

## Review



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# KAAACI Allergic Rhinitis Guidelines: Part 2. Update in Non-pharmacological Management

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## ABSTRACT

Allergic rhinitis is the most common chronic disease worldwide. Various upper airway symptoms lower quality of life, and due to the recurrent symptoms, multiple treatments are usually attempted rather than one definitive treatment. There are alternatives to medical (medication-based) and non-medical treatments. A guideline is needed to understand allergic rhinitis and develop an appropriate treatment plan. We have developed guidelines for

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medical treatment based on previous reports. The current guidelines herein are associated with the “KAAACI Evidence-Based Guidelines for Allergic Rhinitis in Korea, Part 1: Update in pharmacotherapy” in which we aimed to provide evidence-based recommendations for the medical treatment of allergic rhinitis. Part 2 focuses on non-pharmacological management, including allergen-specific immunotherapy, subcutaneous or sublingual immunotherapy, nasal saline irrigation, environmental management strategies, companion animal management, and nasal turbinate surgery. The evidence to support the treatment efficacy, safety, and selection has been systematically reviewed. However, larger controlled studies are needed to elevate the level of evidence to select rational non-medical therapeutic options for patients with allergic rhinitis.

**Keywords:** Rhinitis, allergic; guideline; surgery; immunotherapy; safety

## INTRODUCTION

Allergic rhinitis (AR) is an inflammatory condition of the nasal cavity caused by an immunoglobulin E-mediated type 1 hypersensitivity reaction to a specific external allergen, characterized by 4 symptoms: watery rhinorrhea, nasal congestion, itching, and sneezing.<sup>1</sup> AR has a very high prevalence and tends to increase gradually with various factors including environmental stimuli. As a result, medical costs for care tend to increase.<sup>2</sup> AR is known to diminish the quality of life (QOL), with comparable levels even to other severe respiratory diseases.<sup>3,4</sup>

The high prevalence of this condition, the severe deterioration in QOL, and the social burden of care have led to various treatment options, including anti-allergy medications, immunotherapy, environmental controls, nasal irrigation, and surgery. Moreover, there have been many studies regarding the selection and appropriate combination of these various treatments. Around the world, major allergy societies have produced guidelines suitable for the medical environment of each country. Despite this, there have been social and environmental changes including the medical system, and current guidelines still need revision.

Because of the need for appropriate guidelines in response to changes in the medical environment, the Korean Academy of Asthma, Allergy, and Clinical Immunology (KAAACI) organized a development committee to update its previous guideline.<sup>5</sup> The new guideline was updated in 2 parts. Part 1 introduced the background and purpose of the guideline update, detailed the selection criteria and analytic methods of the study, and described pharmacotherapy for AR. Part 2 reports on the application and effectiveness of non-pharmacological management including immunotherapy, environmental control, nasal irrigation, and surgical interventions. Part 2 of the guideline will focus on recommendations for the effective and safe non-pharmacological management of Korean patients with AR based on the meta-analyses of the literature.

## KEY QUESTIONS AND RECOMMENDATIONS

All recommendations for the non-pharmacological management of AR are summarized in **Table**. Details regarding the evidence supporting each recommendation are given in the following text.

**Table.** Summary of recommendations for non-pharmacological management of allergic rhinitis

Key questions	Recommendations	Quality of evidence	Strength of recommendation
Can allergen-specific immunotherapy reduce the incidence of asthma in patients with allergic rhinitis without asthma?	We suggest AIT can be selectively recommended to prevent asthma in patients with allergic rhinitis.	High	Conditional
In patients with allergic rhinitis, is subcutaneous immunotherapy more effective than sublingual immunotherapy in relieving symptoms and reducing the need for rescue medications?	In patients with allergic rhinitis, subcutaneous and sublingual immunotherapy are equally effective, but there are differences in compliance and side effects. We suggest treatment can be selected considering the patient's values, preferences, and potential obstacles.	Moderate	Conditional
Is nasal saline irrigation effective for symptom relief in allergic rhinitis patients?	We suggest saline nasal lavage can be selectively recommended in patients with allergic rhinitis.	Low	Conditional
Are environmental management strategies such as air purifiers, impermeable bedding, and cleaning effective in alleviating symptoms for patients with allergic rhinitis caused by house dust mites?	We suggest that various environmental management strategies, including air purifiers, impermeable bedding, and cleaning, can be selectively recommended to reduce the indoor dust mite concentration and alleviate the symptoms of AR caused by house dust mites.	Very low	Conditional
In patients with allergic rhinitis whose symptoms are caused by companion animals, can (active/multi-faceted) avoidance therapy and environmental management effectively relieve symptoms and reduce the need for relief medications?	For patients with AR whose symptoms are caused by companion animals, we suggest that the use of air purifiers, bathing of the animals, and avoidance therapy or environmental management of the animals can be selectively recommended.	Very low	Conditional
Is inferior turbinate volume reduction surgery effective for a long time in patients with allergic rhinitis?	In patients with allergic rhinitis, we suggest that inferior turbinate volume reduction surgery can be selectively recommended, considering that rhinitis symptoms can be improved for more than 1 year.	Very low	Conditional

AIT, allergen immunotherapy; AR, allergic rhinitis.

### Key Question 1: Can allergen-specific immunotherapy (AIT) reduce the incidence of asthma in patients with AR?

#### Background

AIT is a disease-modifying treatment that can induce desensitization or tolerance to allergens. Through this, the therapeutic effect of preventing a new occurrence of asthma can be expected by inducing immune tolerance in patients with AR. Therefore, there is a need for the systematic analysis of AIT.

#### Recommendation

We suggest AIT can be selectively recommended to prevent asthma in patients with AR (conditional recommendation, high quality of evidence).

#### Summary of evidence

A total of 11 randomized controlled studies were included in this systematic review.<sup>6-16</sup> The study results that began an investigation with the same subjects but reported results separately according to the follow-up period were considered duplicates, so these studies were excluded. The asthma prevention effect of AIT was analyzed in the remaining 8 studies, and the asthma incidence rate was significantly lower in the intervention group that received AIT compared to the control group. AIT was effective in preventing asthma (relative risk [RR], 0.50; 95% confidence interval [CI], 0.40–0.63). AIT can be divided into subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT), depending on the application method. Accordingly, each subgroup was classified and analyzed, and asthma occurred less often in the intervention group treated with either SCIT or SLIT compared to the control group (RR, 0.37; 95% CI, 0.23–0.59 vs. RR, 0.57; 95% CI, 0.44–0.74). When each subgroup was classified and analyzed according to the follow-up period after treatment, the incidence of asthma was lower in the intervention group than in the control group during the three-year immunotherapy period (RR, 0.31; 95% CI, 0.22–0.43). Even after long-term follow-up, up to 7 years after treatment, asthma was less prevalent in the intervention group (RR, 0.65; 95%

CI, 0.50–0.84). When the risk of bias was assessed for the 11 studies included in the analysis, in all studies, the probability of bias arising from the randomization process, deviations from intended interventions, outcome measurements, and missing outcome data was low.

#### *Remarks*

Since AIT administers a larger quantity of allergen than the living environment, the patient may experience hypersensitivity reactions when the causative allergen is administered. As for local adverse events, SCIT may cause itching, urticaria, swelling, and pain at the injection site, while SLIT may induce itching in the mouth and swelling of the lips. As for systemic adverse events, potentially fatal situations, such as dyspnea and anaphylaxis may occur, so a specialist should perform therapy in a hospital with sufficient emergency capacities. In addition, AIT requires continuous treatment for a long period of time (3–5 years), so it can be both time-consuming and costly. Therefore, AIT, as a disease-modifying treatment, must be explained well in terms of the side effects and time and cost burdens. It will be considered a treatment for alleviating AR symptoms and preventing the occurrence of new asthma. AR and asthma often appear together as a single airway disease. A family history of allergic diseases increases the risks of both AR and asthma. With severe persistent AR, AIT can be administered to prevent the occurrence of asthma. Since it is better to start early for disease prevention, many studies have been conducted on children. Therefore, early AIT for preventing asthma in children over 5 years old with AR may be more helpful.

### **Key Question 2: In patients with AR, is SCIT more effective than SLIT in relieving symptoms and reducing the need for rescue medications?**

#### *Background*

Until now, domestic and international guidelines for AR have recommended AIT for patients with moderate-to-severe AR that cannot be controlled with avoidance and medication therapies. Current AIT can be divided into SCIT and SLIT, depending on the route of administration, and both treatments have been proven to relieve or eliminate symptoms in patients with AR. However, a more thorough investigation is needed to evaluate which therapeutic benefit is better, and whether there is a difference in the risk of adverse events.

#### *Recommendation*

In patients with AR, SCIT and SLIT are equally effective, but there are differences in compliance and adverse events. Therefore, we suggest treatment is selectively recommended with consideration of the patient's values, preferences, and potential obstacles (conditional recommendation, moderate quality of evidence).

#### *Summary of evidence*

A total of 14 studies were included in the analysis, comprising 6 randomized studies on the benefits of treatment, 6 randomized and 3 non-randomized studies on the risks of treatment, and 5 non-randomized studies evaluating the balance of benefits and risks.<sup>17-30</sup> The studies included in the outcome analysis of immunotherapy benefits were 6 randomized and 5 non-randomized controlled studies.<sup>17-27</sup>

A total of 6 randomized studies were meta-analyzed for the rhinitis symptom score.<sup>17-22</sup>

As a result of meta-analysis, SCIT seemed to improve symptoms more than SLIT after treatment, but it was not statistically significant (standardized mean difference, SMD –0.18). The difference was even smaller when the period was unified after 1 year of treatment<sup>17-20</sup> (SMD –0.08). On the other hand, in a study conducted in Turkey, both treatments showed

significant improvement in symptoms after 3 years of treatment, but only SCIT showed symptom improvement after 6 years.<sup>22</sup> A meta-analysis of the medication score for SCIT and SLIT was included, with 3 randomized studies.<sup>17,20,21</sup> On meta-analysis, SCIT was likely to show a lower medication use score after treatment than SLIT (SMD -0.15), albeit with no significant difference between the two groups. Five non-randomized studies underwent meta-analysis on adherence to treatment.<sup>23-27</sup> As a result, SCIT showed significantly higher treatment compliance than SLIT (RR, 1.11). When evaluated by treatment period, the difference between SCIT and SLIT was not significant in the second year of treatment (RR, 0.99).<sup>23,24</sup> In the third year of treatment, SCIT showed 1.18 times higher adherence than SLIT. The longer the treatment period lead to higher the adherence to SCIT. The immunotherapy risk outcome was analyzed in 6 randomized and 3 non-randomized studies.<sup>17,18,21,22,24,26,28-30</sup> Treatment-induced systemic adverse reactions, such as anaphylaxis and asthma occurred more frequently in SCIT than SLIT in 6 randomized studies (RR, 6.69)<sup>17,18,21,22,28,29</sup> and 3 non-randomized studies (RR, 5.76).<sup>24,26,30</sup> Therefore, SCIT had a higher risk for systemic adverse events than SLIT. In 1 out of 8 studies, there was an increased risk of bias arising from the randomization process, and in 5 studies, there was a risk of bias arising from the randomization process. There was also a risk of bias due to deviations from intended interventions in 6 studies, and a risk of bias due to missing outcome data in 2 studies.

#### Remarks

Meta-analyses revealed no significant difference between SCIT and SLIT regarding symptom relief and reduction in the need for rescue medications. In patients with AR, both methods were equally effective. However, the meta-analyses showed that SCIT had significantly higher risks for systemic adverse events, such as anaphylaxis during the induction period than SLIT; compliance was also significantly higher in SCIT than SLIT. The risk of systemic adverse events in SCIT was significantly higher. In most cases, however, they were well controlled. Since AIT demands long-term maintenance treatment of at least 3 years to obtain maximum effects, there was a benefit to SCIT with its higher compliance rates. It is recommended to explain these benefits and disadvantages fully and to select the treatment with the patient's consent and in consideration of the patient's values and preferences.

### Key Question 3: Is nasal saline irrigation effective for symptom relief in AR patients?

#### Background

Nasal saline irrigation is known to improve nasal symptoms by physically washing out mucus, crust, and allergens in the nose, removing various inflammatory mediators in the nasal cavity, and improving mucociliary transport ability.<sup>31,32</sup> Nasal saline irrigation is a simple and inexpensive treatment method used to treat upper respiratory tract infections and chronic rhinosinusitis. Although it is sometimes prescribed as an auxiliary treatment for AR, the treatment effect and its adverse events have not been sufficiently verified.

#### Recommendation

We suggest that saline nasal lavage can be selectively recommended in patients with AR (conditional recommendation, low quality of evidence).

#### Summary of evidence

Twelve randomized studies evaluated the effects of nasal saline irrigation in patients with AR.<sup>33-44</sup> One study of AR patients not receiving medications compared the symptoms of a group performing nasal irrigation with a control group.<sup>33</sup> Eleven studies analyzed the effects

of nasal saline irrigation with medications such as intranasal steroids or antihistamines.<sup>34-44</sup> In one study assessing the effects of nasal saline irrigation in a group not taking the anti-allergy medication, adult patients sensitized to mugwort pollen were subjected to nasal washing for 7–8 weeks from 2 weeks before the pollen dissipated. The total nasal symptom scores were compared between the nasal and non-nasal irrigation groups ( $6.0 \pm 2.1$  vs.  $8.0 \pm 1.3$ ). The score was significantly lower in the nasal irrigation group ( $P < 0.01$ ). However, the number of study participants was as small as 20, and the difference in treatment effects was not large, so the level of evidence was evaluated as very low.<sup>33</sup> Among the studies analyzing the effects of nasal irrigation on patients also using a medication, there were 9 studies including nasal symptom scores within one month. There were 6 and 2 studies analyzing nasal symptom scores and QOL between 1–3 months, respectively. Among the studies comparing nasal symptom scores within one month, there were 4 studies targeting adults<sup>34-37</sup> and 5 studies focusing on children.<sup>38-42</sup> One of the pediatric studies did not provide standard deviation scores, and it was excluded from the meta-analysis. Nasal irrigation significantly decreased the nasal symptom score within 1 month in both adults and children (SMD  $-1.68$ ; 95% CI,  $-2.22$  to  $-1.13$ ;  $P < 0.00001$ ;  $I^2 = 80\%$ ). Of the 6 studies that analyzed nasal symptom scores between 1 and 3 months, 2 were conducted in adults,<sup>35,43</sup> and 4 were conducted in children.<sup>38-41</sup> In two adult studies, the nasal symptom score did not decrease significantly (SMD  $-1.64$ ; 95% CI,  $-4.34$  to  $1.05$ ;  $P = 0.23$ ;  $I^2 = 96\%$ ). However, in the 4 pediatric studies, the nasal symptom score was significantly reduced in the 3 studies where evidence could be synthesized (SMD  $-1.36$ ; 95% CI,  $-2.31$  to  $-0.40$ ;  $P = 0.005$ ;  $I^2 = 69\%$ ). When the evidence was synthesized, including adults and children, the nasal symptom score was significantly reduced (SMD  $-1.45$ ; 95% CI,  $-2.51$  to  $-0.40$ ;  $P = 0.007$ ;  $I^2 = 87\%$ ). One study of adults and children analyzed QOL between 1–3 months. There was a significant difference between the groups with and without nasal irrigation in adults, but none in children. There was also no significant difference even when the evidence of adults and children was synthesized (SMD  $-0.50$ ; 95% CI,  $-1.17$  to  $0.17$ ;  $P = 0.15$ ;  $I^2 = 35\%$ ).<sup>43,44</sup> Based on these results, nasal irrigation with or without medication is effective in alleviating the symptoms of AR.

#### Remarks

Nasal irrigation is effective in alleviating the symptoms of AR, with or without medications. In addition, adverse reactions from nasal washing are minimal or can be prevented by using saline prepared according to an appropriate concentration, temperature, and preparation regulations. However, although serious adverse events, such as meningitis from amoeba infection can occur when contaminated water is used, many patients possibly use unsterilized tap water. Therefore, patients should be instructed to perform nasal irrigation only after fully explaining the importance of proper methods and the use of sterile saline. Nasal saline irrigation is effective in patients with AR, and additional effects can be obtained when taking medication. Since the effect of nasal irrigation using physiological saline is lower than that of topical steroid use, it is recommended that it is applied as an auxiliary treatment.

#### **Key Question 4: Are environmental management strategies such as air purifiers, impermeable bedding, and cleaning effective in alleviating symptoms for patients with AR caused by house dust mites?**

##### Background

Due to climate change, temperature and humidity are rising in Korea; thus, an environment conducive to increasing house dust mites continues. Air pollution also plays a role in exacerbating allergic reactions caused by house dust mites. As the number of indoor dwellings increases with urbanization, exposure to house dust mite allergens has also

increased. For this reason, various environmental management remedies to reduce house dust mite allergens have been introduced, although their effectiveness has not yet been sufficiently verified.

#### *Recommendation*

We suggest that various environmental management strategies, including air purifiers, impermeable bedding, and cleaning, can be selectively recommended to reduce the indoor dust mite concentration and alleviate the symptoms of AR caused by house dust mites (conditional recommendation, very low quality of evidence).

#### *Summary of evidence*

A total of 5 randomized studies were included in the analysis. Four reported a decrease in house dust mite concentration, and four reported AR symptom improvements.<sup>45-49</sup> Five randomized studies included in the systematic review compared prospectively randomized groups with and without environmental therapy. Studies evaluating the improvement of AR symptoms comprised 191 test and 195 control patients. Those assessing the reduction of house mites included 184 test and 192 control participants. With such small numbers, it is difficult to come to sufficient conclusions. There were 5 randomized studies included in the analysis of environmental management benefits. The improvement of the total rhinitis symptoms score, which is the AR symptom score, was reported in 4 studies. The study period was 2 weeks to 12 months. In each of the 4 studies, various environmental management strategies were implemented, including house dust mite impermeable covers, vacuum cleaning of bedding, air purifiers, and house dust mite impermeable pillows, but all of these were analyzed together under the broad heading of environmental management. The test group implementing environmental management improved symptoms more than the control group, but the difference was not significant (SMD  $-0.30$ ;  $P = 0.42$ ). The results related to house dust mite concentration reductions were reported in 4 studies. The test group that implemented environmental management showed a significant decrease in concentrations compared to the control group (SMD  $-0.34$ ;  $P = 0.003$ ). Based on these results, this guideline concluded that environmental management strategies, such as air purifiers, impermeable bedding, and special cleaning were effective in reducing dust mite concentrations, but limited in alleviating AR symptoms. In all of these studies, there was a risk of bias due to deviations from the intended interventions, because there was no clear description of whether all subjects who began the study completed it. Also, the risk of bias due to missing outcome data was high in 2 studies, and there was a possibility of selection bias in the reported results in 2 studies.

#### *Remarks*

There is no risk to implementing environmental management, but the cost of purchasing equipment and the consumables needed to implement these strategies should be considered. Although AR symptoms did not improve significantly within the study period, long-term benefits likely ensue because of the significant reductions in house dust mite concentrations. Therefore, the patient's AR discomfort must be thoroughly evaluated, and the resulting information must be used to decide whether to implement environmental management.

**Key Question 5: In patients with AR whose symptoms are caused by companion animals, can (active/multi-faceted) avoidance therapy and environmental management effectively relieve symptoms and reduce the need for relief medications?**

*Background*

As the number of people with companion animals increases, interest in AR also increases. Unfortunately, for patients with AR experiencing symptoms from exposure to companion animals, there is no significant benefit for prevention; instead, avoidance therapy has been recommended. However, the effects of environmental and avoidance therapies in relieving symptoms and reducing the need for relief medication use have yet to be sufficiently verified.

*Recommendation*

For patients with AR whose symptoms are caused by companion animals, we suggest that the use of air purifiers, bathing of the animals, and avoidance therapy or environmental management of the animals can be selectively recommended (conditional recommendation, very low quality of evidence).

*Summary of evidence*

Two randomized studies that controlled environmental management strategies and avoidance were included in this systematic review. One study evaluated the use of a high-efficiency particulate absorbing (HEPA) filter to reduce companion animal allergens, and the other study examined avoidance therapy and environmental management overall. For these studies, 35 and 40 study subjects aged 15–65 years were enrolled, respectively.

Fel d 1, a well-known cat allergen, was analyzed in the induced allergen study. Air samples were collected from the control and the test groups, which implemented avoidance and environmental interventions. Samples from both groups were collected and analyzed in the same manner, but there was a difference in the final follow-up duration of 3 to 8 months. However, the analysis time of up to 3 months was comparable. The concentration (ng/g) of Fel d 1 was significantly lower in the test group, and the difference was significant after 2 months (SMD -1.11; 95% CI, -1.64 to -0.58;  $P < 0.0001$ ;  $I^2 = 13\%$ ). When comparison was made on a single scale, including the symptoms of nasal congestion, rhinorrhea, and itching, there was no difference in overall nasal symptoms for those using avoidance therapy or environmental management for companion animals (SMD -0.15; 95% CI, -0.87 to 0.57;  $P = 0.68$ ;  $I^2 = 59\%$ ). Bjornsdottir *et al.*<sup>50</sup> reported significant differences in nasal congestion and itching, but none in runny nose. Both studies included in this analysis had a high risk of bias in outcome measurement.

*Remarks*

Avoidance therapy and environmental management of companion animals do not improve overall nasal symptoms, but there are aspects that can help alleviate nasal congestion and itching. A limitation here is that all studies were conducted with cats only. Also, although indoor allergens were reduced, there was no difference in AR activity and no reduced need for rescue medications. In addition, as environmental management and allergen evasion may incur costs, and there are often psychological effects involved with adopting companion animals, it is important to explain the benefits and risks to the patient. The following warnings should be given: 1) Remove carpets from the bedroom, 2) Keep closets closed, 3) Clean floors, furniture, and carpets weekly, 4) Wash bedding at 60°C each week and keep it

covered, 5) Wash pets every 2 weeks, 6) Keep pets out of the bedroom, 7) Use air purifiers or vacuum cleaners with HEPA filters.

### **Key Question 6: Is inferior turbinate volume reduction surgery effective for a long time in patients with AR?**

#### *Background*

To date, domestic and international guidelines for AR have recommended surgical treatment for patients who do not respond well to medication. However, sufficient verification regarding which AR symptoms and indicators are most improved by surgical treatment and how long the effects last is not available.

#### *Recommendation*

In patients with AR, we suggest that inferior turbinate volume reduction surgery can be selectively recommended; rhinitis symptoms can be improved for more than 1 year (conditional recommendation, very low quality of evidence).

#### *Summary of evidence*

A total of 18 studies were included in this systematic review, and study participants were those with a follow-up period of 1 year or more after rhinitis surgery.<sup>51-68</sup> Excluded were all subjects who had diagnoses other than rhinitis, such as sinusitis or sleep apnea, or whose surgery was performed on other sites in addition to the inferior turbinate. There were 12 case series comparing the effects before and after surgery,<sup>51,52,54-57,59,60,62,66-68</sup> 5 randomized control trials,<sup>53,58,61,63,65</sup> and 1 prospective cohort study.<sup>64</sup> The randomized control trials and prospective cohort studies divided participants into two groups and compared the effects of surgical treatment between the two groups. Among 18 studies with benefits analysis, studies that confirmed an improvement index for AR were evaluated. Subjective symptoms, such as nasal congestion, runny nose, sneezing, and itching were all evaluated on a Visual Analog Scale (VAS) scale, with 0 representing no discomfort and 10 the most severe discomfort imaginable. In 9 studies analyzing nasal obstruction, the VAS score improved significantly after rhinitis surgery compared to the preoperative value (SMD 4.60; 95% CI, 3.43 to 5.76;  $P < 0.00001$ ;  $I^2 = 100\%$ ).<sup>52,53,58,61-65,67</sup> In addition, 6 studies analyzing the symptoms of rhinorrhea showed significant symptom improvement after surgery (SMD 3.12; 95% CI, 1.97 to 4.28;  $P < 0.00001$ ;  $I^2 = 99\%$ ).<sup>53,58,62,63,65,67</sup> Six studies showed post-surgical improvement in sneezing (SMD 2.64; 95% CI, 1.74 to 3.54;  $P < 0.00001$ ;  $I^2 = 99\%$ )<sup>53,58,62,64,65,67</sup> and three studies in nasal itching (SMD 1.75; 95% CI, 1.20 to 2.30;  $P < 0.00001$ ;  $I^2 = 87\%$ ).<sup>58,62,67</sup> Regarding duration, significant improvement in nasal congestion remained at 3 months (SMD 5.05; 95% CI, 4.39 to 5.71;  $P < 0.00001$ ;  $I^2 = 26\%$ )<sup>58,64,67</sup> and 3 years post-surgery (SMD 5.18; 95% CI, 3.00 to 7.37;  $P < 0.00001$ ;  $I^2 = 100\%$ ).<sup>52,62,63,65</sup> Runny nose also remained improved at 3 months (SMD 4.18; 95% CI, 3.16 to 5.21;  $P < 0.00001$ ;  $I^2 = 96\%$ )<sup>58,67</sup> and 3 years after surgery (SMD 4.05; 95% CI, 2.22 to 5.89;  $P < 0.00001$ ;  $I^2 = 100\%$ ).<sup>62,63,65</sup> Likewise, sneezing symptoms maintained significant improvements at 3 months (SMD 3.40; 95% CI, 2.77 to 4.03;  $P < 0.00001$ ;  $I^2 = 88\%$ )<sup>58,67</sup> and 3 years post-operatively (SMD 2.95; 95% CI, 1.58 to 4.32;  $P < 0.00001$ ;  $I^2 = 99\%$ ).<sup>62,63,65</sup> One study that confirmed the therapeutic effect of rhinitis surgery with objective indicators was analyzed. Nasal resistance was significantly improved after surgery compared to the preoperative baseline (SMD 0.16; 95% CI, 0.08 to 0.24;  $P < 0.00001$ ;  $I^2 = 98\%$ ).<sup>52,53,60,61,63,65</sup> Total nasal volume also showed significant improvement compared to baseline values (SMD 0.96; 95% CI, 0.73 to 1.19;  $P = 0.01$ ;  $I^2 = 66\%$ ).<sup>53,58,64</sup> When the degree of symptom improvement was analyzed according to the follow-up period, the total nasal volume showed even more significant improvement at 1 year (SMD 0.96; 95% CI, 0.73

to 1.19;  $P = 0.01$ ,  $I^2 = 66\%$ ) than at 1 month (SMD 0.12; 95% CI,  $-0.53$  to  $0.77$ ;  $P < 0.67$ ;  $I^2 = 0\%$ ) after surgery.<sup>53,58,64</sup> Based on this, this guideline concluded that inferior turbinate volume reduction surgery significantly improved both subjective symptoms and objective indicators in AR patients, and the effects lasted more than 1 year. Of 18 studies in total, 8 reported no complications after surgery.<sup>52,53,56,60-62,66,67</sup> Postoperative complications were reported in 8 studies, none of them serious.<sup>54,55,57-59,63-65</sup> Bleeding occurred with a frequency of 40 per 1,000, and was described, in most studies, as mild and easily controlled (rate 0.04; 95% CI, 0.01 to 0.07;  $P = 0.081$ ;  $I^2 = 51.9\%$ ). Crusting occurred at a frequency of 170 per 1,000 (rate 0.17; 95% CI, 0.05 to 0.29;  $P = 0.000$ ;  $I^2 = 87.5\%$ ).<sup>55,63,65</sup> Nasal dryness was seen in 20 per 1,000 (rate 0.02; 95% CI,  $-0.01$  to 0.05;  $P = 0.790$ ;  $I^2 = 0\%$ ).<sup>63,65</sup> Overall, postoperative complications were low. Based on this, this guideline concluded that while inferior turbinate volume reduction surgery did cause minor complications, such as bleeding, crusting, and dry nasal passages after surgery, the incidence of these was low, and there were no serious complications. The risk of bias assessment for the 18 studies included in the analysis (ROBINS-I) identified 8 studies at high risk for confounding variables bias<sup>51-57,60</sup> and 4 studies with medium risk.<sup>58,62,67,68</sup> There were 8 studies at high risk of subject selection bias,<sup>51,53,54,56,59,60,62,67</sup> and the risk of randomization bias and bias due to deviations from intended intervention was low in all 18 cases. Missing outcome data was a high risk of bias in 10 studies<sup>51,53,54,56,59,60,62,63,65,67</sup> and medium risk in three.<sup>52,55,57</sup> Outcome measurement was a high risk of bias in all 18 cases. As for the selection bias of the reported results, 7 studies were at high risk<sup>51,54-57,62,67</sup> and seven were at medium risk.<sup>52,58-61,66,68</sup> Based on the evaluation of bias in the individual studies, all of the measurement variables used in the outcome and risk analyses were rated as very low levels of evidence.

#### Remarks

Inferior turbinate volume reduction surgery significantly improved subjective symptoms and objective indicators of AR patients and showed a long-term effect of more than 1 year. Complications such as bleeding, crusting, and dry nasal passages may occur at a low rate after surgery, so surgery should be recommended only after fully explaining the benefits and risks to the patient. After surgery, treatment effects and the potential for adverse reactions must be sufficiently evaluated. Patients with AR should receive clear and thorough explanations regarding the therapeutic effects and adverse events of inferior turbinate volume reduction surgery to select the best treatment plan. Inferior turbinate volume reduction surgery can be recommended for patients whose symptoms do not improve despite medication. It is particularly recommended because long-term effects lasting longer than 1 year have been reported in patients whose symptoms of nasal congestion and runny nose have not otherwise improved. After surgery, sufficient feedback regarding treatment effects as well as the occurrence and severity of adverse events should be collected. Surgical site care and regular follow-up are required.

## CONCLUSIONS

This guideline was produced according to a systematic selection and review of varied research with proper evidence. It focused on the perspective of the physician managing AR in a real clinical practice environment. In this Part 2 of the guidelines, we have detailed the recommendations for immunotherapy, environmental management strategies, nasal irrigation, and surgery for 6 key questions regarding the non-pharmacological management of AR based on many verified studies. However, these studies were primarily conducted in

countries other than Korea, and we consider this a limitation. Further evaluation among Korean populations will be needed to determine whether the therapeutic efficacy and safety of AR treatment will diverge from those detailed here. The recommendations issued in this guideline should be updated regularly as new evidence emerges.

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## REFERENCES

1. Brożek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic rhinitis and its impact on asthma (ARIA) guidelines-2016 revision. *J Allergy Clin Immunol* 2017;140:950-8.  
[PUBMED](#) | [CROSSREF](#)
2. Park HS, Choi GS, Cho JS, Kim YY. Epidemiology and current status of allergic rhinitis, asthma, and associated allergic diseases in Korea: ARIA Asia-Pacific workshop report. *Asian Pac J Allergy Immunol* 2009;27:167-71.  
[PUBMED](#)
3. Bousquet J, Schünemann HJ, Togias A, Bachert C, Erhola M, Hellings PW, et al. Next-generation allergic rhinitis and its impact on asthma (ARIA) guidelines for allergic rhinitis based on grading of recommendations assessment, development and evaluation (GRADE) and real-world evidence. *J Allergy Clin Immunol* 2020;145:70-80.e3.  
[PUBMED](#) | [CROSSREF](#)
4. Bousquet J, Hellings PW, Agache I, Amat F, Annesi-Maesano I, Ansotegui IJ, et al. Allergic rhinitis and its impact on asthma (ARIA) phase 4 (2018): change management in allergic rhinitis and asthma multimorbidity using mobile technology. *J Allergy Clin Immunol* 2019;143:864-79.  
[PUBMED](#) | [CROSSREF](#)
5. Korean Academy of Asthma, Allergy and Clinical Immunology. Clinical diagnostic guidelines for management of allergic rhinitis [Internet]. Seoul: Korean Academy of Asthma, Allergy and Clinical Immunology; 2015 [cited 2022 Jul 15]. Available from: <https://www.allergy.or.kr/content/member/file/allergic2015.pdf>.
6. Novembre E, Galli E, Landi F, Caffarelli C, Pifferi M, De Marco E, et al. Coseasonal sublingual immunotherapy reduces the development of asthma in children with allergic rhinoconjunctivitis. *J Allergy Clin Immunol* 2004;114:851-7.  
[PUBMED](#) | [CROSSREF](#)
7. Grembale RD, Camporota L, Naty S, Tranfa CM, Djukanovic R, Marsico SA. Effects of specific immunotherapy in allergic rhinitic individuals with bronchial hyperresponsiveness. *Am J Respir Crit Care Med* 2000;162:2048-52.  
[PUBMED](#) | [CROSSREF](#)
8. Marogna M, Tomassetti D, Bernasconi A, Colombo F, Massolo A, Businco AD, et al. Preventive effects of sublingual immunotherapy in childhood: an open randomized controlled study. *Ann Allergy Asthma Immunol* 2008;101:206-11.  
[PUBMED](#) | [CROSSREF](#)
9. Möller C, Dreborg S, Lanner A, Björkstén B. Oral immunotherapy of children with rhinoconjunctivitis due to birch pollen allergy. A double blind study. *Allergy* 1986;41:271-9.  
[PUBMED](#) | [CROSSREF](#)
10. Möller C, Dreborg S, Ferdousi HA, Halken S, Høst A, Jacobsen L, et al. Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study). *J Allergy Clin Immunol* 2002;109:251-6.  
[PUBMED](#) | [CROSSREF](#)

11. Valovirta E, Petersen TH, Piotrowska T, Laursen MK, Andersen JS, Sørensen HF, et al. Results from the 5-year SQ grass sublingual immunotherapy tablet asthma prevention (GAP) trial in children with grass pollen allergy. *J Allergy Clin Immunol* 2018;141:529-538.e13.  
[PUBMED](#) | [CROSSREF](#)
12. Jacobsen L, Niggemann B, Dreborg S, Ferdousi HA, Halken S, Høst A, et al. Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study. *Allergy* 2007;62:943-8.  
[PUBMED](#) | [CROSSREF](#)
13. Niggemann B, Jacobsen L, Dreborg S, Ferdousi HA, Halken S, Høst A, et al. Five-year follow-up on the PAT study: specific immunotherapy and long-term prevention of asthma in children. *Allergy* 2006;61:855-9.  
[PUBMED](#) | [CROSSREF](#)
14. Polosa R, Li Gotti F, Mangano G, Paolino G, Mastruzzo C, Vancheri C, et al. Effect of immunotherapy on asthma progression, BHR and sputum eosinophils in allergic rhinitis. *Allergy* 2004;59:1224-8.  
[PUBMED](#) | [CROSSREF](#)
15. Song W, Lin X, Chai R. Evaluation of long-term effect for house dust mite subcutaneous immunotherapy for patients with allergic rhinitis. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2015;50:632-5.  
[PUBMED](#)
16. Song W, Lin X, Chai R. Efficacy evaluation of standardized dust mite allergen specific immunotherapy to patients of allergic rhinitis. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2014;28:300-2.  
[PUBMED](#)
17. Eifan AO, Akkoc T, Yildiz A, Keles S, Ozdemir C, Bahceciler NN, et al. Clinical efficacy and immunological mechanisms of sublingual and subcutaneous immunotherapy in asthmatic/rhinitis children sensitized to house dust mite: an open randomized controlled trial. *Clin Exp Allergy* 2010;40:922-32.  
[PUBMED](#) | [CROSSREF](#)
18. Quirino T, Iemoli E, Siciliani E, Parmiani S, Milazzo F. Sublingual versus injective immunotherapy in grass pollen allergic patients: a double blind (double dummy) study. *Clin Exp Allergy* 1996;26:1253-61.  
[PUBMED](#) | [CROSSREF](#)
19. Wang ZX, Shi H. Single-allergen sublingual immunotherapy versus multi-allergen subcutaneous immunotherapy for children with allergic rhinitis. *J Huazhong Univ Sci Technol Med Sci* 2017;37:407-11.  
[PUBMED](#) | [CROSSREF](#)
20. Xian M, Feng M, Dong Y, Wei N, Su Q, Li J. Changes in CD4+CD25+FoxP3+ regulatory T cells and serum cytokines in sublingual and subcutaneous immunotherapy in allergic rhinitis with or without asthma. *Int Arch Allergy Immunol* 2020;181:71-80.  
[PUBMED](#) | [CROSSREF](#)
21. Karakoc-Aydiner E, Eifan AO, Baris S, Gunay E, Akturk E, Akkoc T, et al. Long-term effect of sublingual and subcutaneous immunotherapy in dust mite-allergic children with asthma/rhinitis: a 3-year prospective randomized controlled trial. *J Investig Allergol Clin Immunol* 2015;25:334-42.  
[PUBMED](#)
22. Tahamiler R, Saritzali G, Canakcioglu S, Ozcora E, Dirican A. Comparison of the long-term efficacy of subcutaneous and sublingual immunotherapies in perennial rhinitis. *ORL J Otorhinolaryngol Relat Spec* 2008;70:144-50.  
[PUBMED](#) | [CROSSREF](#)
23. Borg M, Løkke A, Hilberg O. Compliance in subcutaneous and sublingual allergen immunotherapy: a nationwide study. *Respir Med* 2020;170:106039.  
[PUBMED](#) | [CROSSREF](#)
24. Zhu L, Lu JH, Xie Q, Wu YL, Zhu LP, Cheng L. Compliance and safety evaluation of subcutaneous versus sublingual immunotherapy in mite-sensitized patients with allergic rhinitis. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2010;45:444-9.  
[PUBMED](#)
25. Lemberg ML, Berk T, Shah-Hosseini K, Kasche EM, Mösges R. Sublingual versus subcutaneous immunotherapy: patient adherence at a large German allergy center. *Patient Prefer Adherence* 2017;11:63-70.  
[PUBMED](#) | [CROSSREF](#)
26. Liu W, Zeng Q, He C, Chen R, Tang Y, Yan S, et al. Compliance, efficacy, and safety of subcutaneous and sublingual immunotherapy in children with allergic rhinitis. *Pediatr Allergy Immunol* 2021;32:86-91.  
[PUBMED](#) | [CROSSREF](#)
27. You SH, Qin XY, Xu C, Qiu X, Luan ZL, Jia HX, et al. Comparison study of subcutaneous immunotherapy and sublingual immunotherapy in patients with allergic rhinitis. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2016;30:689-93.  
[PUBMED](#)

28. Mungan D, Misirligil Z, Gürbüç L. Comparison of the efficacy of subcutaneous and sublingual immunotherapy in mite-sensitive patients with rhinitis and asthma—a placebo controlled study. *Allergy Asthma Immunol* 1999;82:485-90.  
[PUBMED](#) | [CROSSREF](#)
29. Khinchi MS, Poulsen LK, Carat F, André C, Hansen AB, Malling HJ. Clinical efficacy of sublingual and subcutaneous birch pollen allergen-specific immunotherapy: a randomized, placebo-controlled, double-blind, double-dummy study. *Allergy* 2004;59:45-53.  
[PUBMED](#) | [CROSSREF](#)
30. Rossi RE, Monasterolo G, Coco G, Silvestro L, Operti D. Evaluation of serum IgG4 antibodies specific to grass pollen allergen components in the follow up of allergic patients undergoing subcutaneous and sublingual immunotherapy. *Vaccine* 2007;25:957-64.  
[PUBMED](#) | [CROSSREF](#)
31. Hermelingmeier KE, Weber RK, Hellmich M, Heubach CP, Mösges R. Nasal irrigation as an adjunctive treatment in allergic rhinitis: a systematic review and meta-analysis. *Am J Rhinol Allergy* 2012;26:e119-25.  
[PUBMED](#) | [CROSSREF](#)
32. Park DY, Choi JH, Kim DK, Jung YG, Mun SJ, Min HJ, et al. Clinical practice guideline: nasal irrigation for chronic rhinosinusitis in adults. *Clin Exp Otorhinolaryngol* 2022;15:5-23.  
[PUBMED](#) | [CROSSREF](#)
33. Ning X, Xing Z, Wang M, Gao Z. To investigate the effect of pretreatment with budesonide spray in patients with allergic rhinitis. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2011;25:633-5.  
[PUBMED](#)
34. Di Berardino F, Zanetti D, D'Amato G. Nasal rinsing with an atomized spray improves mucociliary clearance and clinical symptoms during peak grass pollen season. *Am J Rhinol Allergy* 2017;31:40-3.  
[PUBMED](#) | [CROSSREF](#)
35. Garavello W, Somigliana E, Acaia B, Gaini L, Pignataro L, Gaini RM. Nasal lavage in pregnant women with seasonal allergic rhinitis: a randomized study. *Int Arch Allergy Immunol* 2010;151:137-41.  
[PUBMED](#) | [CROSSREF](#)
36. Rogkakou A, Guerra L, Massacane P, Baiardini I, Baena-Cagnani R, Zanella C, et al. Effects on symptoms and quality of life of hypertonic saline nasal spray added to antihistamine in persistent allergic rhinitis—a randomized controlled study. *Eur Ann Allergy Clin Immunol* 2005;37:353-6.  
[PUBMED](#)
37. Zhang Y, Li W. Effects of oral desloratadine citrate disodium combined with physiological seawater nasal irrigation on IgE levels, IL-4, IL-6, IL-13 and IFN- $\gamma$  expression and treatment of intermittent allergic rhinitis. *Cell Mol Biol* 2020;66:54-8.  
[PUBMED](#) | [CROSSREF](#)
38. Chen JR, Jin L, Li XY. The effectiveness of nasal saline irrigation (seawater) in treatment of allergic rhinitis in children. *Int J Pediatr Otorhinolaryngol* 2014;78:1115-8.  
[PUBMED](#) | [CROSSREF](#)
39. Garavello W, Di Berardino F, Romagnoli M, Sambataro G, Gaini RM. Nasal rinsing with hypertonic solution: an adjunctive treatment for pediatric seasonal allergic rhinoconjunctivitis. *Int Arch Allergy Immunol* 2005;137:310-4.  
[PUBMED](#) | [CROSSREF](#)
40. Garavello W, Romagnoli M, Sordo L, Gaini RM, Di Berardino C, Angrisano A. Hypersaline nasal irrigation in children with symptomatic seasonal allergic rhinitis: a randomized study. *Pediatr Allergy Immunol* 2003;14:140-3.  
[PUBMED](#) | [CROSSREF](#)
41. Li H, Sha Q, Zuo K, Jiang H, Cheng L, Shi J, et al. Nasal saline irrigation facilitates control of allergic rhinitis by topical steroid in children. *ORL J Otorhinolaryngol Relat Spec* 2009;71:50-5.  
[PUBMED](#) | [CROSSREF](#)
42. Marchisio P, Varricchio A, Baggi E, Bianchini S, Capasso ME, Torretta S, et al. Hypertonic saline is more effective than normal saline in seasonal allergic rhinitis in children. *Int J Immunopathol Pharmacol* 2012;25:721-30.  
[PUBMED](#) | [CROSSREF](#)
43. Wu M, Wang Q, Zhang K, Wu K, Zhang Y, Wang Z, et al. The effect of nasal irrigation in the treatment of allergic rhinitis. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2014;28:287-9.  
[PUBMED](#)
44. Jung M, Lee JY, Ryu G, Lee KE, Hong SD, Choi J, et al. Beneficial effect of nasal saline irrigation in children with allergic rhinitis and asthma: a randomized clinical trial. *Asian Pac J Allergy Immunol* 2020;38:251-7.  
[PUBMED](#)

45. Reisman RE, Mauriello PM, Davis GB, Georgitis JW, DeMasi JM. A double-blind study of the effectiveness of a high-efficiency particulate air (HEPA) filter in the treatment of patients with perennial allergic rhinitis and asthma. *J Allergy Clin Immunol* 1990;85:1050-7.  
[PUBMED](#) | [CROSSREF](#)
46. Terreehorst I, Hak E, Oosting AJ, Tempels-Pavlica Z, de Monchy JG, Bruijnzeel-Koomen CA, et al. Evaluation of impermeable covers for bedding in patients with allergic rhinitis. *N Engl J Med* 2003;349:237-46.  
[PUBMED](#) | [CROSSREF](#)
47. Jeon YH, Lee YJ, Sohn MH, Lee HR. Effects of vacuuming mattresses on allergic rhinitis symptoms in children. *Allergy Asthma Immunol Res* 2019;11:655-63.  
[PUBMED](#) | [CROSSREF](#)
48. Park KH, Sim DW, Lee SC, Moon S, Choe E, Shin H, et al. Effects of air purifiers on patients with allergic rhinitis: a multicenter, randomized, double-blind, and placebo-controlled study. *Yonsei Med J* 2020;61:689-97.  
[PUBMED](#) | [CROSSREF](#)
49. Stillerman A, Nachtsheim C, Li W, Albrecht M, Waldman J. Efficacy of a novel air filtration pillow for avoidance of perennial allergens in symptomatic adults. *Ann Allergy Asthma Immunol* 2010;104:440-9.  
[PUBMED](#) | [CROSSREF](#)
50. Björnsdóttir US, Jakobinudóttir S, Runarsdóttir V, Juliusson S. The effect of reducing levels of cat allergen (Fel d 1) on clinical symptoms in patients with cat allergy. *Ann Allergy Asthma Immunol* 2003;91:189-94.  
[PUBMED](#) | [CROSSREF](#)
51. Manzi B, Sykes KJ, Wei JL. Sinonasal quality of life in children after outfracture of inferior turbinates and submucosal inferior turbinoplasty for chronic nasal congestion. *JAMA Otolaryngol Head Neck Surg* 2017;143:452-7.  
[PUBMED](#) | [CROSSREF](#)
52. Neri G, Cazzato F, Mastronardi V, Pugliese M, Centurione MA, Di Pietro R, et al. Ultrastructural regenerating features of nasal mucosa following microdebrider-assisted turbinoplasty are related to clinical recovery. *J Transl Med* 2016;14:164.  
[PUBMED](#) | [CROSSREF](#)
53. Banhiran W, Assanasen P, Tantilipikorn P, Nujchanart N, Voraprayoon S, Bunnag C. A randomized study of temperature-controlled versus bipolar radiofrequency for inferior turbinate reduction. *Eur Arch Otorhinolaryngol* 2015;272:2877-84.  
[PUBMED](#) | [CROSSREF](#)
54. Arganbright JM, Jensen EL, Mattingly J, Gao D, Chan KH. Utility of inferior turbinoplasty for the treatment of nasal obstruction in children: a 10-year review. *JAMA Otolaryngol Head Neck Surg* 2015;141:901-4.  
[PUBMED](#) | [CROSSREF](#)
55. Deenadayal DS, Kumar MN, Sudhakshin P, Hameed S. Radiofrequency reduction of inferior turbinates in allergic and non allergic rhinitis. *Indian J Otolaryngol Head Neck Surg* 2014;66 Suppl 1:231-6.  
[PUBMED](#) | [CROSSREF](#)
56. Assanasen P, Banhiran W, Tantilipikorn P, Pinkaew B. Combined radiofrequency volumetric tissue reduction and lateral outfracture of hypertrophic inferior turbinate in the treatment of chronic rhinitis: short-term and long-term outcome. *Int Forum Allergy Rhinol* 2014;4:339-44.  
[PUBMED](#) | [CROSSREF](#)
57. Akdag M, Dasdag S, Ozkurt FE, Celik MY, Degirmenci A, Demir H, et al. Long-term effect of radiofrequency turbinoplasty in nasal obstruction. *Biotechnol Biotechnol Equip* 2014;28:285-94.  
[PUBMED](#) | [CROSSREF](#)
58. Lee JY. Efficacy of intra- and extratubinal microdebrider turbinoplasty in perennial allergic rhinitis. *Laryngoscope* 2013;123:2945-9.  
[PUBMED](#) | [CROSSREF](#)
59. Kojima Y, Tsuzuki K, Takebayashi H, Oka H, Sakagami M. Therapeutic evaluation of outpatient submucosal inferior turbinate surgery for patients with severe allergic rhinitis. *Allergol Int* 2013;62:479-85.  
[PUBMED](#) | [CROSSREF](#)
60. Garzaro M, Pezzoli M, Landolfo V, Defilippi S, Giordano C, Pecorari G. Radiofrequency inferior turbinate reduction: long-term olfactory and functional outcomes. *Otolaryngol Head Neck Surg* 2012;146:146-50.  
[PUBMED](#) | [CROSSREF](#)
61. Gunhan K, Unlu H, Yuceturk AV, Songu M. Intranasal steroids or radiofrequency turbinoplasty in persistent allergic rhinitis: effects on quality of life and objective parameters. *Eur Arch Otorhinolaryngol* 2011;268:845-50.  
[PUBMED](#) | [CROSSREF](#)

62. Lin HC, Lin PW, Friedman M, Chang HW, Su YY, Chen YJ, et al. Long-term results of radiofrequency turbinoplasty for allergic rhinitis refractory to medical therapy. *Arch Otolaryngol Head Neck Surg* 2010;136:892-5.  
[PUBMED](#) | [CROSSREF](#)
63. Liu CM, Tan CD, Lee FP, Lin KN, Huang HM. Microdebrider-assisted versus radiofrequency-assisted inferior turbinoplasty. *Laryngoscope* 2009;119:414-8.  
[PUBMED](#) | [CROSSREF](#)
64. Wu CC, Lee SY, Hsu CJ, Yeh TH. Patients with positive allergen test have less favorable outcome after endoscopic microdebrider-assisted inferior turbinoplasty. *Am J Rhinol* 2008;22:20-3.  
[PUBMED](#) | [CROSSREF](#)
65. Chen YL, Tan CT, Huang HM. Long-term efficacy of microdebrider-assisted inferior turbinoplasty with lateralization for hypertrophic inferior turbinates in patients with perennial allergic rhinitis. *Laryngoscope* 2008;118:1270-4.  
[PUBMED](#) | [CROSSREF](#)
66. Huang TW, Cheng PW. Changes in nasal resistance and quality of life after endoscopic microdebrider-assisted inferior turbinoplasty in patients with perennial allergic rhinitis. *Arch Otolaryngol Head Neck Surg* 2006;132:990-3.  
[PUBMED](#) | [CROSSREF](#)
67. Lin HC, Lin PW, Su CY, Chang HW. Radiofrequency for the treatment of allergic rhinitis refractory to medical therapy. *Laryngoscope* 2003;113:673-8.  
[PUBMED](#) | [CROSSREF](#)
68. Mori S, Fujieda S, Igarashi M, Fan GK, Saito H. Submucous turbinectomy decreases not only nasal stiffness but also sneezing and rhinorrhea in patients with perennial allergic rhinitis. *Clin Exp Allergy* 1999;29:1542-8.  
[PUBMED](#) | [CROSSREF](#)