

Conventional Versus Holmium: YAG Laser-assisted Resection of Concha Bullosa: A Comparative Study

Konvansiyonel ve Holmium: YAG Lazer ile Yapılan Konka Bulloza Rezeksiyonlarının Karşılaştırılması

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Abstract

Objective: This study aims to compare the surgical outcomes of conventional concha bullosa resection and holmium: YAG laser-assisted lateral laminectomy, focusing on efficacy, safety, and postoperative recovery in patients with symptomatic concha bullosa.

Methods: A total of 46 patients (54 concha bullosa surgeries) were included. Patients were divided into two groups: group 1 underwent holmium: YAG laser-assisted lateral laminectomy (n=23), and group 2 underwent conventional lateral laminectomy (n=23). Primary outcomes included surgical duration, intraoperative bleeding, and postoperative complications. Symptom evaluation was conducted using the visual analog scale (VAS) for headaches and the sinonasal outcome test-22 (SNOT-22), recorded preoperatively and three months postoperatively.

Results: The mean surgical duration was significantly shorter in group 1 (15.0±5.7 minutes) compared to group 2 (28.0±7.5 minutes, p<0.05). Group 1 demonstrated a clearer surgical field with visibly reduced bleeding. Both groups exhibited statistically significant improvements in VAS and SNOT-22 scores (p<0.05); however, intergroup comparisons showed no significant differences. Crusting persisted longer in group 2, and one case of postoperative epistaxis requiring nasal packing was reported in this group. No major complications occurred in either group.

Conclusion: Holmium: YAG laser-assisted concha bullosa resection is a safe and effective alternative to conventional lateral laminectomy. It offers distinct intraoperative advantages, including shorter operative time, better visualization, and reduced bleeding. Despite similar symptomatic improvement in both groups, laser-assisted resection may enhance surgical efficiency and patient recovery. Further prospective studies with long-term follow-up are warranted to evaluate recurrence and delayed complications.

Keywords: Concha bullosa, endoscopic sinus surgery, holmium, laser therapy, visual analog scale

Öz

Giriş: Bu çalışmanın amacı, semptomatik konka bulloza hastalarında konvansiyonel konka bulloza rezeksiyonu ile holmium: YAG lazer destekli lateral laminektominin cerrahi sonuçlarını; etkinlik, güvenlik ve postoperatif iyileşme açısından karşılaştırmaktır.

Yöntem: Çalışmaya toplam 46 hasta (54 konka bulloza cerrahisi) dahil edilmiştir. Hastalar iki gruba ayrılmıştır: grup 1'de holmium: YAG lazer destekli lateral laminektomi (n=23), grup 2'de ise konvansiyonel lateral laminektomi (n=23) uygulanmıştır. Birincil sonuç ölçütleri arasında cerrahi süresi, intraoperatif



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Öz

kanama ve postoperatif komplikasyonlar yer almıştır. Semptom değerlendirmesi baş ağrısı için görsel analog skala (GAS) ve sinonazal semptomlar için sinonazal sonuç testi-22 (SNOT-22) kullanılarak, ameliyat öncesi ve ameliyat sonrası üçüncü ayda yapılmıştır.

Bulgular: Ortalama cerrahi süresi grup 1'de anlamlı derecede daha kısa bulunmuştur (15,0±5,7 dakika) (grup 2: 28,0±7,5 dakika; $p<0,05$). Grup 1'de daha net bir cerrahi alan ve belirgin şekilde azalmış kanama gözlenmiştir. Her iki grupta da GAS ve SNOT-22 skorlarında istatistiksel olarak anlamlı düzeltilmeler elde edilmiştir ($p<0,05$); ancak gruplar arası karşılaştırmada anlamlı fark bulunmamıştır. Kabuklanma grup 2'de daha uzun sürmüş ve bu grupta bir hastada nazal tampon gerektiren postoperatif epistaksis gözlenmiştir. Her iki grupta da majör komplikasyon izlenmemiştir.

Sonuç: Holmium: YAG lazer destekli konka bulloza rezeksiyonu, konvansiyonel lateral laminektomiye güvenli ve etkili bir alternatiftir. Daha kısa operasyon süresi, daha iyi görüş alanı ve azalmış kanama gibi belirgin intraoperatif avantajlar sunmaktadır. Her iki yöntemde semptomatik iyileşme benzer olsa da lazer destekli rezeksiyon cerrahi etkinliği ve hasta iyileşmesini artırabilir. Nüks ve geç komplikasyonların değerlendirilmesi için uzun dönem takipli prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Konka bulloza, endoskopik sinüs cerrahisi, holmium, lazer tedavisi, görsel analog skala

Introduction

Concha bullosa, commonly defined as the pneumatization of the middle nasal turbinate, is reported in the literature as the most prevalent anatomical variation in the sinonasal region. The prevalence of concha bullosa ranges from 14% to 53%. Although the etiology of turbinate pneumatization remains uncertain, factors such as nasal septum deviation, mouth breathing, and trauma are thought to play a role⁽¹⁻³⁾.

Although most cases of concha bullosa are asymptomatic, the condition can obstruct the middle meatus by enlarging the middle turbinate, which may lead to blockage of the osteomeatal complex. This obstruction can impair the mucociliary drainage of the maxillary sinus, resulting in sinusitis. Symptomatic cases have also been linked to headaches, chronic sinusitis, and deviation of the nasal septum^(4,5). In such cases, surgical intervention becomes necessary to restore nasal airflow and improve sinus ventilation.

Several surgical techniques have been described for the treatment of concha bullosa. The conventional approach, which involves resecting the portion obstructing the nasal airway and sinus ventilation, is commonly preferred⁽⁶⁾. These techniques include lateral or medial laminectomy, crushing, turbinoplasty, and intrinsic stripping, each with its own risk-benefit profile depending on the extent and type of conchal pneumatization.

In recent years, laser-assisted procedures have gained popularity in otolaryngologic surgery due to their precision, hemostatic effect, and reduced tissue trauma. Among various laser modalities, the holmium: YAG laser offers

specific advantages such as minimal penetration depth and strong water absorption, enabling controlled tissue ablation with limited collateral damage. However, its use in middle turbinate surgery, particularly for concha bullosa resection, remains underexplored in the literature.

In this study, we compared the outcomes of two surgical techniques: the conventional method and the holmium: YAG laser-assisted approach. Our aim was to evaluate their effectiveness, safety, and influence on intraoperative parameters and postoperative symptom improvement.

Materials and Methods

Study Design

This retrospective case-control study was conducted at the Clinic of Otorhinolaryngology of Medipol University Esenler Hospital between 2018 and 2023. The study protocol was approved by the İstanbul Medipol University Institutional Ethics Committee (approval no: 213, date: 20.02.2025) in accordance with the Declaration of Helsinki.

Patient Selection

Data from 54 concha bullosa surgeries performed on 46 patients were analyzed. The demographic data and primary complaints of the patients were evaluated. The most frequently reported symptoms were nasal obstruction and intermittent headaches. Classification of concha bullosa was based on nasal endoscopic examination. Preoperative computed tomography (CT) of the paranasal sinuses was performed using a multidetector CT unit.

Inclusion and Exclusion Criteria

Patients were included if they had symptomatic concha bullosa and underwent either laser-assisted or conventional resection. Exclusion criteria were as follows:

- Asymptomatic concha bullosa
- Age below 18 years
- Previous nasal surgery
- Concomitant nasal pathologies such as chronic rhinosinusitis with or without nasal polyps
- Incomplete follow-up data

Surgical Groups and Procedure

Patients were divided into two groups based on the surgical method used:

- Group 1: Holmium: YAG laser-assisted lateral laminectomy (n=23)
- Group 2: Conventional lateral laminectomy (n=23)

The surgical method was selected based on surgeon discretion and patient preference; randomization was not performed. All surgeries were performed by the same senior surgeon with assistance from the same team. Blinding was not applied during outcome assessments, as postoperative evaluations were performed by the operating surgeon.

Bilateral and unilateral concha bullosa cases were present in both groups. For resection time analysis, each concha was evaluated independently. In patients with bilateral concha bullosa, the resection times were summed and averaged per concha to maintain consistency.

Surgical and Clinical Assessment

All surgeries were performed under general anesthesia using endoscopic guidance with a 4 mm, 0° rigid telescope (Karl Storz, Tuttlingen, Germany). Intraoperative parameters included operative time, surgical field visibility, and bleeding. Because a significant number of patients underwent simultaneous septoplasty and/or inferior turbinate reduction, efforts were made to isolate the outcomes of concha bullosa resection. Therefore, intraoperative parameters such as operative time and bleeding were evaluated specifically during the concha bullosa phase of surgery. Septoplasty and inferior turbinate reduction durations were not included in the recorded concha bullosa resection time. The degree of

bleeding was assessed subjectively by the surgeon using a binary descriptive scale: "less" or "more", based on visual clarity during the procedure. Simultaneous nasal procedures, including septoplasty and inferior turbinate reduction, were noted. Postoperative recovery and complications were recorded.

All patients underwent preoperative and postoperative evaluations using:

- Visual analog scale (VAS) for headache
- Sinonasal outcome test-22 (SNOT-22) for sinonasal symptom severity

Postoperative assessments were conducted at three months. Concha bullosa volume was assessed through nasal endoscopy and was scored using a 3-point scale (0-3) for size and prominence. This scale was adopted from previous studies and validated through consistent application by the same surgeon across all cases.

Statistical Analysis

Data analysis was performed using SPSS software (version 22.0, Chicago, IL, USA). A parametric paired-sample t-test was used to compare pre- and postoperative scores within groups. Independent-sample t-tests were applied for intergroup comparisons. Categorical variables were analyzed using the chi-square (χ^2) test. A p-value less than 0.05 was considered statistically significant.

Operative Technique

After the administration of general anesthesia, a local anesthetic solution consisting of lidocaine hydrochloride (2%) and adrenaline (0.1%) was injected submucosally into the anterior and posterior regions of the middle turbinate. In cases requiring simultaneous septoplasty or inferior turbinate reduction, these procedures were performed prior to concha bullosa intervention. Both groups were treated using a 0° rigid endoscope (Karl Storz, Tuttlingen, Germany).

In the holmium: YAG laser-assisted group, a 0.7 mm flexible quartz laser fiber (LISA, SPHINX® JR, Germany) was utilized by inserting it through an aspirator tube for maneuverability and visibility. Energy levels ranging from 0.5 to 1.5 J were applied at a frequency of 3 to 5 Hz. The mucosa was initially marked with laser shots to delineate the resection area, followed by precise ablation and resection of the bony conchal segment using direct laser contact. Subsequently, the complete mobilization of the lateral segment was verified

with the assistance of a Cottle elevator. Finally, the resected portion was removed from the nasal cavity using a punch (Figure 1).

In the conventional lateral laminectomy group, the concha was accessed using a hooked knife at the most ventilated area, followed by resection of the obstructing lateral portion with turbinate scissors. Hemostasis was successfully achieved in all cases using bipolar cautery (Valleylab Force 2 ESU, USA).

Patients were discharged the day after surgery and prescribed a one-week course of amoxicillin-clavulanate and analgesics. A Doyle splint tampon was applied at the

end of the procedure and removed on postoperative day four. Saline irrigation and moisturizing nasal drops were prescribed three times daily for 2.5 weeks.

Results

A total of 46 patients were included in the study, with 23 patients in group 1 (laser-assisted) and 23 patients in group 2 (conventional). There was no statistically significant difference in gender distribution between the groups ($p=0.750$). The mean age was 39.56 ± 13.35 years in group 1 and 37.44 ± 11.64 years in group 2 ($p=0.378$) (Table 1).

Table 1. Patient characteristics and surgical details (n=46)

Characteristics	Group 1 (laser-assisted)	Group 2 (conventional)	p-value*
Gender (M/F)	8:15	10:13	0.750
Age (years, mean \pm SD)	39.56 ± 13.35	37.44 ± 11.64	0.378
Side of concha bullosa, n (%)			0.686
Unilateral	18 (78%)	20 (87%)	
Bilateral	5 (22%)	3 (13%)	
Types of concha bullosa, n (%)			
Lamellar	4 (15%)	6 (24%)	
Bulbous	10 (35%)	8 (30%)	
Extensive	14 (50%)	12 (46%)	
Concurrent surgery, n			0.552
Septoplasty+reduction of inferior turbinates	19	21	
Reduction of inferior turbinates	4	2	

*: Statistical significance was set at $p<0.05$, SD: Standard deviation

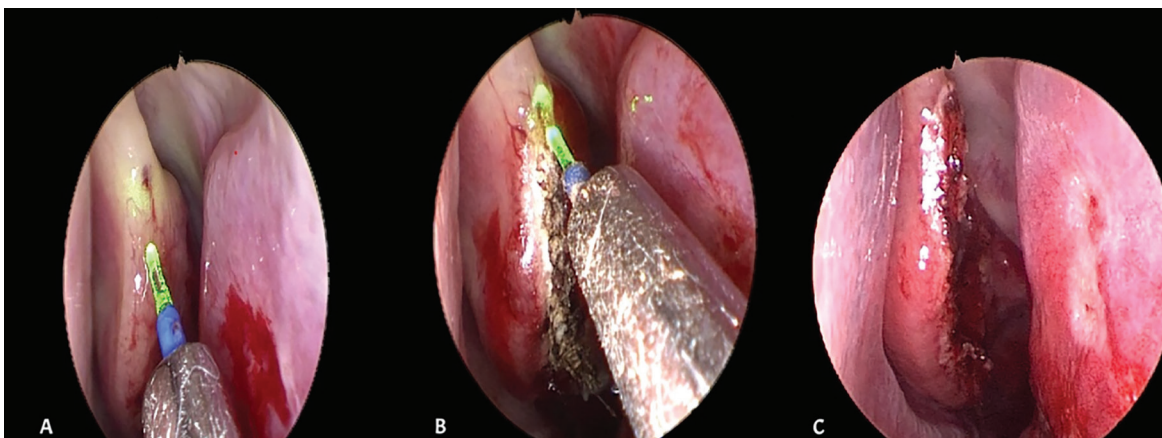


Figure 1. Intraoperative views of holmium: YAG laser-assisted resection of concha bullosa

(A) Initial laser marking of the mucosa to define the resection area. **(B)** Lateral laminectomy of the aerated middle turbinate resection using direct laser contact. **(C)** Post-resection view showing the treated area

Regarding laterality, unilateral concha bullosa was present in 78% of group 1 and 87% of group 2 patients, while bilateral involvement was seen in 22% and 13% of patients, respectively ($p=0.686$). The types of concha bullosa-lamellar, bulbous, and extensive-were similarly distributed between groups. Concurrent nasal surgeries were common in both groups, primarily septoplasty combined with inferior turbinate reduction, with no significant differences noted ($p=0.552$).

The mean follow-up duration was 6.5 ± 1.8 months in group 1 and 6.6 ± 1.5 months in group 2 ($p>0.05$). Mean resection time was significantly shorter in group 1 (15 ± 5.7 minutes) compared to group 2 (28 ± 7.5 minutes) ($p<0.001$). Additionally, the surgical field was consistently reported as clearer and less bloody in the laser-assisted group (Table 2). In subgroup analysis, no significant difference in resection time was observed between unilateral and bilateral cases when calculated per turbinate. The reported 28-minute average in the conventional group reflects cumulative intraoperative challenges such as intraoperative bleeding and limited visualization, rather than septoplasty or turbinate reduction time.

Endoscopic image classification showed significant postoperative reductions in concha bullosa scores in both groups, at the three-month follow-up ($p<0.001$ for each); however, the difference between groups was not statistically significant (Table 3).

Both groups demonstrated statistically significant improvement in VAS scores for headache and SNOT-22 scores for sinonasal symptoms ($p<0.001$ within groups). However, comparisons between groups revealed no significant intergroup differences in either VAS or SNOT-22 outcomes (Table 3). Figure 2 visually illustrates the pre- and postoperative improvements in both symptom domains across groups, confirming clinical benefit independent of the surgical technique.

Postoperative endoscopic follow-ups revealed temporary crusting and mucosal edema in both groups, more commonly persisting into the second week in group 2. One patient in group 2 experienced epistaxis on postoperative day five, which was successfully managed with bipolar cautery under local anesthesia. No further complications were reported. Importantly, there were no occurrences of cerebrospinal fluid (CSF) leakage, orbital injury, anosmia, synechiae, exposed bone, lateralized turbinates, or persistent symptoms in either group.

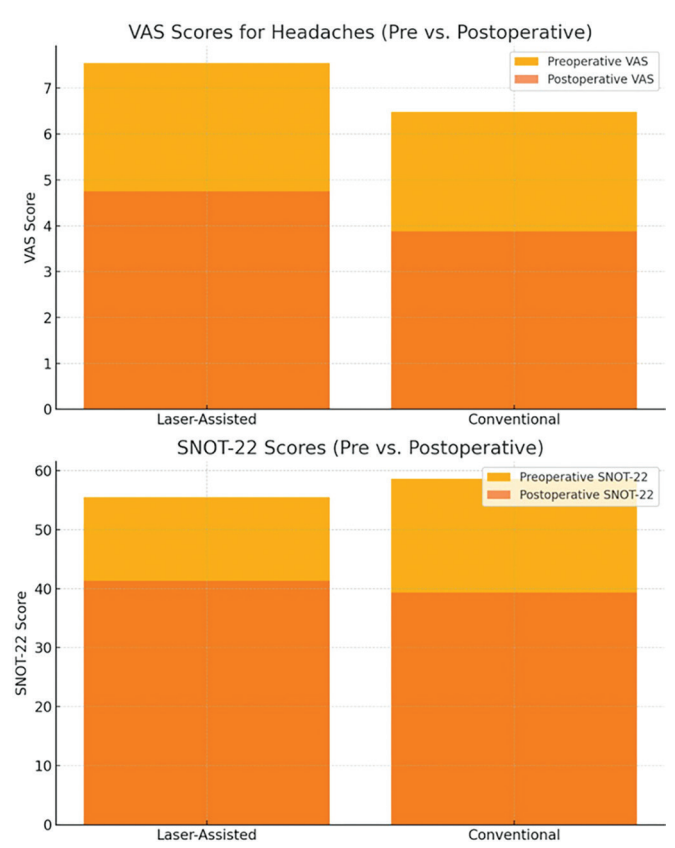


Figure 2. Comparison of preoperative and postoperative VAS and SNOT-22 scores between groups
VAS: Visual analog scale, SNOT-22: Sinonasal outcome test-22

Table 2. Comparison of the intraoperative and postoperative parameters of each group of patients			
Parameter	Group 1 (laser-assisted)	Group 2 (conventional)	p-value
Mean resection time ± SD (minutes)	15±5.7	28±7.5	0.000*
Surgical field bleeding	Less	More	
Mean follow-up duration ± SD (months)	6.5±1.8	6.6±1.5	>0.05
Major complications	None	None	

*: p<0.05, independent samples t-test, SD: Standard deviation

Table 3. Comparative analysis of endoscopic classification scores, VAS, and SNOT-22 results in laser-assisted and conventional concha bullosa resection groups

The concha bullosa scores of endoscopic image classification			
	Endoscopy preoperative (mean ± SD)	Endoscopy postoperative 3 rd month (mean ± SD)	Paired student t-test (p-value)
Group 1 (laser-assisted, n=23)	2.60±0.35	1.90±0.58	0.000*
Group 2 (conventional, n=23)	2.50±0.46	1.85±0.55	0.000*
Unpaired student t-test (p-value)	0.140	0.115	
Evaluation of VAS for headaches results in patients undergoing middle turbinate surgery			
	Preoperative VAS (mean ± SD)	Postoperative VAS 3 rd month (mean ± SD)	Paired student t-test (p-value)
Group 1 (laser-assisted, n=23)	7.55±1.95	4.75±2.12	0.000*
Group 2 (conventional, n=23)	6.48±2.16	3.88±2.18	0.000*
Unpaired student t-test (p-value)	0.247	0.355	
Evaluation of SNOT-22 scores results in patients undergoing middle turbinate surgery			
	Preoperative SNOT-22 (mean ± SD)	Postoperative SNOT-22 3 rd month (mean ± SD)	Paired student t-test (p-value)
Group 1 (laser-assisted, n=23)	55.45±12.95	41.35±13.72	0.004*
Group 2 (conventional, n=23)	58.64±11.16	39.29±15.18	0.000*
Unpaired student t-test (p-value)	0.557	0.672	

*: p-value considered significant at <0.05, SD: Standard deviation, VAS: Visual analog scale, SNOT-22: Sinonasal outcome test-22

Regression analysis (Table 4) identified that shorter resection time and higher preoperative SNOT-22 scores significantly predicted greater VAS improvement ($\beta=-0.0297$ and $+0.0585$, respectively; $p<0.001$). For SNOT-22 score improvement, significant predictors included longer resection time and higher baseline VAS scores (coefficients of $\beta=0.4782$ and 0.9033 , respectively; $p<0.001$). These results emphasize the dual role of symptom severity and surgical dynamics in influencing postoperative recovery.

Figure 3 presents a correlation heatmap summarizing the strong associations between symptom severity, surgical time, and postoperative improvement. These patterns reinforce the internal consistency of clinical outcomes across both subjective and procedural variables.

Discussion

Although middle concha bullosa is a common anatomical variation, surgical intervention is not always recommended. Surgery is primarily indicated in symptomatic cases where concha bullosa contributes to the obstruction of the

osteomeatal complex. Various surgical techniques have been described in the literature, including lateral or medial partial resection, total resection, turbinoplasty, crushing, and crushing with intrinsic stripping. However, there is no clear consensus on the optimal surgical technique yet^(7,8).

In another study, the intrinsic stripping technique was shown to significantly reduce concha bullosa volume while also lowering recurrence rates⁽⁹⁾. No significant postoperative functional differences have been observed between medial and lateral partial resections, commonly referred to as classical resection. However, medial resection has been noted to offer advantages in terms of preventing synechiae in the lateral nasal wall-frontal recess area and facilitating frontal sinus drainage⁽¹⁰⁾.

The crushing technique provides advantages such as a shorter operative time and the ability to be performed simultaneously with other nasal surgeries. However, it carries a risk of long-term recurrence, as noted in previous studies^(11,12).

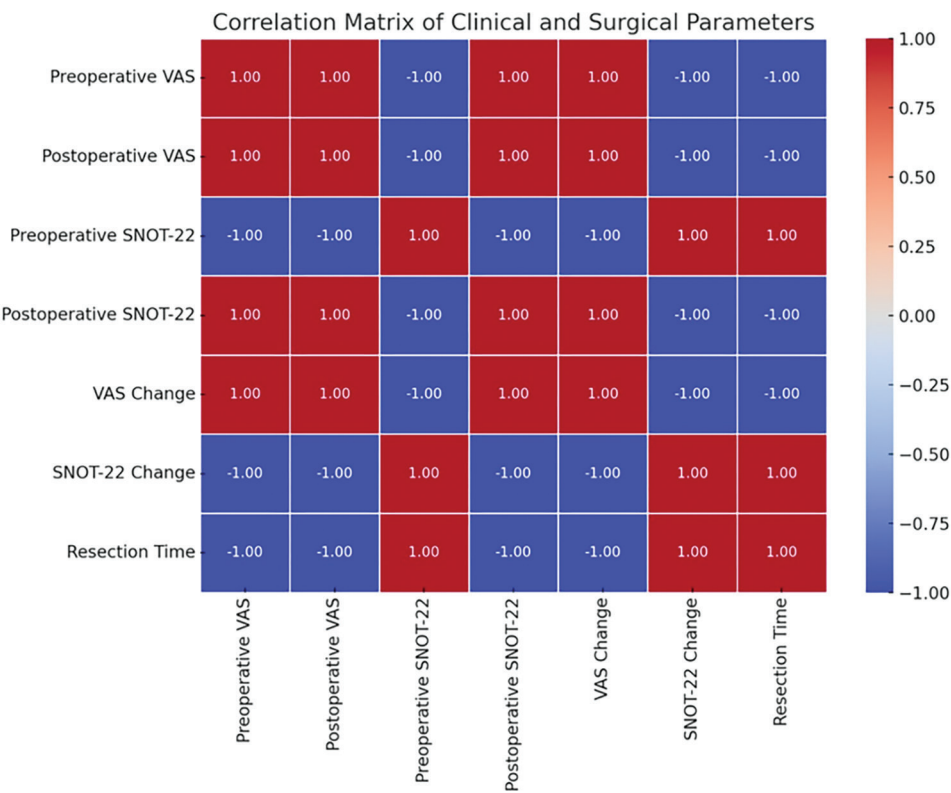


Figure 3. Correlation heatmap of symptom scores and surgical parameters in concha bullosa resection
VAS: Visual analog scale, SNOT-22: Sinonasal outcome test-22

Table 4. Regression analysis of predictors for VAS and SNOT-22 improvement				
Outcome variable	Predictor	Beta coefficient (β)	p-value	Interpretation
VAS change	Resection time	−0.0297	<0.001	Shorter resection time is associated with greater VAS improvement.
VAS change	Preoperative SNOT-22	+0.0585	<0.001	Higher symptom burden predicts more headache relief.
SNOT-22 change	Resection time	+0.4782	<0.001	Longer surgery duration is associated with greater SNOT-22 improvement.
SNOT-22 change	Preoperative VAS	+0.9033	<0.001	More severe headache symptoms predict greater improvement in SNOT-22.

[†]: All models had R²=1.000 due to dataset uniformity. Beta values indicate direction and strength of association, VAS: Visual analog scale, SNOT-22: Sinonasal outcome test-22

All concha bullosa cases were classified into three types: lamellar, bulbous, and extensive. A prospective study evaluating the crushing technique in all three types reported a significant reduction in concha volume on preoperative and postoperative tomography. Additionally, no cases of re-pneumatization were observed during long-term follow-up⁽¹³⁾. In our case series, the type and volume of concha bullosa were evaluated preoperatively through nasal endoscopic

examination and paranasal sinus CT. In group 1, 16 bulbous and 7 extensive concha bullosa were observed, while in group 2, 14 bulbous, 8 extensive, and 1 lamellar type were identified. In the postoperative period, concha volume was assessed only through nasal endoscopic examination to avoid unnecessary radiation exposure. A fundamental principle of surgery is minimizing tissue damage while effectively resolving the pathology in a short

time. This principle is particularly relevant in concha bullosa surgery, where limited and controlled resection of the affected portion is the primary goal^(14,15).

The conventional resection technique, lateral excision of the middle turbinate, is the most commonly used approach for isolated concha bullosa. Since the medial part of the middle turbinate is connected to the skull base, lateral resection is considered safer in terms of preventing CSF fistula formation⁽¹⁶⁾. In our study, lateral resection was performed in both patient groups.

Ismail et al.⁽¹¹⁾ prospectively evaluated three surgical techniques for the treatment of symptomatic concha bullosa: crushing, lateral laminectomy with mucosal preservation, and lateral laminectomy without mucosal preservation. Postoperative headache assessment using the VAS showed a statistically significant improvement in patients who underwent lateral laminectomy (with and without mucosal preservation) compared to the crushing group. However, no significant difference was observed between the two lateral laminectomy groups⁽¹¹⁾. In our study, in both groups undergoing lateral laminectomy, the resected bony segment was excised along with its inner and outer mucosal surfaces.

However, postoperative complications such as bleeding, synechiae, sinusitis, and olfactory dysfunction have been reported following middle turbinate surgery^(17,18). In our study, one patient from each group required hospitalization and re-tamponade due to nasal bleeding within the first postoperative week.

In some cases, the middle turbinate has a direct anatomical relationship with the skull base. Excessive mobilization (destabilization of the middle turbinate) or forceful maneuvers during surgery in such cases may lead to CSF leakage. This potential complication has been previously reported following septal and turbinate surgeries^(19,20).

The use of a holmium: YAG laser in group 1 aimed to achieve sufficient resection without excessive manipulation of the middle turbinate. Compared to the conventional technique, laser-assisted resection provided a clearer surgical field with reduced intraoperative bleeding and a shorter resection time, which are significant advantages.

Winters and Worley⁽²¹⁾ previously reported the use of the LightForce Gold Laser for concha bullosa resection, highlighting its ease of use and hemostatic. However, to our knowledge, no prior studies have investigated holmium: YAG

laser-assisted concha bullosa resection. In our case series, holmium: YAG laser was utilized not only for concha bullosa resection but also for inferior turbinate reduction. The lower incidence of postoperative crusting in group 1 compared to group 2 may be attributed to the reduced need for bipolar cauterization for hemostasis in the laser-assisted technique.

Study Limitations

This study has several limitations. First, its retrospective design may introduce selection and information biases, as randomization and blinding were not applied. Second, although efforts were made to isolate the outcomes of concha bullosa resection, many patients underwent concurrent nasal procedures such as septoplasty and inferior turbinate reduction, which may have influenced postoperative symptom scores. Third, the relatively small sample size and short follow-up period (mean 6.5 months) limit the generalizability of the findings and prevent a comprehensive evaluation of long-term outcomes, such as recurrence or empty nose syndrome. Additionally, the subjective assessment of intraoperative bleeding and the absence of objective bleeding quantification may reduce the reproducibility of this outcome. Finally, the study did not include an economic analysis of the laser device's cost-effectiveness, which is an important consideration for wider clinical adoption.

Future prospective studies with larger cohorts and extended follow-up periods (>2 years) are warranted to better evaluate the long-term outcomes of these techniques. Furthermore, comparative studies involving other laser modalities, such as CO₂ or diode lasers, could provide further insights into optimizing surgical approaches for concha bullosa resection.

Conclusion

Holmium: YAG laser-assisted lateral laminectomy is a safe and effective alternative to conventional surgical techniques for the treatment of symptomatic concha bullosa. While both methods significantly improve headache and sinonasal symptoms, the laser-assisted approach offers advantages in terms of reduced operative time, improved surgical field visibility, and minimal intraoperative bleeding. These findings suggest that incorporating laser technology may enhance surgical efficiency without compromising clinical outcomes. Further studies with long-term follow-up and broader patient populations are recommended to validate these results.

Ethics

Ethics Committee Approval: The study protocol was approved by the İstanbul Medipol University Institutional Ethics Committee (approval no: 213, date: 20.02.2025) in accordance with the Declaration of Helsinki.

Informed Consent: This retrospective case-control study was conducted at the Clinic of Otorhinolaryngology of Medipol University Esenler Hospital between 2018 and 2023.

Footnotes

Authorship Contributions

Surgical and Medical Practises: E.A., Concept: N.Ö., A.A., Design: E.A., N.Ö., A.A., Data Collection or Processing: E.A., Analysis or Interpretation: N.Ö., Literature Search: E.A., A.A., Writing: E.A., N.Ö., A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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