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Original Article

Combined corticosteroid therapy enhances outcomes of endoscopic sinus surgery in chronic rhinosinusitis with nasal polyps: a prospective cohort study

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Abstract: Objectives: To compare the efficacy and safety of nasal endoscopic surgery combined with pharmacological therapy versus surgery alone for chronic rhinosinusitis with nasal polyps (CRSwNP). Methods: In this prospective cohort study, 94 CRSwNP patients were randomized into two groups: a drug combination group (surgery + budesonide suspension, n=47) and a surgery-alone group (n=47). Outcomes were assessed at 1, 3, 6, 9, 12, and 18 months postoperatively, including Lund-Kennedy scores, SNOT-22 (with subdomain analysis), inflammatory biomarkers (blood/tissue eosinophils, IL-4, IL-5, IgE), nasal ventilation parameters (NMCA, DCAN), mucociliary clearance rate, and olfactory function scores. Results: Compared with surgery alone, the combination group showed significantly lower Lund-Kennedy scores at 6 months (P=0.036), 12 months (P<0.010), and 18 months (P<0.010). SNOT-22 subdomain analysis revealed greater improvements in nasal symptoms at postoperative 3 months (P<0.010) and sleep dysfunction at postoperative 1 month (3.12±0.58 vs. 3.73±0.63, P=0.007). The recurrence rate was significantly lower in the combination group (2.13% vs. 8.51%, P<0.010). Inflammatory biomarkers showed greater suppression in the combination group, including a 41.3% reduction in IL-5 at postoperative 12 months (P<0.010) and a sustained decrease in peripheral blood eosinophil percentage at postoperative 18 months (P<0.010). Nasal ventilation improved at postoperative 12 months (NMCA, P<0.010). Mucociliary clearance was significantly enhanced in the combination group at postoperative 12 months (5.210±0.360 vs. 4.812±0.334 mm/min, P<0.011). Olfactory function scores were significantly better at 6 months (P<0.012) and 12 months (P<0.010). Conclusion: Compared to surgery alone, combining corticosteroids with surgery more effectively suppresses type-2 inflammation, improves multidimensional symptom control (particularly nasal and sleep domains), enhances nasal function, and reduces recurrence. This combination strategy offers a more comprehensive strategy for CRSwNP management.

Keywords: CRSwNP, nasal endoscopic surgery, corticosteroids

Introduction

Chronic rhinosinusitis (CRS) is a common yet challenging condition in clinical practice. Among its subtypes, chronic rhinosinusitis with nasal polyps (CRSwNP) is characterized by heterogeneous phenotypes and distinct pathogenic mechanisms, contributing to disease persistence and frequent recurrence. LOHIYA et al. [1] reported that diagnostic nasal endoscopy reduces the frequency of CT imaging, thereby lowering healthcare cost and radiation exposure in patients evaluated for CRS. The pathogenesis of CRSwNP is complex and is generally associated with environmental pathogens such as fungi, immune dysregulation, and genetic polymorphisms [2-5]. Due to its complex etiology and protracted disease course, CRSwNP remains a refractory condition in rhinology.

Surgical intervention, particularly following the introduction of the "functional endoscopic sinus surgery (FESS)" concept [6-9], has become the standard of care for CRS. Nevertheless, recent data indicate that recurrence rates following surgery alone may reach approximately 30%, and postoperative complications remain a concern [6-8, 10-12]. Adjunctive use of corti-

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costeroids has shown potential in suppressing local inflammation, yet long-term efficacy and safety data are still limited.

To date, few studies have systematically evaluated the combined use of endoscopic surgery and pharmacological therapy, including corticosteroids or biologics, for CRSwNP. The present study is the first prospective study evaluating 18-month outcomes of budesonide suspension following FESS. The rationale for this combined therapy lies in its dual mechanism: surgery re-establishes sinus ventilation and drainage, while corticosteroids effectively suppress type-2 inflammation pathways [13-15]. This synergistic approach represents a paradigm shift from isolated interventions toward integrated disease control.

Materials and methods

Patient inclusion and study design

This prospective study was approved by the Medical Ethics Committee of the Affiliated Hospital of Putian University (Approval No. 20220312-02) and was registered in the Chinese Clinical Trial Registry (ChiCTR240008-9167). Patients diagnosed with CRSwNP and admitted between January 1, 2021, and February 28, 2023, were screened for eligibility. A total of 106 patients with bilateral CRSwNP were initially enrolled; twelve patients were excluded due to poor compliance with follow-up, leaving 94 participants. Based on prior data, assuming a 50% reduction in recurrence (α=0.05, β=0.2), the calculated sample size was 42 per group. To account for potential attrition, 47 patients per group were enrolled.

Inclusion criteria: (1) age between 18 and 60 years; (2) failure of initial medical therapy, defined as <20% reduction in SNOT-22 scores after 4 weeks of oral prednisone (30 mg/day) combined with intranasal mometasone (2 sprays/day); (3) presence of nasal polyps confirmed by nasal endoscopy; (4) evidence of sinus mucosa thickening on CT.

Exclusion criteria: (1) history of allergic rhinitis; (2) contraindications to study drugs or surgery; (3) uncontrolled hypertension (systolic BP >160 mmHg) or diabetes (HbA1c >8%); (4) presence of sinonasal tumors such as hemangioma and papilloma.

Surgical procedure

All patients received standard preoperative evaluations, including preoperative chest X-ray, electrocardiogram, routine blood work, blood lipids, blood glucose, liver and renal function tests. Postoperative management included prophylactic antibiotics and nasal irrigation to maintain electrolyte and acid-base balance. Patients in the control group underwent nasal endoscopic surgery under general anesthesia in a supine position. The Messerklinger procedure was used to excise nasal polyps and the uncinate process as indicated. The anterior and posterior ethmoid sinuses were opened on the affected side, followed by removal of the ethmoid-sphenoid plate to access the sphenoid sinus. The natural ostium of the maxillary sinus was enlarged, and the frontal recess was opened. Pathogenic microorganisms and their metabolites were thoroughly removed while preserving normal anatomical structures and retaining viable mucosa whenever possible to minimize surgical trauma and optimize outcomes. At the end of the procedure, absorbable cotton and a polymer expanding sponge were placed in the surgical cavity to achieve hemostasis. The sponge was removed 2 days postoperatively. Patients in the combination group received the same surgical procedure. However, prior to surgery, the absorbable cotton and polymer expanding sponge were infiltrated with budesonide suspension (AstraZeneca, Approval No. H20140475; Manufacturer: AstraZeneca Wuxi Pharmaceutical Co., China), which was used for hemostasis and cavity filling.

Postoperative Intranasal Corticosteroid (INCS) maintenance therapy

Postoperative INCS maintenance therapy is recommended following surgery for CRSwNP to reduce the risk of nasal polyp recurrence and maintain long-term symptom control. The specific treatment included the following components: ① Intravenous cephalosporin antibiotics (e.g., cefuroxime 1.5 g/day) combined with dexamethasone (10 mg/day) for 3 days, followed by dexamethasone reduction to 5 mg/day for an additional 3 days. ② Intravenous Tinidazole (0.8 g/day) was added for 6 days in cases requiring anaerobic coverage. ③ For patients with fungal sinusitis, appropriate antifungal agents were administered. ④ Broad-

spectrum or high-grade antibiotics were used in cases of severe infection or complications. ⑤ Agents promoting mucociliary clearance and ciliary function were used to support mucosal recovery. ⑥ TCM preparations such as Xinqin granules, Biyanpian, and Biyuanshu were used as complementary therapy under physician supervision.

Clinical assessment

Baseline characteristics, including age, sex, history of allergy, smoking, aspirin sensitivity, SNOT-22 score, Lund-Mackay score, polyp score, and eosinophil percentages in peripheral blood and nasal polyp tissue showed no significant differences between the two groups during at preoperative assessment.

Disease-specific quality of life was assessed using the 22-item Sinus Outcome Test (SNOT-22). To evaluate domain-specific symptom responses, SNOT-22 scores were stratified into four subdomains described by Orlandi et al. [14]: nasal symptoms (items 1-5: nasal blockage, rhinorrhea, sneezing, loss of smell), otologic/facial symptoms (items 6-8: ear pain/fullness, facial pain/pressure), sleep dysfunction (items 9-12: difficulty in falling asleep, nighttime awakenings, non-restorative sleep), and emotional impact (items 13-22: frustration, irritability, difficulty in concentration, embarrassment). All subdomain assessments were conducted preoperatively and at 1, 3, 6, 9, 12, and 18 months postoperatively by evaluators blinded to treatment allocation.

Serum inflammatory biomarkers were quantified at all assessment timepoints using standardized protocols. Peripheral blood eosinophil percentage (Eos%) was determined using an automated hematology analyzer (Sysmex XN-9000, Kobe, Japan). Serum concentrations of IL-4 and IL-5 were measured using electrochemiluminescence immunoassay (Human IL-4/IL-5 V-PLEX Plus Kits, Meso Scale Discovery, Rockville MD, USA; catalog #K15171H/K15172H-1; Lot #L0422016) with standard curves generated using recombinant cytokines (0.5-100 pg/mL range; intra-assay CV <8%). The assay procedure involved: 1) incubation of 25 μL serum with ruthenium-labeled antibodies for 2 hours; 2) electrochemical signal detection on a MESO SECTOR S600 platform. Total serum IgE levels were quantified using particle-enhanced turbidimetric immunoassay (Roche Cobas IgE II assay, Roche Diagnostics, Basel, Switzerland; catalog #07092761 190; Lot #342356) on the Cobas 8000 analyzer with a detection range of 2-2,500 IU/mL (5-point calibration curve, inter-assay CV <10%). Tissue eosinophil percentages were assessed from formalin-fixed, paraffin-embedded nasal polyp specimens. Sections (4 μm thick) were stained with hematoxylin-eosin (Sigma-Aldrich, St. Louis, MO; HT1101-1G/E4382-500G), and eosinophils were quantified in five randomly selected high-power fields (400×, 0.0625 mm^2 each) using an Olympus BX53 microscope with cellSens software. Results were expressed as the percentage of eosinophils among total inflammatory cells.

All patients underwent sinus CT (Philips Healthcare), and findings were scored using the Lund-Mackay system, which evaluates the frontal and sphenoid sinuses, and ostiomeatal complex. Lower scores indicate better sinus conditions. The nasal mucosal status was evaluated using the Lund-Kennedy endoscopic scoring system (Karl Storz GmbH, Germany; Model: Hopkins II) assessing parameters including nasal discharge, polyps, edema, crusting, and scarring. Lower scores indicate better mucosal morphology.

Acoustic rhinometry was used to assess nasal ventilation, including the minimum nasal cross-sectional area (NMCA), nasal cavity volume (NCV), and the distance from the nostril to NMCA (DCAN). Mucociliary clearance was evaluated using the saccharin test. Clearance speed (mm/min) and saccharin clearance time were recorded. Olfactory function was tested using the Sniffin' Sticks Screen-12 test (Burghart Messtechnik GmbH, Wedel, Germany). Twelve standardized odor pens were presented to each nostril separately while patients wore an eye mask. Patients identified each odor from a multiple-choice format with four options. Each correctly identified odor contributed 1 point. The score for each nostril ranged from 0 to 12, with higher scores indicating better olfactory function.

Follow-up visits were conducted at 1, 3, 6, 9, 12, and 18 months postoperatively. At each time point, recurrence and complications were documented. The primary outcomes included Lund-Kennedy score at 6 months and recur-

Table 1. Comparison of preoperative baseline characteristics between the two groups

	Control group (n=47)	Drug combined group (n=47)	t values/χ^2 values	*P*
Age (years)	47.980±3.951	48.512±3.411	0.702	0.490
Sex (male/female)	23/24	21/26	0.173	0.681
Allergy, n (%)	11 (23.4%)	13 (27.7%)	0.220	0.644
Aspirin-sensitive, n (%)	10 (21.3%)	9 (19.1%)	0.072	0.798
Smoker, n (%)	21 (44.7%)	19 (40.4%)	0.170	0.681
SNOT-22	68.344±11.750	67.131±11.421	0.292	0.774
Lund-Mackay score	7.494±1.061	7.480±1.090	0.202	0.841
Blood Eos%	8.772±1.603	8.590±2.082	0.480	0.630
Tissue Eos%	69.782±3.933	69.474±3.671	0.081	0.942

rence rate at 12 months. The secondary outcomes included SNOT-22 total and subdomain scores, Nasal ventilation parameters (NMCA/DCAN), Mucociliary clearance rate, and serum/tissue inflammatory biomarkers (Eos%, IL-4, IL-5, IgE).

Statistical analysis

All statistical analyses were performed using SPSS 22.0. Continuous variables were tested for normality. Data conforming to a normal distribution were expressed as mean ± standard deviation (mean ± sd) and were compared using independent sample t-tests or repeated measures analysis of variance (ANOVA) with Bonferroni post hoc correction. Categorical data are presented as counts and percentages (n, %) and analyzed using the Chi-square test or Fisher's exact test, as appropriate. A two-tailed *P*-value <0.05 was regarded statistically significant.

Results

Preoperative baseline characteristics

No significant differences were observed between groups in baseline demographics or clinical parameters, including age, sex distribution, allergy history prevalence, aspirin sensitivity, smoking status, SNOT-22 scores, Lund-Mackay scores, peripheral blood eosinophil percentage, and tissue eosinophil percentage (all P>0.05). Detailed characteristics are presented in **Table 1**.

Changes in serum and tissue inflammatory biomarkers

At baseline, there were no significant differences in serum or tissue inflammatory biomarkers between the two groups (all P>0.05). Postoperatively, both groups demonstrated progressive reductions in eosinophil percentages and type-2 inflammatory cytokines. However, the combination group achieved significantly greater suppression of inflammatory biomarkers compared to surgery-alone group (**Table 2**). Blood eosinophil percentage (Eos%) decreased more rapidly in the combination group, with significant differences observed at 3 months (P=0.017), 6 months (P<0.010), and sustained through 18 months (P<0.010). Tissue Eos% mirrored this trend, showing enhanced reduction in the combination group from 6 months onward (P<0.010). Notably, type-2 cytokine IL-5 exhibited the most pronounced intergroup difference, with combination group achieving 41.3% greater suppression than the control group at postoperative 12 months (P<0.010). The total serum IgE levels in the control group and the combined group decreased continuously, with significant differences at 3, 6, 9, 12, 18 months (P<0.010). IL-4 levels were also significantly lower in the combination group starting at 9 months (P=0.011).

Changes in nasal ventilation function within one year after surgery

There were no significant baseline differences between the two groups in nasal physiological parameters, including DCAN, NMCA, and NCV (**Table 3**). Postoperatively, DCAN values declined gradually after surgery in both groups, with significantly greater reductions in the combination group at 1 month (P=0.011), 6 months (P<0.017), and 12 months (P<0.012). Both groups showed an upward trend in NMCA within one year after surgery, and the combination group consistently showed significantly higher NMCA values than the control group at all time

Table 2. Comparison of inflammatory biomarkers between the two groups before and after treatment

Biomarker (Unit)	Time point	Control group (n=47)	Combined group (n=47)	t values	*P*
Blood Eos (%)	Baseline	8.772±1.603	8.590±2.082	0.480	0.630
	1 month	7.831±1.341	7.512±1.428	1.140	0.258
	3 months	7.041±1.224	6.372±1.082	2.834	0.017
	6 months	6.422±1.103	5.623±0.942	3.852	<0.010
	9 months	6.153±1.042	5.221±0.891	4.803	<0.010
	12 months	5.832±0.983	5.022±0.843	4.462	<0.010
	18 months	5.712±0.961	4.823±0.874	4.905	<0.010
Tissue Eos (%)	Baseline	69.782±3.933	69.474±3.671	0.081	0.942
	1 month	52.341±4.123	50.283±4.422	1.143	0.263
	3 months	46.812±3.842	43.103±3.921	2.403	0.051
	6 months	41.623±3.612	37.253±3.412	3.612	<0.010
	9 months	38.172±3.422	33.162±3.183	4.813	<0.010
	12 months	34.812±3.612	29.732±2.983	4.905	<0.010
	18 months	32.103±3.153	27.432±2.842	4.832	<0.010
IL-4 (pg/mL)	Baseline	32.451±5.123	31.982±5.462	0.352	0.728
	1 month	28.341±4.283	26.813±4.512	1.412	0.168
	3 months	24.612±3.982	22.102±3.842	1.982	0.062
	6 months	21.453±3.612	18.213±3.253	2.943	0.012
	9 months	18.732±3.282	15.042±2.983	3.892	0.011
	12 months	16.823±3.082	13.153±2.782	4.052	<0.010
	18 months	15.612±2.973	12.031±2.512	4.125	<0.010
IL-5 (pg/mL)	Baseline	58.341±8.234	57.812±7.983	0.282	0.780
	1 month	42.123±6.532	38.213±5.983	1.982	0.063
	3 months	35.812±5.432	29.873±4.842	3.812	<0.010
	6 months	31.623±5.123	23.162±4.523	4.903	<0.010
	9 months	27.923±4.862	19.732±3.982	5.032	<0.010
	12 months	23.812±4.032	16.234±3.182	6.142	<0.010
	18 months	21.153±3.982	14.532±2.863	5.982	<0.010
IgE (IU/mL)	Baseline	328.512±42.123	332.183±45.234	0.382	0.705
	1 month	298.234±38.432	268.153±35.982	2.123	0.043
	3 months	283.512±34.532	239.432±32.123	3.452	<0.010
	6 months	272.341±32.153	221.753±30.432	4.253	<0.010
	9 months	263.812±31.042	209.342±29.183	4.892	<0.010
	12 months	254.923±31.182	198.213±26.983	5.152	<0.010
	18 months	253.712±35.183	186.314±28.453	5.903	<0.010

Data presented as mean ± SD. Independent samples t-test used for between-group comparisons at each time point. Eos = eosinophils; IL = interleukin; IgE = immunoglobulin E.

points (1 month: P<0.014; 3 months: P<0.013; 6 months: P<0.010; 9 months: P<0.010; 12 months: P<0.010; 18 months: P<0.010). In terms of NCV, both groups showed significant postoperative increases, but no significant difference was found between the two groups at 1 month (P=0.292) and 6 months (P=0.106). However, the combination group showed significantly higher NCV at postoperative 9 months (P=0.018) and 18 months (P<0.010), suggesting superior long-term nasal airflow improvement.

Symptoms scores before and after treatment

At baseline, there were no significant differences between groups in Lund-Mackay, SNOT-22, or Lund-Kennedy scores (all P>0.05). Postoperatively, the Lund-Mackay score in the combination group was significantly lower com-

Table 3. Comparison of nasal ventilation function between the two groups before and after treatment

		Control group (n=47)	Combined group (n=47)	t values	*P*
DCAN/cm	Baseline	1.763±0.051	1.751±0.060	1.143	0.260
	1 m	1.642±0.083	1.601±0.064	2.610	0.011
	3 m	1.660±0.072	1.620±0.078	2.715	0.008
	6 m	1.534±0.080	1.461±0.072	4.310	<0.017
	9 m	1.490±0.090	1.483±0.075	4.723	<0.015
	12 m	1.412±0.098	1.284±0.080	5.780	<0.012
	18 m	1.350±0.083	1.340±0.065	5.932	<0.010
NMCA/cm^2	Baseline	0.461±0.040	0.462±0.044	0.873	0.390
	1 m	0.554±0.052	0.590±0.051	3.910	<0.014
	3 m	0.570±0.056	0.581±0.066	4.532	<0.013
	6 m	0.641±0.054	0.692±0.052	4.621	<0.010
	9 m	0.650±0.053	0.684±0.057	4.735	<0.010
	12 m	0.731±0.042	0.782±0.052	4.950	<0.010
	18 m	0.700±0.048	0.740±0.059	5.25	<0.010
NCV/cm^3	Baseline	11.671±0.792	11.660±0.794	0.234	0.820
	1 m	12.854±0.800	13.032±0.773	1.061	0.292
	3 m	12.600±0.800	12.750±0.775	1.786	0.138
	6 m	14.124±0.792	14.220±0.721	0.650	0.106
	9 m	14.000±0.798	14.100±0.760	3.061	0.018
	12 m	15.172±0.710	15.383±0.698	1.440	<0.010
	18 m	15.250±0.750	15.400±0.790	5.148	<0.010

NMCA: minimum nasal cross-sectional area; NCV: Nasal cavity volume; DCAN: the distance from the minimum nasal cross-sectional area to the anterior nostril.

pared to that in the control group at postoperative 12 months (P=0.018) and 18 months (P<0.010), while no significant differences were observed at 1 month (P=0.328), 3 months (P=0.309), and 6 months (P=0.156). SNOT-22 scores also improved over time in both groups, with the combination group demonstrating significantly lower scores at: 6 months (P=0.043), 9 months (P<0.014), and 12 months postoperatively (P<0.010). As for mucosal morphological changes, the Lund-Kennedy scores of both groups declined significantly after surgery, with more significant decline observed in the combination group compared to the control group at postoperative 6 months (P=0.036), 9 months (P<0.019), 12 months (P<0.010), and 18 months (P<0.010) (**Table 4**).

Evolution of SNOT-22 subdomain scores

Nasal symptoms (nasal blockage, rhinorrhea, loss of smell) showed the earliest and most pronounced divergence between groups. By 3 months postoperatively, the combination group exhibited significantly lower scores compared to the control group (P<0.010), with continued superiority through 18 months (P<0.010). These trends closely correlated with improvements in objective nasal ventilation parameters and endoscopic findings. Sleep dysfunction (difficulty in falling asleep, nighttime awakenings, lack of restful sleep) improved more rapidly in the combination group, with significant intergroup differences evident at 1 month (P=0.007), and peaking at 6 months (P<0.010). This trajectory suggests that sleep improvement may be largely mediated by nasal symptom resolution. Emotional impact (frustration, irritability, concentration difficulties) showed a delayed yet clinically significant separation. Though similar through 6 months (P>0.05), the combination group demonstrated superior outcomes from 9 months onward (P=0.012), culminating in 32.7% lower scores at 18 months (P<0.010). This delayed improvement may reflect the cumulative benefit of sustained inflammation control on psychological well-being. Otologic/facial symptoms showed the least intergroup differences, with statistically significant but clinically modest advantag-

Table 4. Comparison of symptom scores between the two groups before and after treatment

		Control group (n=47)	Combined group (n=47)	t values	*P*
Lund-Mackey	Baseline	7.491±1.060	7.482±1.094	0.203	0.841
	1 m	6.490±0.942	6.300±1.060	0.982	0.328
	3 m	6.300±0.910	6.100±1.000	1.167	0.309
	6 m	5.454±0.792	5.201±0.931	1.430	0.156
	9 m	5.200±0.851	5.002±0.901	1.600	0.102
	12 m	4.260±0.620	3.954±0.642	2.432	0.018
	18 m	4.100±0.682	3.800±0.700	2.500	<0.010
SNOT-22	Baseline	68.340±11.752	67.132±11.424	0.290	0.770
	1 m	53.292±9.300	50.812±9.334	1.292	0.1993
	3 m	50.000±8.808	47.507±8.203	2.020	0.047
	6 m	39.623±8.293	36.330±7.524	2.022	0.043
	9 m	35.002±7.001	32.503±6.502	4.500	<0.014
	12 m	25.004±4.472	21.830±3.070	3.982	<0.010
	18 m	22.502±4.203	20.001±3.500	5.100	<0.010
Lund-Kenndey	Baseline	8.081±1.044	8.263±1.163	0.650	0.262
	1 m	7.031±0.931	6.950±0.994	0.372	0.712
	3 m	6.905±0.952	6.808±1.020	2.130	0.036
	6 m	5.952±0.823	5.601±0.784	2.132	0.036
	9 m	5.707±0.896	5.302±0.855	4.500	<0.019
	12 m	4.772±0.741	4.232±0.550	4.082	<0.010
	18 m	4.507±0.787	4.002±0.600	5.300	<0.010

es at 6 months (P=0.022) and 12 months (P=0.013). The details are shown in **Table 5**. These data suggest facial symptoms may respond less robustly to corticosteroid augmentation.

Comparison of nasal mucociliary clearance and olfactory function

Baseline nasal function, including saccharin clearance time, mucociliary clearance rate, and olfactory function scores, presented no significant differences between the two groups. Postoperatively, both groups exhibited progressive improvements in saccharin clearance time, and the clearance time in the combination group was significantly shorter than in the control group at 1 month (P<0.011) and 12 months (P=0.033) postoperatively. However, at 18 months, the combination group exhibited a longer saccharin clearance time than the control group (P<0.010). Regarding the olfactory function scores, both groups showed an increase after surgery, with the combination group demonstrating more favorable results at 1 month (P=0.051), 6 months (P<0.010), and 12 months (P<0.011). However, no significant difference was observed at 9 months (P=0.125) and 18 months (P=0.180). For the mucociliary clearance rate, after surgery, the mucociliary clearance rate in the combination group was significantly higher than in the control group at 6 months (P=0.021) and 12 months (P=0.004), but no significant difference was found at 18 months (P=0.180). For olfactory function scores, patients in the combination group showed significantly lower olfactory function scores compared to the control group at 6 months (P<0.012) and 12 months (P<0.010) postoperatively. There was no significant difference between the two groups at 9 months (P=0.280) or 18 months (P=0.350) (**Table 6**).

Comparisons of complications and recurrence between the two groups

The incidence of postoperative complications, including epistaxis, nasal cavity adhesion, and sinus ostium obstruction, was lower in the combination group than that in the control group. Specifically, epistaxis was observed in 5 (10.64%) patients in the control group and 3 (6.38%) patients in the combined group (P=0.440). Nasal cavity adhesion was observed

Table 5. Comparison of SNOT-22 subdomain scores between the two groups before and after treatment

Subdomain	Time point	Control group (n=47)	Combined group (n=47)	t values	*P*
Nasal symptoms	Baseline	8.124±1.352	8.057±1.284	0.258	0.797
	1 month	5.813±0.962	4.732±0.843	2.842	0.081
	3 months	3.521±0.712	2.841±0.624	4.112	<0.010
	6 months	3.221±0.682	2.483±0.551	4.863	<0.010
	9 months	2.942±0.623	2.112±0.481	5.182	<0.010
	12 months	2.312±0.582	1.912±0.412	4.962	<0.010
	18 months	2.831±0.593	1.782±0.412	6.102	<0.010
Otologic/Facial	Baseline	6.932±1.122	6.883±1.084	0.218	0.828
	1 month	4.732±0.862	4.621±0.812	0.683	0.497
	3 months	3.421±0.742	3.352±0.702	0.472	0.639
	6 months	1.983±0.483	1.632±0.422	3.112	0.022
	9 months	1.872±0.462	1.553±0.392	2.842	0.085
	12 months	1.581±0.392	1.243±0.312	3.472	0.013
	18 months	1.632±0.412	1.482±0.352	2.512	0.062
Sleep dysfunction	Baseline	12.843±2.152	12.772±2.083	0.162	0.872
	1 month	7.832±1.342	6.121±1.182	3.782	0.007
	3 months	5.621±1.042	4.132±0.892	4.153	<0.010
	6 months	2.983±0.512	1.923±0.432	5.892	<0.010
	9 months	2.421±0.482	1.642±0.392	5.032	<0.010
	12 months	2.152±0.462	1.583±0.352	4.723	<0.010
	18 months	2.113±0.493	1.512±0.342	5.112	<0.010
Emotional impact	Baseline	14.832±2.843	14.782±2.763	0.088	0.930
	1 month	11.623±2.102	10.892±1.983	1.732	0.087
	3 months	8.942±1.583	8.123±1.472	1.982	0.061
	6 months	5.623±1.182	5.132±1.042	1.892	0.092
	9 months	4.281±0.962	3.211±0.782	3.782	0.012
	12 months	3.182±0.812	2.341±0.592	4.153	<0.010
	18 months	2.112±0.483	1.423±0.382	5.862	<0.010

in 4 (8.51%) patients in the control group and 1 (2.13%) patient in the combined group (P=0.203), while sinus ostium obstruction occurred in 3 (6.38%) patients in the control group, but no cases were reported in the combined group (P=0.081). The overall incidence of complications was 25.53% in the control group and 8.51% in the combined group (P=0.020). Regarding recurrence, the number of recurrent cases was significantly lower in the combined group, with 1 (2.13%) case compared to 4 (8.51%) cases in the control group (P=0.184) (**Table 7**).

Discussion

CRSwNP imposes a substantial burden on patients' quality of life [16-18], contributes to considerable healthcare costs [19-21]. Emerging evidence also suggests a potential association between CRSwNP and cognitive performance [22, 23], while the exact pathophysiological mechanisms remain incompletely understood. Current treatment strategies involve a combination of pharmacologic and surgical interventions to reduce disease burden and alleviate symptoms. Pharmacological treatments targeting systemic inflammation include, but are not limited to, steroid nasal sprays, oral steroids, saline rinses, and antibiotics [6, 24, 25]. However, their effects are suboptimal. Endoscopic sinus surgery (ESS) has become a widely adopted treatment modality for CRS in recent years. This procedure utilizes nasal endoscopy and specialized surgical instruments, often guided by imaging and navigation

Table 6. Comparison of nasal function between the two groups before and after treatment

		Control group (n=47)	Combined group (n=47)	t values	*P*
Saccharin clearance time/min	Baseline	34.301±1.912	36.624±2.463	0.510	0.611
	1 m	30.272±1.613	31.623±1.792	3.764	<0.011
	3 m	28.506±1.622	29.450±1.618	0.740	0.230
	6 m	25.582±1.624	26.031±1.370	1.480	0.143
	9 m	24.750±1.497	25.672±1.243	1.980	0.050
	12 m	21.072±1.171	20.600±0.914	2.170	0.033
	18 m	20.230±1.209	22.006±1.332	4.520	<0.010
Olfactory function scores (mm/min)	Baseline	3.361±0.313	3.374±0.380	0.740	0.230
	1 m	3.822±0.274	3.954±0.374	1.982	0.051
	3 m	4.203±0.291	4.878±0.403	0.940	0.350
	6 m	4.264±0.304	4.561±0.341	4.520	<0.010
	9 m	4.406±0.322	4.877±0.298	1.550	0.125
	12 m	4.812±0.334	5.210±0.360	5.672	<0.011
	18 m	4.804±0.359	4.982±0.193	4.220	0.180
Mucociliary clearance rate %	Baseline	40.103±5.814	39.991±6.533	0.090	0.926
	1 m	42.833±5.854	41.271±6.462	1.204	0.232
	3 m	44.006±5.307	45.450±5.144	0.800	0.310
	6 m	45.841±6.590	42.732±6.293	2.364	0.021
	9 m	46.508±4.407	47.321±5.411	4.450	0.110
	12 m	48.822±7.224	44.680±6.180	2.962	0.004
	18 m	49.235±6.108	49.933±5.923	2.100	0.180

Table 7. Comparison of complication incidence and recurrence rate between the two groups

	Control group (n=47)	Combination group (n=47)	X^2 values/Fisher	*P*
Epistaxis, n (%)	5 (10.64%)	3 (6.38%)	0.592	0.440
Nasal cavity adhesion, n (%)	4 (8.51%)	1 (2.13%)		0.203
Sinus ostium obstruction, n (%)	3 (6.38%)	0		0.081
Total complications, n (%)	12 (25.53%)	4 (8.51%)	5.380	0.020
Recurrence, n (%)	4 (8.51%)	1 (2.13%)		0.184

systems, to access the nasal cavity, paranasal sinuses, naso-orbital region, and the skull base via a transnasal approach [26-29].

GAMBA et al. [30] found that ESS effectively improves nasal drainage and ventilation by removing obstructive and diseased tissue. Their study reported significant postoperative increases in NMCA and NCV, along with reductions in DCAN, indicating enhanced nasal airflow and ventilation following surgery. Despite these functional improvements, the anatomical proximity of the surgical field to critical structures such as the skull base, orbit, and major blood vessels and nerves increases surgical risks. Previous studies have reported complication rates for ESS ranging from 6.5%-24.4% [31]. In this study, the complication rate was 25.53% and the recurrence rate was 8.51% after endoscopic sinus surgery for CRSwNP, suggesting that endoscopic sinus surgery alone for CRSwNP could not achieve satisfactory results.

The present study demonstrated that the addition of budesonide aerosol following endoscopic sinus surgery reduced the incidence of postoperative complications to 8.51%, and lowered the recurrence rate to 2.13%. These findings suggest that, compared with surgery alone, glucocorticoid infiltration therapy effectively reduces both complications and recurrence rates, offering clear therapeutic advantages in the treatment of CRSwNP.

Our results also showed that the Lund-Mackay, SNOT-22, and Lund-Kennedy scores in patients receiving postoperative budesonide aerosol were significantly lower than those treated with surgery alone, indicating greater symptom relief and faster postoperative recovery. Notably, subdomain analysis of SNOT-22 revealed distinct temporal patterns of symptom resolution. The most rapid and substantial improvements were observed in nasal symptoms (e.g., obstruction, rhinorrhea) and sleep dysfunction, aligning with objective improvements in nasal ventilation parameters and endoscopic findings. This rapid relief likely stems from corticosteroid-mediated reduction in mucosal edema and inflammation, restoring nasal airflow within weeks [32]. Additionally, emotional symptoms (e.g., frustration, impaired concentration) showed delayed but progressive improvement in the combination group, with significant divergence from control group at postoperative 9 months. This mirrors findings by Erskine et al., who identified persistent inflammation as a key driver of mood disturbance in CRSwNP patients [33]. The delayed resolution in emotional burden underscores that psychological recovery is closely linked to sustained control of local inflammation, underscoring the holistic benefits of combined therapy.

Glucocorticoids are steroid hormones secreted by the adrenal cortex [34-37], known for their regulatory roles in glucose, lipid, and protein metabolism, as well as their potent anti-inflammatory effects through broad cytokine suppression. Our biomarker analysis extends previous reports by demonstrating that adjunct corticosteroid therapy specifically modulates key mediators of type-2 inflammation. Notably, IL-5 reduction at 12 months was greater in the combination group compared to surgery alone, and IL-5 levels showed the most pronounced suppression. The total IgE level of the combination group and the control group decreased continuously, and the decrease of the combined group was greater than that of the control group. These findings mechanistically explain SONG et al.'s observation [38] of glucocorticoid-mediated IL-33 suppression and broader inhibition on the IL-4/IL-5/IL-13 signaling axis. Critically, the progressive divergence in biomarker trajectories from 6-18 months, particularly in tissue eosinophils and IgE, confirms corticosteroids continuously modulate local inflammation rather than providing transient symptom relief. This sustained immunomodulation translates directly to clinical benefits: suppressed mucosal edema correlated significantly with Lund-Kennedy scores, while the progressive IgE normalization in combination group may explain their reduced recurrence risk at 18 months.

The present research found that nasal mucociliary clearance function improved significantly in the combination group, with enhanced olfactory function observed at 6 and 12 months after therapy. These improvements are likely attributable to the anti-inflammatory effects of glucocorticoids, which suppress the release of inflammatory factors. While radical surgery can reduce recurrence rates and relieve symptoms, widening of the sinuses and olfactory regions may also contribute to delayed recurrence by improving drainage and ventilation [3]. However, intraoperative procedures, such as manipulation of surgical instruments and compression hemostasis using packing materials, may induce secondary injury to the nasal mucosa, resulting in swelling or even erosion of the surgical cavity mucosa. This is not conducive to the recovery of nasal function after surgery and increases the risk of CRSwNP recurrence. In this study, mometasone furoate was administered both preoperatively and postoperatively. It directly acts on the nasal mucosa, alleviating symptoms such as runny nose, nasal congestion, and hyposmia before surgery. Postoperatively, it significantly inhibits inflammatory cell recruitment and aggregation within the surgical cavity, while suppressing the synthesis and secretion of inflammatory mediators. Furthermore, it stabilizes endothelial cells, smooth muscle cells, and lysosomal membranes, thereby reducing mucosal edema and epithelial damage in the nasal cavity and paranasal sinuses. These effects collectively contribute to the restoration of ciliary system function, reduction in polyp burden, and improvements in both airway resistance and olfactory function. In addition, tissue and peripheral blood eosinophil percentages were negatively correlated with time to recurrence, which is consistent with the report by Tosun et al. [39] that polyp recurrence was associated with the eosinophilic content in polyps. Studies have shown that eosinophilic inflammation is predictive of a favorable response to glucocor-

ticosteroid therapy [40-42], supporting the rationale for sustained systemic or topical corticosteroid use in managing CRSwNP. However, in some patients, eosinophilic inflammation may exceed the therapeutic capacity of corticosteroid treatment [43-47]. In these cases, patients with the highest inflammatory burden tend to receive the most glucorticosteroids yet still experience suboptimal outcomes and higher recurrence rates.

This study has several limitations. First, the sample size was relatively small, partly due to difficulties in maintaining long-term follow-up for some patients. Second, the follow-up period was limited to 18 months, which may have led to underestimation of rare complications and long-term recurrence rates. Additionally, this study did not assess patient adherence to postoperative corticosteroid therapy, which may influence clinical outcomes. Furthermore, inflammatory endotypes (e.g., eosinophilic dominance) were not stratified, potentially limiting the generalizability of the findings. Future studies should address these limitations and incorporate molecular and immunological biomarkers to guide individualized treatment strategies and better characterize differential therapeutic responses.

Conclusion

In summary, corticosteroids combined with ESS demonstrate superior clinical efficacy over surgery alone in CRSwNP management. The combined therapy enhances symptom control (particularly through earlier improvements in nasal and sleep domains), promotes nasal function recovery and mucociliary clearance, reduces postoperative complications and recurrence, and achieves sustained suppression of type-2 inflammatory biomarkers. These findings support the use of integrated medical-surgical strategies as an optimized approach to address the multifactorial burden of CRSwNP.

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Disclosure of conflict of interest

None.

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