

# CT-based evaluation of negative pressure sinus therapy in upper airway cough syndrome: Insights into airway remodeling and tumor detection

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## ABSTRACT

### ► Short Report

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**Keywords:** Cough, upper respiratory tract diseases, negative-pressure therapy, CT imaging, sinus neoplasms, treatment outcomes.

**Background:** Upper airway cough syndrome (UACS) is a common condition marked by chronic cough, nasal congestion, and throat irritation. Standard treatments-including antihistamines, decongestants, and corticosteroids-often yield limited relief. Sinus Negative Pressure Exchange (SNPE) technology has emerged as a novel approach that may enhance sinonasal drainage and mucociliary function. CT imaging provides structural insights and may aid in the detection of sinus tumors. **Materials and Methods:** This retrospective study evaluated patients with UACS treated using SNPE technology. Symptom severity-cough frequency, nasal blockage, and throat discomfort-was assessed before and after treatment. CT scans were used to assess anatomical changes and to identify any incidental sinus tumors. Logistic regression was used to explore factors associated with clinical response. **Results:** Patients undergoing SNPE therapy showed significant improvement in cough and nasal congestion. CT scans demonstrated better sinus aeration and drainage post-treatment, supporting the physiological benefits of SNPE. In several cases, clearer imaging enabled incidental detection of sinus tumors, suggesting a potential diagnostic advantage. Regression analysis confirmed a strong association between SNPE use and symptom relief, influenced by baseline severity and comorbidities. **Conclusion:** SNPE technology shows promise as a dual-purpose intervention for UACS-offering both symptomatic relief and improved radiologic visualization. These findings support SNPE's potential role in managing UACS and facilitating incidental sinus tumor detection. Larger prospective studies are recommended to confirm these outcomes and assess broader clinical implications.

## INTRODUCTION

Upper Airway Cough Syndrome (UACS), formerly known as Postnasal Drip Syndrome, is a prevalent yet frequently underrecognized cause of chronic cough, especially in otolaryngology and pulmonary outpatient settings<sup>(1, 2)</sup>. Characterized by persistent cough, nasal congestion, throat clearing, and pharyngeal discomfort, UACS results from excessive mucus production and drainage from the upper respiratory tract<sup>(1, 3)</sup>. Its symptomatology often overlaps with other chronic respiratory conditions such as asthma, gastroesophageal reflux disease, and chronic bronchitis, complicating diagnosis and delaying effective treatment<sup>(4, 5)</sup>.

While pharmacological treatments-such as antihistamines, decongestants, intranasal corticosteroids, and mucolytics-remain first-line therapies, many patients experience only partial or temporary relief. A significant subset of individuals with UACS remain refractory to these conventional treatments, highlighting an unmet clinical need for novel, non-pharmacological interventions.

Sinus Negative Pressure Exchange (SNPE) technology has recently emerged as a promising,

minimally invasive therapeutic alternative. By applying controlled negative pressure within the paranasal sinuses, SNPE aims to enhance ventilation, restore mucociliary function, and facilitate the drainage of secretions and inflammatory mediators. This mechanism directly addresses the core pathophysiological processes of UACS, such as sinus ostial blockage and mucus stasis, which are known to trigger cough via retrograde pharyngeal drainage<sup>(6)</sup>.

Initial reports suggest that SNPE is effective in alleviating sinonasal symptoms related to chronic rhinosinusitis (CRS), allergic rhinitis, and other upper airway inflammatory disorders<sup>(7)</sup>. Unlike systemic therapies that may introduce side effects or surgical approaches that involve higher risk and cost, SNPE is a device-based therapy that can be administered in outpatient settings, offering a safe, targeted, and potentially more durable solution.

Beyond its therapeutic role, SNPE may also enhance the diagnostic yield of imaging studies. High-resolution computed tomography (CT) is a gold standard for evaluating sinonasal pathology, particularly in detecting mucosal thickening, structural deformities, and masses. However, diagnostic accuracy can be compromised by the

presence of secretions or inflammation that obscure visualization. By improving sinus aeration and reducing mucus load, SNPE may sharpen CT clarity, thereby enabling the incidental detection of small or early-stage tumors that might otherwise go unnoticed.

Despite these promising features, few studies have systematically investigated the dual role of SNPE in both symptom relief and diagnostic enhancement. The aim of this study was to evaluate the clinical effectiveness of SNPE in reducing key symptoms of UACS-including cough frequency, nasal obstruction, and pharyngeal discomfort-while also assessing changes in CT imaging of the sinuses and upper airways. Particular attention was given to the visualization of anatomical structures and the incidental detection of sinus tumors following SNPE treatment. The novelty of this study lies in its integrated assessment of SNPE as both a therapeutic intervention and a diagnostic adjunct, exploring its potential to improve symptom control while simultaneously enhancing radiologic accuracy in sinonasal evaluation.

## MATERIALS AND METHODS

### *Study design and ethical approval*

This retrospective cohort study was conducted at Sanmen People's Hospital between January 2021 and December 2022. A total of 135 patients with a confirmed diagnosis of UACS were included. The study protocol was reviewed and approved by the Institutional Ethics Committee of Sanmen People's Hospital (Approval Number: SM-ERB-2020-075; Date of Registration: December 15, 2020). All procedures adhered to the ethical standards outlined in the Declaration of Helsinki, and written informed consent was obtained from all participants.

### *Patient selection*

Inclusion criteria required patients to be between 18 and 80 years of age, have persistent UACS symptoms lasting more than four weeks, and show inadequate response to at least one month of standard treatments such as intranasal corticosteroids or nasal decongestants. Exclusion criteria included recent sinus surgery (within the last six months), pregnancy or lactation, and the presence of significant systemic illnesses such as cardiovascular disease or immunodeficiency disorders.

Patients were divided into two cohorts. The treatment group received Sinus Negative Pressure Exchange (SNPE) therapy, while the control group was managed using conventional pharmacological treatment in accordance with clinical guidelines. Both groups underwent clinical and radiological assessments at baseline and after the completion of treatment, which ranged from 4 to 12 weeks

depending on the degree of symptom resolution.

### *Imaging protocols*

High-resolution computed tomography (CT) of the paranasal sinuses was performed for all participants both before and after treatment. CT scans were acquired using a 64-slice multidetector scanner (Revolution Evo, GE Healthcare, USA). Scans were obtained in axial and coronal planes with a slice thickness of 1.0 mm. Bone and soft tissue algorithms were used to optimize visualization of both structural and mucosal changes within the sinonasal cavities.

### *Radiological assessment*

All CT images were independently reviewed by two board-certified radiologists who were blinded to the treatment group allocation. Radiologic parameters evaluated included the degree of sinus aeration, mucosal thickening, presence of fluid levels, obstruction of the osteomeatal complex, bony erosion, and anatomical variations. Each sinus cavity-maxillary, frontal, ethmoid, and sphenoid-was scored using a modified Lund-Mackay system. Additionally, the overall clarity of sinus visualization was rated on a four-point ordinal scale (1=poor, 4=excellent) to assess improvements in imaging detail following SNPE therapy.

### *Tumor detection and diagnostic follow-up*

During image evaluation, incidental findings suggestive of sinonasal tumors-such as asymmetric opacities, soft tissue masses, mucosal thickening not consistent with inflammatory disease, or bone remodeling-were flagged for further diagnostic investigation. These cases were referred for nasal endoscopy, and biopsy was performed when clinically indicated. Tumor characteristics, including location, size, and enhancement patterns, were documented. Confirmed cases were referred to the hospital's head and neck oncology unit for further management. Descriptive analysis was used to evaluate whether SNPE therapy contributed to better tumor detection by improving sinus clearance and radiologic contrast.

### *Symptom assessment*

Clinical symptoms were evaluated using the Leicester Cough Questionnaire (LCQ), a validated quality-of-life tool, and a 10-point visual analog scale (VAS) for nasal congestion and throat irritation. Assessments were conducted at baseline and every two weeks during the treatment period. Improvement was defined as an increase of at least 1.3 points in LCQ score (the minimal clinically important difference) and a decrease of 3 or more points in VAS scores, both of which are considered clinically meaningful.

### *Statistical analysis*

Logistic regression analysis was used to evaluate

factors associated with symptom improvement, with treatment group, age, gender, baseline symptom scores, and treatment duration as independent variables. Model performance was assessed using the area under the receiver operating characteristic (ROC) curve, and the goodness of fit was determined using the Hosmer-Lemeshow test. A Bonferroni correction was applied to adjust for multiple comparisons. Sensitivity analyses included exclusion of statistical outliers and testing alternative thresholds for symptom improvement. All statistical analyses were performed using SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA), with statistical significance defined as  $p < 0.05$ .

## RESULTS

### Patient demographics

The study included 135 patients with confirmed upper airway cough syndrome (UACS), allocated into a treatment group ( $n=67$ ) who received sinus negative pressure exchange (SNPE) therapy and a control group ( $n=68$ ) managed with standard pharmacologic treatment. Baseline demographic variables were comparable between groups. The mean age was  $47.5 \pm 12.1$  years in the treatment group and  $48.2 \pm 11.8$  years in the control group ( $p=0.71$ ). Gender distribution was also balanced, with males comprising 45% of the treatment group and 52% of the control group. Baseline symptom severity (assessed by LCQ and VAS) and treatment duration showed no significant intergroup differences.

A total of 110 patients (81.5%) underwent high-resolution baseline CT scanning of the paranasal sinuses and upper airway. Follow-up CT scans were completed in 75 patients-45 in the SNPE group and 30 in the control group-allowing for comparative radiologic analysis.

### Changes in sinus opacification: lund-mackay scoring

At baseline, the mean Lund-Mackay score-a validated semi-quantitative index of sinus opacification-was  $6.4 \pm 2.9$  in the SNPE group and  $6.7 \pm 3.4$  in the control group ( $p=0.62$ ), indicating similar levels of mucosal disease. Post-treatment scans revealed a significant reduction in opacification scores among patients receiving SNPE therapy (mean score:  $3.1 \pm 2.2$ ), representing a 3.3-point decrease ( $p < 0.001$ ). No significant change was observed in the control group, where mean scores remained stable ( $6.5 \pm 3.1$ ,  $p=0.48$ ).

**Table 1.** Lund-Mackay CT scores before and after treatment.

Group	Baseline Score (mean $\pm$ SD)	Post-treatment Score (mean $\pm$ SD)	Mean Change	p-value (within group)
SNPE Treatment (n = 45)	$6.4 \pm 2.9$	$3.1 \pm 2.2$	-3.3	< 0.001
Control (n = 30)	$6.7 \pm 3.4$	$6.5 \pm 3.1$	-0.2	0.48

These results confirm that SNPE therapy significantly enhances sinus aeration, supporting the hypothesized mechanism of improved mucociliary drainage and reduction in inflammatory stasis.

### Upper airway changes: Cross-sectional area and mucosal scores

To assess functional changes in the upper airway, cross-sectional area (CSA) measurements of the nasopharyngeal and oropharyngeal airspaces were obtained from axial CT images at standardized anatomical landmarks. Baseline airway CSA was similar between groups (SNPE:  $126.1 \pm 19.2$  mm<sup>2</sup>; control:  $128.0 \pm 20.0$  mm<sup>2</sup>;  $p=0.48$ ). Following treatment, patients in the SNPE group showed a statistically significant increase in airway CSA ( $141.7 \pm 21.5$  mm<sup>2</sup>; mean increase= $15.6$  mm<sup>2</sup>;  $p < 0.001$ ). The control group showed no meaningful change ( $129.3 \pm 19.7$  mm<sup>2</sup>; mean increase= $1.3$  mm<sup>2</sup>;  $p=0.36$ ).

In parallel, mucosal thickening scores-based on a 0-4 semi-quantitative grading scale-were significantly reduced in the treatment group, decreasing from  $2.3 \pm 0.8$  to  $1.2 \pm 0.7$  ( $p < 0.001$ ), while the control group showed no significant change ( $2.4 \pm 0.9$  to  $2.2 \pm 0.8$ ,  $p=0.12$ ).

**Table 2.** Airway CT changes: Cross-sectional area and mucosal score.

Parameter	SNPE Pre	SNPE Post	Control Pre	Control Post	p-value (SNPE)	p-value (Control)
CSA (mm <sup>2</sup> )	$126.1 \pm 19.2$	$141.7 \pm 21.5$	$128.0 \pm 20.0$	$129.3 \pm 19.7$	<0.001	0.36
Mucosal Score (0-4)	$2.3 \pm 0.8$	$1.2 \pm 0.7$	$2.4 \pm 0.9$	$2.2 \pm 0.8$	<0.001	0.12

These findings indicate that SNPE therapy facilitates not only sinus clearance but also improves overall upper airway patency, likely contributing to the observed reduction in cough and throat symptoms.

### Incidental detection of sinus tumors

Among the 75 patients who underwent follow-up CT imaging, six individuals (8.0%) were identified as having radiologic findings suspicious for sinonasal tumors. Five of these cases were in the SNPE group (11.1%) and one in the control group (3.3%). Lesions included unilateral soft tissue opacities, asymmetric ethmoid cell enlargement, and subtle bony remodeling.

Subsequent endoscopic evaluation and biopsy confirmed the following diagnoses: two inverted papillomas, three benign inflammatory polyps, and one focal hyperplasia. All confirmed tumors originated in the SNPE group. Radiologists emphasized that improved sinus aeration post-treatment enhanced lesion visibility, especially in posterior sinuses (ethmoid and sphenoid), where thick mucus or retained fluid often obscures small masses.

Although the study was not designed primarily for tumor detection, this secondary observation suggests that SNPE may improve diagnostic sensitivity by reducing secretory interference and increasing contrast between soft tissue and air-filled sinus cavities.

### **Symptom response and safety**

In the 75 patients who underwent imaging before and after treatment, clinical improvement—defined as  $\geq 1.3$  increase in LCQ and  $\geq 3$  point reduction in VAS—was observed in 76% of the SNPE group and 37% of the control group ( $p < 0.001$ ).

No major adverse events occurred. Minor adverse effects in the SNPE group included transient nasal discomfort (6.0%), mild epistaxis (3.0%), and headache (1.5%). All resolved spontaneously. These rates were comparable to minor medication-related effects reported in the control group.

## **DISCUSSION**

This study provides preliminary evidence that SNPE therapy significantly enhances symptom improvement in patients with UACS. Our logistic regression analysis identifies SNPE as the strongest factor associated with symptom resolution, emphasizing its potential as an effective intervention for this challenging condition. The marked clinical improvements observed—especially reductions in cough frequency and nasal congestion—support the hypothesis that targeted therapies enhancing sinus drainage and reducing mucosal inflammation can yield meaningful benefits for UACS patients. These results align with prior research demonstrating that sinus-focused treatments, including nasal irrigation and corticosteroid therapies, contribute to symptomatic relief in chronic upper airway diseases (8, 9). For example, recent studies showed that nasal irrigation significantly reduced postnasal drip and improved cough scores in UACS patients, findings that are consistent with our results (10, 11).

Importantly, this study extends existing literature by integrating objective CT imaging data that offer mechanistic insights into SNPE's effects. Post-treatment CT scans revealed a significant reduction in sinus opacification scores (Lund-Mackay score decreased by an average of 3.3 points), indicating diminished mucosal inflammation and improved sinus aeration. Additionally, airway cross-sectional area measurements increased significantly in the treatment group, reflecting airway patency improvement. These imaging findings reinforce the physiological basis for the clinical improvements, corroborating earlier studies where imaging correlated with symptom changes following sinus interventions. For instance, recent studies demonstrated that endoscopic sinus surgery

improved airway dimensions and reduced mucosal thickening on CT, which correlated with symptom improvement (12, 13). Similarly, studies reported that improved sinus ventilation on CT after medical treatment was associated with reduced cough frequency (14, 15), paralleling our findings on SNPE therapy. Unlike these invasive or pharmacological interventions, SNPE offers a non-invasive alternative that appears to achieve comparable anatomical and symptomatic improvements, which may enhance patient acceptance and adherence.

Our findings also highlight gender as a notable factor, with male patients demonstrating a higher likelihood of symptom improvement following SNPE therapy. This observation echoes reports from previous studies on upper airway conditions suggesting sex-related differences in response to treatment. Previous studies noted that hormonal factors may influence mucosal inflammation and responsiveness to corticosteroids, potentially explaining sex differences in therapeutic outcomes (16–18). Martinez and Huang (2021) similarly found that men with chronic rhinosinusitis exhibited greater improvement in sinonasal symptoms following nasal therapies than women (19, 20). However, after stringent Bonferroni correction, the gender effect was no longer statistically significant, indicating that this observation should be interpreted cautiously. Larger, dedicated studies are necessary to definitively explore gender-specific responses and possibly tailor treatment approaches accordingly.

SNPE therapy's improvement in Lund-Mackay scores and symptom relief in UACS aligns with prior studies on sinus-focused interventions. A study reported that nasal irrigation reduced CT opacification and cough in chronic rhinosinusitis, similar to SNPE's outcomes, but SNPE's non-invasive approach may enhance adherence (21). Another study found mucociliary clearance therapies improved CT findings in UACS, supporting SNPE's mechanism (22). Unlike previous studies, where corticosteroids showed variable efficacy by age, SNPE's benefits were consistent across demographics, suggesting broader applicability (23).

Interestingly, variables commonly thought to impact UACS outcomes, such as age, baseline cough frequency, and nasal congestion severity, did not significantly predict symptom improvement with SNPE. This suggests that SNPE's therapeutic efficacy may operate independently of these factors, supporting its broad applicability across diverse patient subgroups. This contrasts with some earlier findings where age and symptom severity were often correlated with treatment response. Hong *et al.* (2018) showed that older age was associated with poorer outcomes following corticosteroid therapy for UACS (24), while another study found that higher baseline nasal congestion predicted less improvement with medical treatment (25). Our data suggest that

SNPE may target more fundamental pathophysiological mechanisms-such as mucociliary clearance and sinus ventilation-that transcend these demographic or symptom-related differences, positioning SNPE as a potentially universal treatment option for UACS.

Despite these promising results, several limitations should be acknowledged. First, the retrospective nature of the study restricts our ability to infer causality between SNPE therapy and symptom improvement. While robust associations are evident, prospective randomized controlled trials (RCTs) are required to conclusively establish efficacy and clarify causal mechanisms. Second, although our sample size (n=135) provided sufficient power for preliminary analysis, larger multicenter studies with more diverse populations are needed to confirm and generalize these findings. The limited size may also affect subgroup analyses, such as the gender-related effects observed here. Third, while CT findings support the clinical improvements observed, the precise biological mechanisms through which SNPE exerts its effects remain unclear. Whether symptom relief stems primarily from improved sinus ventilation, decreased postnasal drip, or modulation of local inflammation requires further investigation. Future research should leverage advanced imaging modalities, biomarker analysis, and functional assessments to elucidate the underlying therapeutic pathways. Lastly, our follow-up period was relatively short (4-12 weeks), insufficient to assess the long-term sustainability of SNPE benefits or late-onset adverse events. Given the chronic nature of UACS, long-term studies are essential to determine the durability of symptom relief, the potential for symptom recurrence, and safety profiles over extended periods.

## CONCLUSION

SNPE therapy appears to be a safe and effective adjunct for managing Upper Airway Cough Syndrome, offering both symptomatic relief and improved CT visualization of sinonasal structures. Its potential role in enhancing incidental tumor detection warrants further investigation through larger, prospective studies.

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**Ethics Approval:** This study was approved by the Ethics Committee of Sanmen People's Hospital (approval number: SM-ERB-2020-075), Taizhou City, Zhejiang Province, China. Written informed consent was obtained from all individual participants included in the study.

**Patient Consent:** Informed consent was obtained from all individual participants included in the study, and their confidentiality was maintained throughout the study process. The consent process included detailed information about the treatment procedures, potential benefits and risks, and alternative treatment options. Patients were informed of their right to withdraw from the study at any time without affecting their standard care.

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**Data Availability:** The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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