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ORIGINAL ARTICLE

Temperature-controlled radiofrequency device treatment of the nasal valve for nasal airway obstruction: A randomized controlled trial

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Background: Nasal valve collapse is one of several causes of nasal obstruction. The safety and efficacy of a temperature-controlled radiofrequency (RF) device for the treatment of the nasal valve for nasal airway obstruction (NAO) has been established in single-arm studies. The objective of this trial was to compare active device treatment against a sham procedure (control).

Methods: In a prospective, multicenter, single-blinded, randomized controlled trial (RCT), patients were assigned to bilateral temperature-controlled RF treatment of the nasal valve (n = 77) or a sham procedure (n = 41), in which no RF energy was transferred to the device/treatment area. The device was applied to the mucosa over the lower lateral cartilage on the lateral nasal wall. The primary endpoint was responder rate at 3 months, defined as a ≥20% reduction in Nasal Obstruction Symptom Evaluation (NOSE)-scale score or ≥1 reduction in clinical severity category.

Results: At baseline, patients had a mean NOSE-scale score of 76.7 (95% confidence interval [CI], 73.8 to 79.5) and 78.8 (95% CI, 74.2 to 83.3) ($p = 0.424$) in the active treatment and sham-control arms, respectively. At 3 months, the responder rate was significantly higher in the active treatment arm (88.3% [95% CI, 79.2%-93.7%] vs 42.5% [95% CI, 28.5%-57.8%]; $p < 0.001$). The active treatment arm had a significantly greater decrease in NOSE-scale score (mean, −42.3 [95% CI, −47.6 to −37.1] vs −16.8 [95% CI, −26.3 to −7.2]; $p < 0.001$). Three adverse events at least possibly related to the device and/or procedure were reported, and all resolved.

Conclusion: This RCT shows temperature-controlled RF treatment of the nasal valve is safe and effective in reducing symptoms of NAO in short-term follow-up.

KEYWORDS
nasal valve, nasal valve collapse, nasal obstruction, radiofrequency, nasal congestion, NOSE scale, randomized controlled trial

1 | INTRODUCTION

Nasal valve collapse is recognized as a primary cause of nasal obstruction.[1–3] However, it is also underdiagnosed and often left untreated. Physical nasal exam is habitual, and often omits simple lateral wall observations during breathing or bypasses valve collapse as nasal specula are inserted in pursuit of posterior visualization. Patients with nasal airway obstruction (NAO) and nasal valve collapse suffer from a variety of symptoms that significantly lower their quality of life, including nasal congestion, headache, sleep disturbance, daytime sleepiness, and snoring.[4,5] Treatment options for nasal valve collapse include external/internal nasal dilators and surgical functional rhinoplasty and/or nasal valve repair.[6,7] New graft techniques and technologies have been introduced to treat dynamic nasal valve collapse.[8,9] One reason for the undertreatment of nasal valve collapse may be the scarcity of minimally invasive treatment options as an alternative to surgical repair.

Radiofrequency (RF)-induced heating has been shown to induce tissue tightening and contraction through effects on the collagen fiber network of the tissue. These effects are both acute, through the immediate contraction of existing collagen proteins, and longer term, through the induction of the production of new collagen.[10,11] The safety and efficacy of a minimally invasive temperature-controlled RF device designed to cause these tissue tightening effects within the submucosal layer of the lateral nasal wall, the Vivaer Stylus (Aerin Medical, Sunnyvale, CA), for the treatment of nasal valve collapse and NAO has been established in single-arm studies and demonstrated that early 3-month improvements were durable through 2-year follow-up.[12,13] The objective of this study was to provide higher level evidence to determine the safety and efficacy of the Vivaer Stylus in a randomized controlled trial (RCT) with a sham procedure as the control arm. In this report we detail the primary endpoint at 3-month follow-up.

2 | SUBJECTS AND METHODS

A prospective, single-blinded (patient), randomized sham-controlled trial with enrollment at 16 centers in the United States was conducted between August and December 2020. The Western Institutional Review Board (IRB) (20201804) approved the trial at all enrolling centers except Eastern Virginia Medical School (EVMS), where the trial was approved by the EVMS IRB (20-09-FB-0189). The trial was registered at clinicaltrials.gov (NCT04549545). All site principal investigators were board-certified otolaryngologists.

The design was a superiority trial with crossover available to eligible sham-control arm patients after 3-month follow-up, and these data will be available for future publications. The trial will continue follow-up through 2 years. A complete list of eligibility criteria is available in the Supporting Information. Key inclusion criteria were: age 18 to 85 years; seeking treatment for nasal obstruction; a baseline Nasal Obstruction Symptom Evaluation (NOSE) scale score ≥55, nasal valve collapse as the primary or a significant contributor to the nasal obstruction; a positive response to a temporary nasal dilation measure, such as the modified Cottle maneuver; and patient dissatisfaction with medical management. However, no standard medication regimen before inclusion or intervention was dictated by the protocol. Key exclusion criteria were: previous surgery of the lateral nasal wall; a severe case of septal deviation; turbinate hypertrophy; polyps; or ptotic nose tip believed to be the primary contributor to the nasal obstruction symptoms and warranting surgical intervention. Patients gave written informed consent prior to enrollment.

Patients were randomized to either the active treatment arm or the control arm (sham procedure) via a web-based database. A 2:1 site-stratified block randomization was employed. Identical patient preparation, including administration of topical anesthesia and anesthetic by injection, was used in both arms, with the anesthesia regimen according to investigator preference. A representative anesthesia regimen was to apply tetracaine-saturated pledgets to the mucosal surface of treatment area and waiting approximately 10 minutes for sufficient numbing of the mucosa. This was immediately followed by injection of lidocaine 2% (with epinephrine 1:200,000) into the treatment area. Patients were blindfolded during the procedure. After administration of topical and local anesthesia, active treatment arm patients were treated bilaterally with the Vivaer Stylus on up to 4 non-overlapping areas of the nasal mucosa at the junction of the upper and lower lateral cartilage on the lateral nasal wall (Figure 1). Treatment settings were: temperature, 60°C; power, 4 watts; treatment time, 18 seconds; and cooling time, 12 seconds. For the sham procedure, the stylus was applied in the same manner but without RF energy delivery, while audible tones mimicking activation of the Aerin Console (Aerin Medical, Sunnyvale, CA) were played. No repeat "touch-up" procedures during follow-up were allowed.

Assessments performed at applicable intervals included a physical and endoscopic nasal exam; NOSE-scale score (a validated outcome tool)[14,15]; a 100-mm ease-of-breathing visual analog scale (VAS), where 0 is no difficulty breathing and 100 is extreme difficulty breathing; and a 100-mm VAS for nasal pain,[16] where 0 is no pain and 100 is worst pain imaginable. Adverse events were recorded throughout.

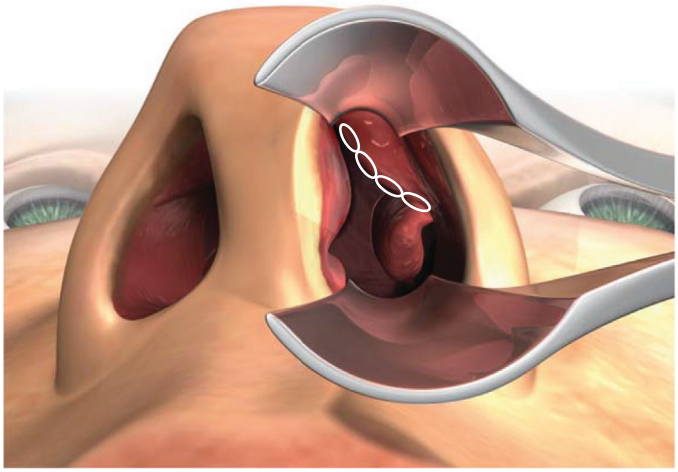

FIGURE 1 Patients were treated bilaterally with the stylus at up to 4 non-overlapping areas on the nasal mucosa at the junction of the upper and lower lateral cartilage of the lateral nasal wall, as indicated

The primary endpoint was the responder rate at 3 months, where a responder was defined as a ≥20% improvement (decrease) in NOSE-scale score or ≥1 NOSE-scale severity category improvement[15] from baseline. Secondary endpoints were the mean change in NOSE-scale score from baseline to 3 months and the frequency of device- and procedure-related serious adverse events through 3 months, where serious adverse events were defined in the protocol in accordance with ISO 14155 Clinical investigation of medical devices for human subjects—Good clinical practice.

Sample size estimation was based on comparison of 2 proportions using an exact test, assuming 80% responder rate in the active treatment arm, 50% in the sham-control arm, treatment allocation 2:1, significance level 0.05 (2-sided), and 80% power. This resulted in a minimum of 99 patients (66 active treatment group, 33 sham-control group). After adjustment to allow for unevaluable patients and a distribution across the sites, 120 was the enrollment target. Demographic and baseline characteristics of the active treatment and sham-control patients were compared using *t* tests for continuous data (after finding insufficient evidence of non-normality in the measures) and Fisher exact test for categorical measures. Mean NOSE-scale scores and 95% confidence intervals (CIs) were calculated at baseline and 3 months. The NOSE-scale score mean change was calculated as the mean of patients' follow-up visit score minus baseline score and compared by *t* test. A negative change indicates an improvement (decrease) in NOSE-scale score. NOSE-scale component score responses were summarized by assigning values of 0 to 4 to the rating categories and computing the mean (95% CI) at baseline and 3 months and compared by *t* test. The ease-of-breathing VAS score mean change was calculated as the mean of patients' follow-up visit score minus baseline score and compared by *t* test. The pain VAS data are reported as the median (interquartile range [IQR]) and were compared by Wilcoxon 2-sample test. Statistical analysis was performed using SAS/STAT version 14.1 (SAS Institute, Cary, NC).

3 | RESULTS

A total of 119 eligible patients were randomized. Figure 2 shows treatment assignment with 78 in the active treatment arm and 41 in the sham-control arm. One patient in the active treatment arm withdrew consent before treatment. One patient in the sham-control arm was lost to follow-up before the 3-month visit (primary endpoint). Therefore, a total of 117 patients (77 active treatment and 40 sham control) were included in the analysis of the 3-month primary endpoint. The baseline demographics and characteristics of the patients in each arm are shown in Table 1. At baseline, 96.1% and 97.5% ($p > 0.999$) had NAO for >1 year in the active treatment and sham-control arms, respectively. The remaining patients in each arm had NAO for 6 to 12 months. Mean baseline NOSE-scale scores in each arm were not significantly different (Tables 1 and 2).

Analysis of the primary endpoint demonstrated that the responder rate in the active treatment arm was significantly higher than in the sham-control arm (88.3% [95% CI, 79.2%-93.7%] vs 42.5% [95% CI, 28.5%-57.8%]; $p < 0.001$) (Figure 3). In addition, the mean change in NOSE-scale score was significantly greater at 3 months in the active treatment arm than in the sham-control arm (−42.3 [95% CI, −47.6 to −37.1] vs −16.8 [95% CI −26.3 to −7.2]; $p < 0.001$) (Table 2). This represents a 55.1% decrease in NOSE-scale score from baseline in the active treatment arm vs a 21.3% decrease in the sham-control arm.

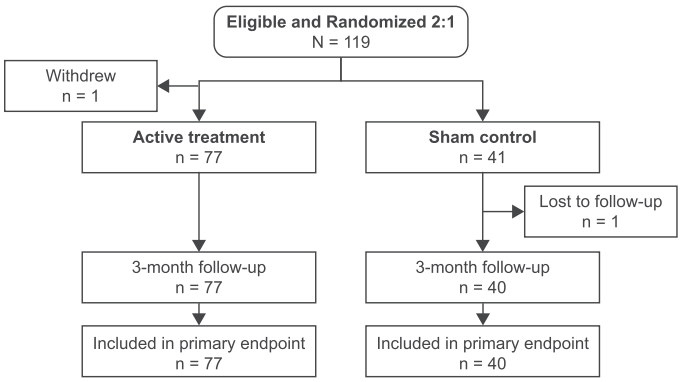

FIGURE 2 Enrollment, treatment arm allocations, and follow-up through 3 months postprocedure

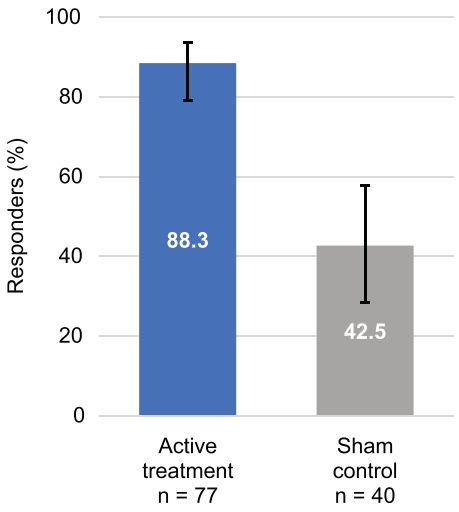

FIGURE 3 Primary endpoint at 3 months postprocedure: the proportion of patients with ≥20% improvement (decrease) in NOSE-scale score or ≥1 NOSE scale severity category improvement from baseline. Active treatment with a temperature-controlled RF energy device was superior to the sham-control procedure ($p < 0.001$). Bars indicate 95% confidence intervals

The mean change in ease-of-breathing VAS score from baseline through 3 months was significantly greater in the active treatment arm than in the sham-control arm (−31.4 [95% CI, −38.5 to −24.2] vs −16.1 [95% CI, −26.3 to −6.0]; $p = 0.015$) (Table 2).

At baseline, all patients were classified as having extreme or severe obstruction, based on the NOSE-scale severity classification system.[15] The distribution was split between extreme and severe categories in both arms at baseline (46.8% extreme, 53.2% severe in the active treatment arm, and 52.5% extreme, 47.5% severe in the sham-control arm; $p = 0.556$ based on a comparison of the distribution of the ordered classifications in each arm using a generalized linear model). At 3 months, there was a significantly larger shift toward lower severity classes in the active treatment arm than in the sham-control arm ($p < 0.001$, again based on a comparison of the distribution of the ordered classifications in each arm) (Figure 4). In particular, 36 patients (46.8%) in the active treatment arm moved from the extreme or severe category at baseline to the mild or no problem category at 3 months, compared with 7 patients (17.5%) who showed the same shift in the sham-control arm (Fisher exact test, $p = 0.002$).

The mean change from baseline through 3 months for all NOSE-scale component scores (ie, nasal congestion/stuffiness, nasal blockage/congestion, trouble breathing through the nose, trouble sleeping, and unable to get enough air through the nose during exercise or exertion) was significantly greater in the active treatment arm than in the sham-control arm ($p < 0.001$ for all components; 95% CIs are shown in Figure 5).

Because patients with both static and dynamic nasal valve collapse were treated in the trial, post-hoc subgroup analysis based on the mechanism of valve collapse was performed. The nasal valve collapse mechanism definitions were: dynamic, movement of the nasal valve during the Cottle Maneuver; static, no movement during the Cottle maneuver; and dynamic and static (combined in 1 nostril), movement and no movement of the nasal valve at different stages of the respiratory cycle. Patients in each arm were divided into 4 groups (bilateral dynamic collapse, bilateral static collapse, bilateral static and dynamic collapse, and complex). The complex group included patients with a different or mixed mechanism on each side; that is, dynamic on one side, static on the other; or static and dynamic on one side, static or dynamic on the other side. Table 3 shows the NOSE-scale score values and changes in each arm for each mechanism of nasal valve collapse. An analysis using a general linear model determined that the mechanism of nasal valve collapse did not significantly affect the NOSE-scale score ($p = 0.597$) in either arm. Furthermore, active treatment was highly significantly better than sham control ($p < 0.001$), regardless of nasal valve collapse mechanism. In summary, subgroup analysis showed active treatment was more effective than sham control regardless of the mechanism of nasal valve collapse assigned to

TABLE 1 Patients' demographics and baseline characteristics by treatment group*

	Active treatment arm, n = 77	Sham-control arm, n = 40	*p* value
Characteristic			
Male sex	30 (39.0)	15 (37.5)	>0.999
Age (years)	47.7 ± 12.4	50.0 ± 11.2	0.338
BMI (kg/m^2)	29.6 ± 6.3	28.9 ± 5.5	0.557
Race/ethnicity			
American Indian or Alaska Native	1 (1.3)	1 (2.5)	0.969
Asian	1 (1.3)	1 (2.5)	
Black or African American	4 (5.2)	2 (5.0)	
White	69 (89.6)	36 (90.0)	
Declined choices	2 (2.6)	0 (0.0)	
Medical history			
Nasal surgery[a]	22 (28.6)	13 (32.5)	0.675
Allergic rhinitis[b]	29 (37.7)	19 (47.5)	0.328
Nonallergic rhinitis[b]	11 (14.3)	6 (15.0)	>0.999
Sinus disease[c]	13 (16.9)	4 (10.0)	0.412
Obstructive sleep apnea	16 (20.8)	8 (20.0)	>0.999
Medical management only[d]	48 (62.3)	18 (45.0)	0.125
Mechanical nasal aids only[e]	3 (3.9)	0 (0.0)	
Medical and mechanical management	19 (24.7)	17 (42.5)	
No medical/mechanical management	7 (9.1)	5 (12.5)	
Scores			
NOSE-scale score	76.7 ± 12.6	78.8 ± 14.3	0.424
Ease-of-breathing VAS score[f]	59.3 ± 21.6	61.8 ± 18.4	0.533

*Continuous variables are presented as mean ± standard deviation. Categorical measures are presented as number (% of total). Characteristics of the arms were compared using *t* tests for continuous data (after finding insufficient evidence of non-normality in the measures) and Fisher exact test for categorical measures.
[a]Includes inferior/middle turbinate reduction/excision, polyp removal, septoplasty, rhinoplasty, sinuplasty, and functional endoscopic sinus surgery. Some patients may have undergone multiple procedures.
[b]Based on patient or provider knowledge, with no tests performed as part of the study.
[c]Combination of acute sinusitis or chronic rhinosinusitis.
[d]Includes medications, saline, and vapor rub.
[e]Includes nasal strips, cones, and nasal pillow.
[f]Ease-of-breathing VAS is a 100-mm scale, where 0 = no difficulty breathing and 100 = extreme difficulty breathing.
BMI = body mass index; NOSE = Nasal Obstruction Symptom Evaluation; VAS = visual analog scale.

TABLE 2 NOSE-scale scores and ease-of-breathing VAS scores at baseline and 3 months in active treatment and sham-control arms and change in score from baseline through 3 months

	Active treatment, n = 77		Sham-control, n = 40		
	Mean	95% CI	Mean	95% CI	*p* value
NOSE-scale score					
Baseline	76.7	73.8 to 79.5	78.8	74.2 to 83.3	0.424
3 months	34.4	28.8 to 39.9	62.0	53.0 to 71.0	—
Change at 3 months[a]	−42.3	−47.6 to −37.1	−16.8	−26.3 to −7.2	<0.001
Ease-of-breathing VAS score[b]					
Baseline	59.3	54.4 to 64.2	61.8	55.9 to 67.7	0.533
3 months	27.9	22.3 to 33.5	45.7	36.5 to 54.8	—
Change at 3 months[a]	−31.4	−38.5 to −24.2	−16.1	−26.3 to −6.0	0.015

[a]Change in score from baseline through 3 months.
[b]Ease-of-breathing VAS is a 100-mm scale, where 0 is no difficulty breathing and 100 is extreme difficulty breathing.
CI = confidence interval; NOSE = Nasal Obstruction Symptom Evaluation; VAS = visual analog scale.

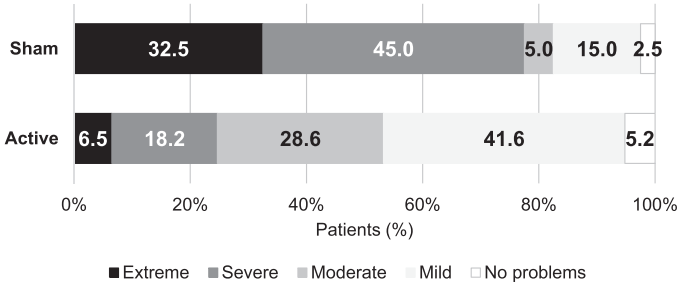

FIGURE 4 The distribution in NOSE-scale severity classifications at 3 months in the active treatment and sham-control arms. NOSE-scale score ranges included in the categories were: extreme (80-100); severe (55-75); moderate (30-50); mild (5-25); and no problems (0-5). All patients were classified as extreme or severe at baseline (46.8% extreme and 53.2% severe in the active treatment arm and 52.5% extreme and 47.5% severe in the sham-control arm; $p = 0.556$ based on a comparison of the distribution of the ordered classifications in each arm using a generalized linear model). At 3 months, the difference in distribution of the ordered classifications was significantly different ($p < 0.001$). NOSE = Nasal Obstruction Symptom Evaluation

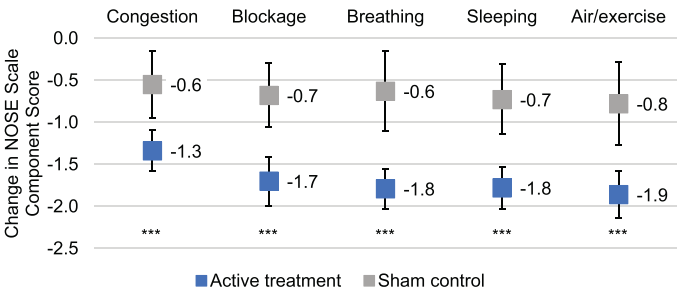

FIGURE 5 Change in NOSE-scale component scores from baseline through 3 months postprocedure in the active treatment arm and sham-control arm. Bars indicate 95% confidence intervals. $^{***}p < 0.001$ comparing changes in the active treatment arm vs sham-control arm. NOSE = Nasal Obstruction Symptom Evaluation

the patients in this trial, when the data were analyzed as a whole.

Nasal pain was recorded on a 100-mm VAS immediately postprocedure (as soon as reasonably possible after the completion of the procedure, typically within 30 minutes of completion), and at 1 month and 3 months. There was no significant difference in pain score immediately postprocedure (active treatment median [n = 76]: 5 mm [IQR, 0-14.5 mm]; sham-control median: 2 mm [IQR, 0-10.5 mm]; $p = 0.235$). Although the level of pain in the active treatment arm remained low at 1 month, the pain score was significantly lower in the sham-control arm (active treatment median (n = 76): 5 mm [IQR, 0-15.5 mm]; sham-control median: 0 mm [IQR, 0-2 mm]; $p < 0.001$). At 3 months, the level of pain was very low in both arms (active treatment median: 1 mm [IQR, 0-6 mm]; sham-control median: 0 mm [IQR, 0-2 mm]; $p = 0.020$), but still significantly lower in the sham-control arm.

The results of the physical and endoscopic nasal exam were generally unremarkable, with no severe findings observed. No saddle nose deformities or orbital bruising were noted postprocedure. Changes to medication regimens and mechanical nasal aid use after the procedures in the active treatment and sham-control arms were also unremarkable. Medications tracked during the trial were antihistamines, decongestants, intranasal steroids, anticholinergics, and immunotherapy. Mechanical nasal aids tracked were nasal cones and strips. To determine the potential effect of an increase in medication use/mechanical nasal aids on the trial outcome, patients

TABLE 3 Subgroup analysis of change in NOSE-scale scores from baseline through 3 months based on mechanism of nasal valve collapse in active treatment and sham-control arms

	Active treatment arm			Sham-control arm		
Valve collapse mechanism	n	Mean change[b]	95% CI	n	Mean change[b]	95% CI
Bilateral dynamic	35	−42.1	−50.8 to −33.4	20	−19.3	−30.8 to −7.7
Bilateral static	25	−42.4	−52.7 to −32.1	11	−12.7	−28.2 to 2.8
Bilateral static and dynamic	10	−43.5	−59.8 to −27.2	5	−3.0	−26.0 to 20.0
Complex[a]	7	−41.4	−60.9 to −22.0	4	−32.5	−58.2 to −6.8

[a]Includes patients with a different or mixed nasal valve collapse mechanism on each side, that is, dynamic on one side, static on the other; or static and dynamic on one side, and static or dynamic on the other side.

[b]Differences between nasal valve collapse mechanisms within arms did not reach statistical significance ($p > 0.05$). Differences between each nasal valve collapse mechanism across arms are statistically significant for bilateral dynamic, bilateral static, and bilateral static and dynamic ($p < 0.01$), but not for complex ($p > 0.05$).

CI = confidence interval; NOSE = Nasal Obstruction Symptom Evaluation.

with an increase in use were assigned to nonresponders if not already nonresponders (4 in the active treatment arm and 2 in the sham-control arm were changed based on medications and 1 in the active treatment arm and 0 in the sham-control arm were changed based on mechanical aids). Primary endpoint analysis with data imputed in this way did not change the overall outcome, with the responder rate in the active treatment arm significantly higher than in the sham-control arm (81.8% [95% CI, 71.8%-88.9%] vs 37.5% [95% CI, 24.2%-53.0%], respectively; $p < 0.001$).

No serious adverse events related to the device/procedure occurred. A total of 3 adverse events were considered at least possibly related to the device and/or procedure. In the active treatment arm, 1 patient had a vasovagal reaction and another had intermittent nasal bleeding with mucus, both of which resolved. In the sham-control arm, 1 patient had intermittent headache, which also resolved.

4 | DISCUSSION

The results of this RCT demonstrate that temperature-controlled RF treatment of the nasal valve is effective in relieving NAO symptoms and is statistically superior to a sham procedure control. The significantly greater change in all components of the NOSE-scale score with active treatment reflects the relief experienced by treated patients in nasal congestion, nasal blockage, breathing, sleeping, and getting air during exercise or exertion. The safety profile of the active device treatment was excellent, with no serious device- or procedure-related adverse events, and with few device- or procedure-related adverse events observed. Pain VAS scores were low in both arms, but scores were statistically significantly greater in the active treatment arm at 1 month and 3 months. This difference is likely due to the healing response occurring after active treatment.

The 80% responder rate in the active treatment arm used for sample size determination was based on the previous single-arm study of the procedure, in which 94% were responders (based on a 15-point improvement in score on the NOSE scale) at 26 weeks.[12,13] The lower 95% confidence bound on the estimate of 94% was 83.5%, which supported the conservative estimate of 80% responder rate for this RCT. The 50% responder rate assumed for the sham-control procedure was based on literature for placebo and sham controls in therapeutic and device studies suggesting 30% to 60% responder rates, with device studies tending to be at the higher end of the range.[17] A randomized trial of a bioabsorbable implant treatment for nasal valve collapse reported a 82.5% responder rate in the active treatment arm and a 54.7% responder rate in the sham-procedure arm of the trial.[9]

To benchmark the effect size observed in the active treatment arm of our RCT (NOSE-scale score −42.3 points, a 55.1% improvement over baseline at 3 months), it is on par with or larger than effects observed after functional rhinoplasty to treat NAO and measured using the NOSE scale, where improvements in scores of 25 points,[18] 30 points,[19] 45 points,[20] and 50 points[21] have been reported.

For further context, NOSE scale–based minimal clinically important differences (MCIDs) from an anchor-based approach have been reported for nasal septoplasty (19.4)[22] and for functional, cosmetic, or combined rhinoplasty (24.4).[23] The mean changes in NOSE-scale score in our RCT were −42.3 in the active treatment arm, which is greater than published MCIDs, and −16.8 in the sham-control arm, which is lower than published MCIDs.

The sham-control arm in our RCT exhibited an improvement in NOSE-scale score of 21.3% from baseline and a responder rate of 42.5% at 3 months, which is below/at the low end of the range of placebo-effect sizes observed in other medical device studies, as outlined earlier. The effect in the sham-control arm could be a consequence of the optimism commonly associated with trial participation. Patients in both arms received topical anesthesia at the treatment site followed by injection of local anesthesia, which was commonly reported to be the most uncomfortable part of treatment. The primary difference in the patient experience between the arms was the 18-second energy delivery phase, during which no energy was delivered through the sham devices. The energy delivery phase of active treatment is generally described as mild discomfort by patients treated in a clinical setting. The sham-control arm patients would still feel the pressure of the stylus head against the treatment site and hear a change in audible tones indicating device activation. It is possible that patients would expect a specific experience from the energy delivery phase that would allow them to guess which arm they were in, but this is unlikely given their lack of any previous experience with the procedure, the generally mild discomfort experienced by patients in the active treatment arm, and the feeling of pressure of the sham device against the lateral nasal wall.

Subgroup analysis of the nasal valve collapse mechanism within this RCT revealed that the results are comparable across static and dynamic nasal valve collapse mechanisms, addressing a limitation of some graft and implant techniques. The small sample size in some subgroups and the absence of a standardized test for static vs dynamic nasal valve collapse are limitations of the subgroup analysis and thus more research is needed in this area.

This RCT was pragmatic in its design in that medication use was not dictated by the protocol, because patients

are usually taking medications such as antihistamines and decongestants for a variety of indications. In this way, the results of this RCT likely reflect the results observed in the real-world clinical practice. To address the possibility that increased medication use could have affected outcome, patients who increased their medication/mechanical nasal aid use during the trial were converted to nonresponders if they were not already nonresponders (5 in the active treatment arm and 2 in the sham-control arm) and the primary endpoint analysis was repeated. However, the overall trial outcome was not changed.

To our knowledge, this trial is the first to compare a minimally invasive RF procedure on the nasal valve to a sham-control for the treatment of nasal valve collapse. The temperature-controlled RF stylus evaluated here is a minimally invasive technique that is highly compatible with an office setting. Cadaveric studies have also shown that the temperature-controlled RF procedure generates almost no additional aerosolized particles above those present in ambient air, which has become a major consideration for patients and providers since the advent of the COVID-19 pandemic.[24] Overall, given the symptom relief in the active treatment arm compared with the sham-control arm, this procedure may reasonably be considered an option for the treatment of NAO in appropriately selected patients.

There are a few limitations of this trial. Among them are those common to randomized sham-controlled studies for medical devices and procedures. Physicians were not blinded to treatment-arm assignment, which may have been a source of bias, but this was mitigated by patient blinding and use of patient-reported outcome measures (ie, NOSE scale, ease-of-breathing VAS, pain VAS). Unlike a placebo in pharmaceutical trials, which can appear identical to the active compound to patient, sham devices and procedures may differ enough from treatment that the patients guess their arm allocation. However, we believe that the sham device and procedure in this trial closely replicated the treatment experience. Medication use was not dictated by the protocol and could potentially have had some confounding effect on symptom relief. However, primary endpoint analysis after converting responders to nonresponders if they increased medication/mechanical nasal aid use did not change the superiority of active treatment over sham control. Finally, the results reported here are through 3 months and longer-term follow-up will reveal the durability of the effect observed in this trial to date.

5 | CONCLUSION

The results of this RCT demonstrate that temperature-controlled RF treatment of the nasal valve is safe and effective in reducing the symptoms of NAO due to nasal valve collapse in short-term follow-up. The procedure is tolerable to patients. The active treatment was superior to a sham procedure control in responder rate and degree of symptom improvement.

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POTENTIAL CONFLICT OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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