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Short-Term Cardiovascular Sequelae Following In-Office Posterior Nasal Nerve Cryoablation

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ABSTRACT

Objective: Evaluate the post-procedural cardiovascular effects of posterior nasal nerve (PNN) cryoablation in comparison to inferior turbinate reduction (ITR).

Methods: Patients over 18 years of age who underwent in-office PNN cryoablation or ITR via submucosal resection via radiofrequency ablation between 2019 and 2022 were enrolled. Cardiovascular parameters including systolic blood pressure (SBP), heart rate (HR), in addition to visual analog pain scale (VAS), were collected at baseline and perioperatively. Maximum changes and time to return to baseline were recorded.

Results: A total of 25 patients were enrolled in the study (16 PNN, 9 ITR). The median maximum change in SBP in the PNN and ITR groups was significant at 36.5 mmHg (IQR 22,50) and 11 mmHg (IQR 0,17) respectively ($p = 0.007$). The median time to return to baseline for SBP was significantly greater at 57.5 min (IQR 30,75) in the PNN group compared to 8.5 (IQR 0,34) in the ITR group ($p = 0.026$). The median duration of time post procedure to the maximal SBP recording for the PNN group was 32.5 min in comparison to 5 min in the ITR group ($p = 0.083$). No differences in HR were noted ($p = 0.293$).

Conclusion: PNN cryoablation is associated with greater and prolonged effects on SBP in comparison to ITR when using a similar in-office anesthesia protocol. Surgeons offering this procedure should be aware of these effects when counseling patients and developing a protocol for post-procedure monitoring.

Level of Evidence: 2

1 | Introduction

Technologic advances have resulted in a shift within the field of rhinology towards office-based procedures to address a variety of sinonasal pathologies [1, 2]. This shift has provided several inherent benefits for patients, including the reduced need for general anesthesia, reduced cost, and improved patient satisfaction [3, 4]. Several studies have also investigated the safety and efficacy of performing these procedures in the office setting with promising results [5–7].

One of the technological advancements that has emerged is posterior nasal nerve (PNN) cryoablation. It is a minimally invasive, low morbidity alternative to vidian neurectomy that can be completed in the office without general anesthesia. PNN cryoablation has been shown to decrease rhinitis symptoms and improve

disease-specific quality of life [8, 9]. Peri-procedural pain control for this procedure is accomplished with topical and/or local anesthesia, with one recent study demonstrating the effectiveness of adding pre-procedural gabapentin for pain control [10].

There is a wide variation in rhinologic procedure setting (i.e., clinic room, procedure room, etc.) and limited data evaluating the peri-procedural hemodynamic effects. Chang et al. recently published a prospective study that found several in-office rhinologic procedures were associated with significant blood pressure fluctuations, particularly present with an older age group [11]. PNN cryoablation was notably associated with the largest increase in SBP at 44.0 ± 17.3 with one case rising to greater than 200 mmHg. The main objective of the current study is to evaluate cardiovascular parameters following submucosal inferior turbinate resection (ITR) via radiofrequency ablation in comparison to PNN cryoablation using an analogous anesthetic protocol.

2 | Materials and Methods

2.1 | Inclusion Criteria

Adult patients age > 18 years were consecutively enrolled as part of a single-institution observational cohort study designed to evaluate cardiovascular parameters following in-office ITR and PNN cryoablation. Study enrollment occurred between 2019 and 2022, and all participants signed an informed consent as part of their enrollment in the study. Participants either underwent in-office PNN cryoablation (Clarifix, Stryker ENT, Kalamazoo, MI) for a diagnosis of allergic or non-allergic rhinitis as defined by the International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis [12] or bilateral diathermy submucosal ITR via radiofrequency ablation (Celon, Olympus, Center Valley, PA) for treatment of inferior turbinate hypertrophy. Atopy was confirmed with blood or skin testing. No study participants underwent inferior meatus cryotherapy. Consecutive patients were enrolled. Participants were excluded if they elected not to participate in the visual analog scale for pain or post-procedural cardiovascular monitoring. Radiofrequency ablation of the inferior turbinate was chosen as a control group as an analogue to PNN because of the similar local anesthetic anesthesia profile, duration, and office-based nature of the procedure. This prospective study was reviewed and approved by the University of California Davis Institutional Review Board (1430003-2).

2.2 | Procedural Anesthesia

Both ITR and PNN cryoablation utilized a comparable anesthetic protocol: Three sprays of 4% lidocaine with oxymetazoline in each nostril, with 5 min allowed for the medication to take effect. Cottonoids soaked with 4% lidocaine were then placed along the inferior turbinate and into the inferior aspect of the middle meatus bilaterally for an additional 5–10 min. For the cryoablation procedure, a sphenopalatine block was performed using 1% lidocaine with 1:100,000 epinephrine injected into the target intervention site. For ITR, three points along the length of the inferior turbinate were injected with the same anesthetic, but the sphenopalatine block was not performed. Five to 10 min were then allotted for anesthesia to take effect and for any cardiovascular parameters to normalize following the injection prior to proceeding [13–15]. PNN cryoablation was then performed using the standard technique as described by Hwang et al. [16]. ITR was also similarly performed in the standard submucosal fashion via radiofrequency ablation [17].

2.3 | Data Collection

Baseline demographic data including age, sex, race, and pertinent past medical history were recorded, including history of coronary artery disease, congestive heart failure, atrial fibrillation, hypertension, and migraine. Any cardiac medications such as anti-hypertensives were also recorded. Periprocedural vital signs including heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded at multiple time points, including at baseline, at the time of injection of local anesthesia, at the time of the procedure, and then every 5 min post procedure until return to baseline. The Wong-Baker visual analog scale (VAS) was used to record the degree of pain at each time point [18].

2.4 | Data Analysis

Treatment arm differences were tested using the unequal variance two-sample t test for continuous, normally distributed variables; the Kruskal–Wallis test for numeric, non-normally distributed variables; and the chi-square test for categorical variables. The normality assumption was assessed using histograms and q–q plots. A p value of less than 0.05 was considered statistically significant. Complete case analysis was employed for each univariate test. All analyses were performed using SAS software version 9.4 for Windows (SAS Institute Inc., Cary, NC).

3 | Results

A total of 25 patients were enrolled in the study, 16 in the PNN group and 9 in the ITR group. The mean (SD) age was 66.9 (±13.6) years in the PNN group and 67.0 (±16.98) years in the ITR group ($p = 0.98$). In the PNN group, 62.5% were male in comparison to 87.5% in the ITR group ($p = 0.20$). Most patients were Caucasian at 93.8% and 87.5% in the PNN and ITR groups respectively ($p = 0.28$). In the PNN group, 31.3% of patients had pre-existing hypertension compared to 12.5% in the ITR group, and there was no significant difference between the two cohorts regarding pre-existing cardiac history ($p = 0.38$). Approximately 26.7% of patients also reported a history of migraine in the PNN group in comparison to 12.5% in the ITR group ($p = 0.43$). There was no difference in baseline blood pressure and heart rate between the two cohorts ($p > 0.05$) (Table 1). There was also no statistically significant difference in the maximum pain VAS between the two cohorts ($p = 0.12$) (Table 2).

The median maximum change in SBP from baseline to post-procedure in the PNN and ITR groups was 36.5 mmHg (IQR

TABLE 1 | Baseline demographic data and pertinent medical history including baseline vital signs of patients in both cohorts.

	Treatment arm			
	PNN (*N* = 16)	**ITR (*N* = 8)**	**Total (*N* = 24)**	**p**
Age				0.9857[a]
N (missing)	16 (0)	8 (0)	24 (0)	
Mean (SD)	66.9 (13.06)	67.0 (16.98)	66.9 (14.11)	
Median (IQR)	70.0 (56.0, 79.0)	72.5 (56.0, 77.5)	71.0 (56.0, 79.0)	
Range	42.0, 82.0	38.0, 86.0	38.0, 86.0	
Sex, *n* (%)				0.2040[b]
F	6 (37.5%)	1 (12.5%)	7 (29.2%)	
M	10 (62.5%)	7 (87.5%)	17 (70.8%)	
Race, *n* (%)				0.2833[b]
African American	0 (0.0%)	1 (12.5%)	1 (4.2%)	
Caucasian	15 (93.8%)	7 (87.5%)	22 (91.7%)	
Pacific Islander	1 (6.3%)	0 (0.0%)	1 (4.2%)	
CardiacHx, *n* (%)				0.3817[b]
CAD	1 (6.3%)	1 (12.5%)	2 (8.3%)	
CAD, CHF, heart valve replacement	0 (0.0%)	1 (12.5%)	1 (4.2%)	
CAD, HTN	1 (6.3%)	0 (0.0%)	1 (4.2%)	
CAD, HTN, aortic stenosis, atrial fibrillation	0 (0.0%)	1 (12.5%)	1 (4.2%)	
Coronary arteriosclerosis, HTN	0 (0.0%)	1 (12.5%)	1 (4.2%)	
HTN	5 (31.3%)	1 (12.5%)	6 (25.0%)	
None	7 (43.8%)	3 (37.5%)	10 (41.7%)	
Atrial fibrillation	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Unspecified arrhythmia	1 (6.3%)	0 (0.0%)	1 (4.2%)	
CardiacMeds, *n* (%)				0.5037[b]
Amlodipine, lisinopril	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Amlodipine, lisinopril	0 (0.0%)	1 (12.5%)	1 (4.2%)	
Amlodipine, hydrochlorothiazide	1 (6.3%)	0 (0.0%)	1 (4.2%)	
HCTZ, lisnopril	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Lisinopril	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Lisinopril, metoprolol	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Losartan, propranolol	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Losartan	0 (0.0%)	1 (12.5%)	1 (4.2%)	
None	4 (25.0%)	3 (37.5%)	7 (29.2%)	
Propranolol, metoprolol	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Spironolactone, propranolol	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Amlodipine, clopidogrel, lisinopril	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Isosorbide mononitrate, carvedilol, a	0 (0.0%)	1 (12.5%)	1 (4.2%)	
Lisinopril, carvedilol, apixaban	1 (6.3%)	0 (0.0%)	1 (4.2%)	

(Continues)

TABLE 1 | (Continued)

	Treatment arm			
	PNN (*N* = 16)	**ITR (*N* = 8)**	**Total (*N* = 24)**	**p**
Metoprolol, losartan, amlodipine	0 (0.0%)	1 (12.5%)	1 (4.2%)	
Nitroglycerin, losartan, propranolol	0 (0.0%)	1 (12.5%)	1 (4.2%)	
None	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Propranolol (for tremors)	1 (6.3%)	0 (0.0%)	1 (4.2%)	
Migraines, *n* (%)				0.4327[b]
No	11 (73.3%)	7 (87.5%)	18 (78.3%)	
Yes	4 (26.7%)	1 (12.5%)	5 (21.7%)	
Missing	1	0	1	
Baseline_SBP				0.4889[a]
N (missing)	16 (0)	8 (0)	24 (0)	
Mean (SD)	135.6 (17.73)	129.9 (18.81)	133.7 (17.89)	
Median (IQR)	133.5 (118.5, 149.0)	123.0 (115.5, 149.0)	131.5 (118.5, 149.0)	
Range	113.0, 172.0	108.0, 156.0	108.0, 172.0	
Baseline_DBP				0.3269[a]
N (missing)	16 (0)	8 (0)	24 (0)	
Mean (SD)	75.0 (9.86)	70.6 (9.98)	73.5 (9.91)	
Median (IQR)	75.0 (66.5, 84.5)	71.0 (62.0, 79.0)	74.5 (66.0, 83.0)	
Range	58.0, 90.0	57.0, 84.0	57.0, 90.0	
Baseline_HR				0.7745[a]
N (missing)	16 (0)	8 (0)	24 (0)	
Mean (SD)	72.9 (13.32)	74.4 (10.32)	73.4 (12.19)	
Median (IQR)	73.5 (63.5, 85.5)	71.5 (67.0, 81.0)	73.0 (65.5, 85.5)	
Range	46.0, 93.0	63.0, 93.0	46.0, 93.0	

[a]Unequal variance two sample *t*-test.
[b]Chi-square *p* value.

22,50) and 11 mmHg (IQR 0,17), ($p = 0.007$) while the median maximum change in DBP was 16.0 mmHg (IQR 10,27) and 6.0 mmHg (3,8, $p = 0.031$). The median maximum change in heart rate was 2.5 beats per minute (bpm) (0.0, 6.5) in the PNN group and 0.0 bpm (0.0, 2.0) in the ITR group ($p = 0.29$).

The median time to the maximum SBP recording was found to be 32.5 min (IQR 22.5,40) in the PNN group and 5 min (IQR 0,35) in the ITR group ($p = 0.083$). The difference in median time to maximum DBP was not statistically significant at 32.5 min (IQR 20,42.5) in the PNN group and 7 min (IQR 5,30) in the ITR group ($p = 0.131$).

The median time to return to baseline for SBP was statistically significant at 57.5 min (IQR 30,75) in the PNN group compared to 8.5 (IQR 0,34) in the ITR group ($p = 0.026$). There was also a significant difference found in the time it took to return to baseline for DBP at 50.5 min (IQR 22,50) in the PNN group compared to 12 min (IQR 7,25) in the ITR group ($p = 0.020$) (Table 2).

4 | Discussion

There has been a dynamic shift within the field of rhinology towards more office-based and minimally invasive approaches to the treatment of a variety of pathologies, including the development of PNN cryoablation for the treatment of chronic rhinitis. PNN cryoablation has been well studied, with several studies demonstrating its clinical efficacy [8, 9, 16]. However, less is known regarding the hemodynamic effects of this procedure.

Chang et al. previously reported on the hemodynamic effects of various in-office rhinologic procedures and found that factors such as age were associated with the greatest increase in SPB fluctuations [11]. This is consistent with previous studies

TABLE 2 | Measurements of periprocedural vital signs including maximum VAS for pain, time to maximum (TTM), time to baseline (TTB), and maximum change (delta max) during the peri-procedural time period for both SBP and DBP.

	Treatment arm			
	PNN (*N* = 16)	**ITR (*N* = 9)**	**Total (*N* = 25)**	***p***
Max_VAS				0.0699[a]
N (missing)	16 (0)	9 (0)	25 (0)	
Mean (SD)	4.6 (3.16)	2.1 (2.89)	3.7 (3.25)	
Median (IQR)	5.0 (2.0, 7.0)	1.0 (0.0, 2.0)	4.0 (0.0, 7.0)	
Range	0.0, 10.0	0.0, 7.0	0.0, 10.0	
TTM_SBP				0.0834[a]
N (missing)	16 (0)	9 (0)	25 (0)	
Mean (SD)	32.3 (15.30)	17.8 (20.83)	27.1 (18.48)	
Median (IQR)	32.5 (22.5, 40.0)	5.0 (0.0, 35.0)	30.0 (14.0, 40.0)	
Range	5.0, 60.0	0.0, 50.0	0.0, 60.0	
TTB_SBP				0.0260[a]
N (missing)	10 (6)	8 (1)	18 (7)	
Mean (SD)	54.4 (26.37)	21.9 (31.31)	39.9 (32.38)	
Median (IQR)	57.5 (30.0, 75.0)	8.5 (0.0, 34.0)	32.5 (10.0, 67.0)	
Range	20.0, 94.0	0.0, 90.0	0.0, 94.0	
TTM_DBP				0.1313[a]
N (missing)	16 (0)	9 (0)	25 (0)	
Mean (SD)	31.2 (17.26)	22.2 (30.13)	28.0 (22.54)	
Median (IQR)	32.5 (20.0, 42.5)	7.0 (5.0, 30.0)	30.0 (7.0, 40.0)	
Range	0.0, 55.0	0.0, 90.0	0.0, 90.0	
TTB_DBP				0.0200[a]
N (missing)	12 (4)	7 (2)	19 (6)	
Mean (SD)	45.1 (28.02)	15.0 (11.72)	34.0 (27.35)	
Median (IQR)	50.5 (17.5, 61.0)	12.0 (7.0, 25.0)	25.0 (12.0, 60.0)	
Range	0.0, 94.0	0.0, 35.0	0.0, 94.0	
d_max_SBP				0.0071[a]
N (missing)	16 (0)	9 (0)	25 (0)	
Mean (SD)	34.9 (20.34)	11.1 (11.47)	26.4 (20.94)	
Median (IQR)	36.5 (22.0, 50.0)	11.0 (0.0, 17.0)	27.0 (6.0, 44.0)	
Range	2.0, 67.0	0.0, 35.0	0.0, 67.0	
d_max_DBP				0.0310[a]
N (missing)	16 (0)	9 (0)	25 (0)	
Mean (SD)	18.3 (13.17)	8.3 (11.01)	14.7 (13.15)	
Median (IQR)	16.0 (10.0, 27.0)	6.0 (3.0, 8.0)	12.0 (5.0, 21.0)	
Range	0.0, 54.0	0.0, 36.0	0.0, 54.0	

(Continues)

TABLE 2 | (Continued)

	Treatment arm			
	PNN (*N* = 16)	**ITR (*N* = 9)**	**Total (*N* = 25)**	***p***
d_max_HR				0.2931[a]
N (missing)	16 (0)	9 (0)	25 (0)	
Mean (SD)	4.8 (6.80)	3.9 (7.52)	4.5 (6.93)	
Median (IQR)	2.5 (0.0, 6.5)	0.0 (0.0, 2.0)	1.0 (0.0, 4.0)	
Range	0.0, 24.0	0.0, 21.0	0.0, 24.0	

[a]Kruskal–Wallis *p* value.

that have looked at hemodynamic changes of in-office laryngology procedures, which found similarly that patients over the age of 50 were at the greatest risk of SBP fluctuations, although BP fluctuations were noted to vary more significantly during operating room procedures compared to in the office [19]. This study demonstrates sustained elevations in blood pressure for patients undergoing PNN ablation independent of age as compared to inferior turbinate reduction. These findings are clinically relevant in the setting of patients who are electing to undergo an in-office procedure and who may be at increased risk of cardiovascular adverse events with BP fluctuations. Notably, most participants in this study were greater than 65 years old, which could impact cardiovascular parameters [20].

It should be noted that while the PNN group did receive a submucosal SPA block with 1% lidocaine with 1:100,000 epinephrine in which that injection alone can result in hemodynamic changes, these changes are documented to be short lived, lasting approximately 5–10 min [13–15]. The study authors therefore completed a period of observation of 5–10 min after the SPA injection in the PNN cohort to allow for any temporary hemodynamic changes to normalize prior to proceeding, thereby creating an analogous anesthetic protocol between the two cohorts to limit any confounding effect from the injection. With this analogous protocol in place, the current study found that the hemodynamic changes were noted to be significantly higher in the PNN cryoablation group in comparison to the ITR group.

Notably, the hemodynamic changes found to be statistically different were the maximum change in SBP and time to return to baseline. Specifically, the median time for SBP to return to baseline (57.5 min for the PNN group in comparison to 8.5 min for the ITR group) can potentially be a helpful metric for the development of in-office safety protocols for the duration of time to observe patients after an in-office procedure.

When controlling for pain, these BP changes remained statistically significant, suggesting that there may be an alternate physiological mechanism related to the cryoablation procedure with systemic cardiovascular sequelae. Although identification of a mechanism for this observation is beyond the scope of this current study, proposed mechanisms include stimulation of a neural pathway during the cryoablation procedure that is not seen during the ITR [21]. Future studies could look at radiofrequency ablation to assess if the hypertensive episodes are unique to cryoablation.

There are several limitations to our study. This was a single center, observational cohort study with a limited number of participants. While no clinically significant adverse cardiovascular events were observed in our cohort, it is difficult to extrapolate that data to the general population with only a small cohort of patients. Despite sample size limitations, significant changes were noted consistent with prior literature [11]. In addition, the anatomical location of the submucosal 1% lidocaine with 1:100,000 epinephrine injections were different between the two cohorts. Despite the different anatomic locations, the study protocol allowed for normalization of hemodynamic parameters prior to each procedure. Further large prospective studies are needed to validate the results of this study and to develop guidelines for safety monitoring in the peri-procedural timeline.

5 | Conclusion

In comparison to ITR, patients undergoing PNN cryoablation under local anesthesia were noted to have a statistically significant increase in both maximum SBP change and time to return down to baseline. Surgeons offering this procedure should be aware of these effects when counseling patients and developing a protocol for post-procedure monitoring.

Acknowledgments

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

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