Received: 1 July 2020 | Accepted: 8 August 2020

DOI: 10.1002/lio2.451

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

The safety of in-office laryngologic procedures during active antithrombotic therapy

Jeffrey M. Straub MD[1] | Kevin A. Calamari BS[1] | Timothy J. Shin MD[1] | Sarah A. Janse PhD[2] | Lowell A. Forrest MD[1] | Brad W. deSilva MD[1] | Laura A. Matrka MD[1]

[1]Department of Otolaryngology—Head and Neck Surgery, The Ohio State University, Columbus, Ohio

[2]Department of Biomedical Informatics, The Ohio State University, Columbus, Ohio

Correspondence
Jeffrey M. Straub, Department of Otolaryngology—Head and Neck Surgery, The Ohio State University, 915 Olentangy River Road, Suite 4000, Columbus, OH 43212.
Email: jeffrey.straub@osumc.edu

Abstract

Objectives: To determine whether patients undergoing in-office laryngologic procedures on antithrombotic therapy are at increased risk for treatment-related complications.

Methods: Patients were those who underwent at least one in-office laryngologic procedure with any of three fellowship-trained laryngologists. Procedures were identified by current procedural terminology (CPT) code and included biopsies, excisions, laser ablations, and injections (therapeutic and augmentative). Patients were divided into two groups based on the use of antithrombotic therapy at the time of their procedure. Retrospective chart review was performed to identify any complications, with an average follow-up of 186 days.

Results: Five hundred-sixty-four unique individuals were identified with ages ranging from 18 to 93 years old and with a relatively even distribution between females (45%) and males (55%). They underwent 647 procedures in total, 310 of which were performed while on some form of antithrombotic therapy. Sixteen procedures were associated with complications either during or after the procedure. In comparing overall complication rates, there was no significant difference between non-antithrombotic (2.4%) and antithrombotic (3.3%) cohorts (OR 1.09, 95% CI [0.46-2.60], $P = .8454$).

Conclusions: In spite of known risks in other settings, antithrombotic agents do not appear to confer increased risk of treatment-related complications during in-office laryngologic procedures, obviating the need for cessation of therapy prior to these interventions.

Level of evidence: 4.

KEYWORDS

antithrombotics, complications, in-office, laryngologic, procedures

1 | INTRODUCTION

In-office laryngologic procedures are becoming increasingly popular in the practice of otolaryngology as physicians look for the most efficient ways to deliver quality health care to patients with voice, airway, and/or swallowing dysfunction.[1-3] Indeed, these procedures are associated with shorter recovery time, quicker return to work, and decreased cost per case compared to the operating room.[4,5] They are well-tolerated, and the avoidance of general anesthesia makes them a potential option for patients with significant comorbidities.[6-8] Furthermore, the ability in some cases to titrate the effects of intervention based on real-time patient response may promote better outcomes and patient satisfaction.[9-12] However, there is some precision lost in the non-operative setting, and there have been reports of hemodynamic instability with topical anesthetic in older patients.[7,13,14] These considerations must be taken into account before any in-office laryngologic procedure.

Another increasing trend over recent decades has been the number of patients on antithrombotic therapy, which includes both antiplatelet and anticoagulant agents.[15,16] The recommendation for antithrombotic medication is based primarily on annual thromboembolic risk and validated scoring systems like the $CHADS_2$ and $CHADS_2$-VASc criteria, which stratify patients into low- and high-risk groups.[17,18] Antiplatelets are one of the primary treatments for patients with acute coronary syndrome, which affects about 635 000 Americans per year.[19] Similarly, anticoagulants are commonly used in atrial fibrillation, the prevalence of which is expected to rise to 5.6 to 12 million by 2050.[7,20] Use of mechanical heart valves and vessel stents is also increasing, necessitating dual therapy.[21,22]

The increased usage of antithrombotics has led to more complicated clinical decision-making in terms of the risk/benefit of office-based laryngologic procedures, as bleeding in the airway may become a potentially emergent situation. This highlights the need for more formal recommendations in this context, and the following study will seek to establish in-office laryngologic procedures as legitimately safe in patients on active antithrombotic therapy.

2 | MATERIALS AND METHODS

Approval was obtained from the Institutional Review Board. The institution's Research Data Repository was queried for all patients aged 18 or older who, from January 2012 through December 2017, underwent at least one in-office procedure with any of three fellowship-trained laryngologists. Procedures were identified by Current Procedural Terminology (CPT) code and included biopsies, excisions, laser ablations, and injections (therapeutic and augmentative). In general, these all involved some form of topical anesthesia (ie, lidocaine drip, nebulized lidocaine, transtracheal lidocaine) with occasional pre-procedural oral diazepam (usually 2-5 mg) per provider and patient preference. No continuous monitoring of vitals was performed during the procedures unless the patient had an oxygen requirement, in which case pulse oximetry was utilized. On average, procedures lasted less than 10 minutes or up to 15 in more difficult cases.

With the study group identified, retrospective chart review was then performed. Data collection included demographic features (age,

TABLE 2 Type and distribution of procedures performed

	Antithrombotic		
Procedure	No (n = 337)	Yes (n = 310)	Total (n = 647)
Biopsy	55 (16%)	47 (15%)	102 (16%)
Excision	77 (23%)	45 (15%)	122 (19%)
Laser ablation	18 (5%)	14 (5%)	32 (5%)
Injection	187 (55%)	204 (66%)	391 (60%)
Therapeutic	159 (47%)	159 (51%)	318 (49%)
Augmentation	28 (8%)	45 (15%)	73 (11%)

TABLE 1 Demographic characteristics by cohort

		Antithrombotic			
Variable	Level	No (n = 290)	Yes (n = 274)	Total (n = 564)	*P*-value
Gender	Female	144 (50%)	111 (41%)	255 (45%)	.0343
	Male	146 (50%)	163 (59%)	309 (55%)	
Race	Asian	5 (2%)	3 (1%)	8 (1%)	.6584
	Black	28 (10%)	22 (8%)	50 (9%)	
	Hispanic	0 (0%)	1 (0%)	1 (0%)	
	Other/Unknown	11 (4%)	7 (3%)	18 (3%)	
	White	246 (85%)	241 (88%)	487 (86%)	
Smoker	Missing	0 (0%)	1 (0%)	1 (0%)	.0266
	Current	42 (14%)	30 (11%)	72 (13%)	
	Former	102 (35%)	126 (46%)	228 (40%)	
	Never	146 (50%)	117 (43%)	263 (47%)	
Age	Median [IQR] (min, max)	56 [44, 65] (17, 92)	65 [56, 74] (28, 93)	60 [50, 71] (17, 93)	<.0001

TABLE 3 Complications as documented per electronic medical record

Complication	Procedure	Intra/Post	Antithrombotic
Bleeding	Injection	Intra	No
Bleeding	Injection	Intra	Yes
Dysphonia	Injection	Post	Yes
Dyspnea	Injection	Post	No
Dyspnea	Excision	Post	No
Dyspnea, stridor	Injection	Post	Yes
Extruded material	Injection	Intra	Yes
Hemoptysis	Injection	Post	No
Hemoptysis, throat pain	Excision	Post	Yes
Hypotension, vocal fold hemorrhage	Excision	Post	Yes
Inability to cough	Injection	Post	Yes
Increased secretions	Excision	Intra	Yes
Throat swelling	Excision	Post	No
Vagal response	Injection	Intra	No
Vagal response, extruded material	Injection	Intra	No
Vocal fold hemorrhage	Injection	Post	Yes

gender, race, smoking status) and clinical information (procedure type, follow-up, complications, outcomes, antithrombotics if applicable). Complications were defined as any unexpected event—bleeding-related or otherwise—identified by review of procedure notes, follow-up appointments, and telephone encounters. Prior to data analysis, procedures were stratified based on the presence or absence of active antithrombotic therapy, which included antiplatelet (fish oil, ibuprofen, naproxen, etodolac, cilostazol, dipyridamole, aspirin, clopidogrel) and/or anticoagulant (enoxaparin, warfarin, apixaban, rivaroxaban) agents of interest. To test for differences between these two groups, Fisher's exact test was used for categorical variables while a Wilcoxon rank-sum test was used for continuous variables. To explore differences in occurrence of complications, a generalized linear mixed model was used to account for the correlation among repeated measurements on some subjects. Each covariate of interest was first tested in a univariate model for consideration into a multivariate model.

3 | RESULTS

A total of 564 unique patients were identified as having undergone 647 in-office laryngologic procedures. Two hundred-seventy-four of these individuals were on antithrombotic therapy at the time, accounting for 310 procedures. Table 1 summarizes and compares the demographic features of the two study groups. For the 68 patients who underwent more than one procedure, this table includes demographic information at their first recorded procedure only. The types of procedures performed as well as their distribution are listed in Table 2. Average duration of follow-up was 186 days or approximately 6 months. There were 16 procedures with complications, all of which were self-limited and are detailed in Table 3. Overall complication rates (number of complications/procedures performed) were 2.4% and 3.3% for the non-antithrombotic and antithrombotic groups, respectively. There was no statistically significant difference between these rates on univariate analysis (OR 1.09, 95% CI [0.46-2.60], P = .8454). Table 4 summarizes univariate analyses of other clinical variables, none of which were statistically significant, thereby obviating the need to fit a multivariate model.

TABLE 4 Additional univariate and generalized linear mixed model results

Variable	Odds ratio	95% CI	*P*-value
Female vs male	1.32	(0.55, 3.15)	.5270
Smoker			.2880
Current vs never	2.54	(0.78, 8.24)	.1196
Former vs never	1.28	(0.47, 3.43)	.6265
Age	1.01	(0.98, 1.04)	.4384
Race nonwhite vs white	1.04	(0.29, 3.71)	.9460
Procedure excision[a] vs injection	0.33	(0.11, 1.01)	.0511

[a]Includes biopsy and laser ablation.

4 | DISCUSSION

Individuals on antithrombotic therapy have traditionally been considered at increased risk of complications from surgery related to excessive bleeding, and oftentimes recommendations are made to hold antithrombotic therapy beforehand. Doing so, however, is not without its risks, and the potential for thromboembolic events may preclude surgery, particularly in more elective cases.[7,17,23,24] In the otolaryngology literature, operative microlaryngeal surgery was shown to have

no increased risk of bleeding in patients on antithrombotics.[25] Subsequent studies by Fritz et al and Dang et al had similar findings in the office setting and at the bedside, respectively, but the smaller size of these studies prevented them from drawing formal conclusions.[7,26]

The present study sought to validate the findings of those before it while establishing definitive recommendations for the performance of in-office laryngologic procedures in patients on antithrombotic therapy. Demographically, there were predictable differences among the two cohorts, with male gender, smoking status, and older age all associated with antithrombotic usage. Most importantly, patients on antithrombotics were found to be just as likely to experience a complication as those not on antithrombotics. These findings indicate that active antithrombotic therapy is in fact safe during said procedures. No other variables were associated with complications.

Despite these encouraging results, there are some limitations worth mentioning. The identification of complications was reliant on documentation from procedure notes, follow-up visits, and patient telephone encounters. As such, it is possible that inadequate documentation may have led to omissions. There is also a degree of subjectivity in distinguishing expected side effects from true complications, introducing the possibility for observer bias. Moreover, although a major strength of this study rests in its size, it is technically underpowered to detect such a small difference in complication rate between the two cohorts (0.8%), which would require about 5000 patients per group. With the current sample size, the smallest difference that can be detected is about 5%, which the authors would argue is clinically negligible in most cases. Lastly, subgroup analysis (ie, antiplatelet vs anticoagulant vs dual therapy) was not possible due to the relative paucity of complications.

5 | CONCLUSION

In-office laryngologic procedures afford a number of advantages compared to their operating room counterparts, including avoidance of general anesthesia, shorter recovery, quicker return to work, and lower cost. The current study supports that these procedures are safe to perform while patients are on active antithrombotic therapy with no need for cessation. Larger cohorts are expected to corroborate these findings and may allow for subgroup analysis going forward.

ACKNOWLEDGMENTS

The authors would like to acknowledge Beth Miles-Markley for her assistance with the Institutional Review Board approval and renewal process as well as other logistical components of the project. There are otherwise no conflicts of interest or sources of funding to disclose.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

ORCID

Jeffrey M. Straub https://orcid.org/0000-0001-5007-8947
Kevin A. Calamari https://orcid.org/0000-0001-8292-1425
Brad W. deSilva https://orcid.org/0000-0003-0842-9744
Laura A. Matrka https://orcid.org/0000-0002-9558-5202

REFERENCES

1. Sulica L, Rosen CA, Postma GN, et al. Current practice in injection augmentation of the vocal folds: indications, treatment principles, techniques, and complications. *Laryngoscope*. 2010;120:319-325.
2. Rosen CA, Amin MR, Sulica L, et al. Advances in office-based diagnosis and treatment in laryngology. *Laryngoscope*. 2009;119(Suppl 2): S185-S212.
3. Zeitels SM, Franco RA Jr, Dailey SH, Burns JA, Hillman RE, Anderson RR. Office-based treatment of glottal dysplasia and papillomatosis with the 585-nm pulsed dye laser and local anesthesia. *Ann Otol Rhinol Laryngol*. 2004;113:265-276.
4. Yung KC, Courey MS. The effect of office-based flexible endoscopic surgery on hemodynamic stability. *Laryngoscope*. 2010;120:2231-2236.
5. Rees CJ, Postma GN, Koufman JA. Cost savings of unsedated office-based laser surgery for laryngeal papillomas. *Ann Otol Rhinol Laryngol*. 2007;116:45-48.
6. Young VN, Smith LJ, Sulica L, Krishna P, Rosen CA. Patient tolerance of awake, in-office laryngeal procedures: a multi-institutional perspective. *Laryngoscope*. 2012;122:315-321.
7. Dang JH, Liou NE, Ongkasuwan J. Anticoagulation and antiplatelet therapy in awake transcervical injection laryngoplasty. *Laryngoscope*. 2017;127:1850-1854.
8. Rees CJ, Halum SL, Wijewickrama RC, Koufman JA, Postma GN. Patient tolerance of in-office pulsed dye laser treatments to the upper aerodigestive tract. *Otolaryngol Head Neck Surg*. 2006;134:1023-1027.
9. Verma SP, Dailey SH. Office-based injection laryngoplasty for the management of unilateral vocal fold paralysis. *J Voice*. 2014;28: 382-386.
10. Andrade Filho PA, Carrau RL, Buckmire RA. Safety and cost-effectiveness of intra-office flexible videolaryngoscopy with transoral vocal fold injection in dysphagic patients. *Am J Otolaryngol*. 2006;27: 319-322.
11. Barbu AM, Gniady JP, Vivero RJ, Friedman AD, Burns JA. Bedside injection medialization laryngoplasty in immediate postoperative patients. *Otolaryngol Head Neck Surg*. 2015;153:1007-1012.
12. Rosow DE. Trends in utilization of vocal fold injection procedures. *Otolaryngol Head Neck Surg*. 2015;153:812-814.
13. Morrison MP, O'Rourke A, Dion GR, Eller RL, Weinberger P, Postma GN. Hemodynamic changes during otolaryngological office-based flexible endoscopic procedures. *Ann Otol Rhinol Laryngol*. 2012; 121:714-718.
14. Bastian RW, Delsupehe KG. Indirect larynx and pharynx surgery: a replacement for direct laryngoscopy. *Laryngoscope*. 1996;106:1280-1286.
15. Adelborg K, Grove EL, Sundboll J, Laursen M, Schmidt M. Sixteen-year nationwide trends in antithrombotic drug use in Denmark and its correlation with landmark studies. *Heart (British Cardiac Society)*. 2016;102:1883-1889.
16. Katz DF, Maddox TM, Turakhia M, et al. Contemporary trends in oral anticoagulant prescription in atrial fibrillation patients at low to moderate risk of stroke after guideline-recommended change in use of the CHADS2 to the CHA2DS2-VASc score for thromboembolic risk assessment: analysis from the National Cardiovascular Data Registry's Outpatient Practice Innovation and Clinical Excellence Atrial Fibrillation Registry. *Circ Cardiovasc Qual Outcomes*. 2017;10(5):e003476.
17. Hsueh WD, Hwang PH, Abuzeid WM. Perioperative management of antithrombotic therapy in common Otolaryngologic surgical procedures: state of the art review. *Otolaryngol Head Neck Surg*. 2015;153: 493-503.

18. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest*. 2010;137:263-272.
19. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation*. 2015;131:e29-e322.
20. Amerena JV, Walters TE, Mirzaee S, Kalman JM. Update on the management of atrial fibrillation. *Med J Aust*. 2013;199:592-597.
21. Baron TH, Kamath PS, McBane RD. Management of antithrombotic therapy in patients undergoing invasive procedures. *N Engl J Med*. 2013;368:2113-2124.
22. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation*. 2012;125:e2-e220.
23. Burger W, Chemnitius JM, Kneissl GD, Rucker G. Low-dose aspirin for secondary cardiovascular prevention—cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation—review and meta-analysis. *J Intern Med*. 2005;257:399-414.
24. Douketis JD, Berger PB, Dunn AS, et al. The perioperative management of antithrombotic therapy: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, 8th ed. *Chest*. 2008;133:299S-339S.
25. Francis DO, Dang JH, Fritz MA, Garrett CG. Antiplatelet and anticoagulation therapy in microlaryngeal surgery. *Laryngoscope*. 2014;124:928-934.
26. Fritz MA, Peng R, Born H, et al. The safety of antithrombotic therapy during in-office laryngeal procedures-a preliminary study. *J Voice*. 2015;29:768-771.

How to cite this article: Straub JM, Calamari KA, Shin TJ, et al. The safety of in-office laryngologic procedures during active antithrombotic therapy. *Laryngoscope Investigative Otolaryngology*. 2020;5:890–894. https://doi.org/10.1002/lio2.451