The Laryngoscope

Office-Based CO_2 Laser Surgery for Benign and Premalignant Laryngeal Lesions

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Objective: Patients with laryngeal pathology are often treated with CO_2 laser surgery, usually in the operating room under general anesthesia. Although office-based laser surgery using several other laser types has been investigated, prospective studies on office-based CO_2 laser surgery are scarce. Our goal was to investigate the feasibility of office-based CO_2 laser surgery for benign and premalignant laryngeal pathology by analyzing completion rate, safety, effect on voice quality, and success rate (i.e., no residual or recurrent disease).

Methods: A prospective cohort study was performed of 30 consecutive procedures. Inclusion started in June 2016 and was completed in August 2018. Adult patients with clinically benign or premalignant laryngeal lesions who could not undergo transoral laser microsurgery in the operating room under general anesthesia were included. Reasons were either contraindications for general anesthesia, previously failed therapeutic laryngoscopy under general anesthesia, and preference of a procedure under topical anesthesia by the patient. The mean follow-up was 9 months.

Results: Thirty procedures were performed in 27 patients (24 males) with an average age of 62 years. Twenty-nine (97%) procedures were fully completed without complications. The mean preoperative Voice Handicap Index (VHI) score (VHI 44) significantly decreased 2 months (VHI 28, $P = 0.032$) and 6 months (VHI 14, $P < 0.001$) after the procedure. Almost two-thirds of patients showed no residual or recurrent disease at their follow-up visits.

Conclusion: Office-based CO_2 laser surgery is a feasible and safe procedure that results in significant voice-quality improvement. Almost two-thirds of patients did not require further treatment.

Key Words: Laser surgery, CO_2 laser, office-based, larynx, topical anesthesia.

Level of Evidence: 2

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INTRODUCTION

For decades, the CO_2 laser has been the most frequently used laser in the operating room for removal of laryngeal lesions under general anesthesia.[1] After the introduction of digital flexible laryngoscopes with a working channel, a shift has been made in performing surgical procedures on the larynx in an office-based setting under topical anesthesia instead of in the operating room under general anesthesia.[2,3] This evolvement has already led to an extensive practice of office-based laser surgery using the pulsed dye laser and potassium-titanyl-phosphate (KTP) laser.[3] Although these studies demonstrated office-based laser surgery to be feasible, effectiveness was variably reported, often only as partial removal of disease.[3]

In the past, office-based CO_2 laser surgery was impossible to perform due to the absence of a flexible laser fiber that could be passed through the working channel of a flexible laryngoscope. Since this problem has been overcome, flexible fibers for office-based CO_2 laser surgery are now commercially available.[4,5] Currently, few studies have reported on the feasibility of office-based CO_2 laser surgery for laryngeal pathology, and most are retrospective case series.[6–9] Our goal was to prospectively investigate the feasibility of office-based CO_2 laser surgery on patients with benign and premalignant laryngeal lesions. Safety, effect on voice quality, and effectiveness (i.e., no residual or recurrent disease) of office-based CO_2 laser surgery were evaluated.

MATERIALS AND METHODS

Patient Inclusion

This prospective study was conducted in accordance with the guidelines established in the Declaration of Helsinki and was approved by the local medical ethical committee of our institution (file number 2015-2045). The study was conducted in our tertiary referral center. Thirty consecutive procedures were included. Inclusion criteria were adult patients with a clinically benign or premalignant laryngeal lesion. Reasons for undergoing an office-based procedure were either contraindications for general anesthesia,

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previously failed therapeutic laryngoscopy under general anesthesia, or a strong preference for a procedure under topical anesthesia by the patient. Patients underwent flexible endoscopic biopsy (FEB) under topical anesthesia to obtain histology prior to office-based laser surgery according to our department's protocol.[10] An exception was if patients with a medical history of a benign laryngeal tumor (e.g., laryngeal papilloma) were seen with suspicion of recurrent disease during flexible laryngoscopy. In these patients, new biopsies were only obtained in case of doubt on pathology. All patients with malignant pathology found after FEB were excluded. In the early phase of the study, patients underwent FEB just prior to laser treatment in the same session. In a later phase, FEB was performed several days in advance of laser surgery to prevent bleeding that may interfere with the effectiveness of the CO_2 laser. A procedure was considered successful (i.e., success rate) when no residual or recurrent disease was detected after a minimal follow-up of 6 months.

Procedure

Patients were treated in our outpatient clinic surgical procedure room. Patients were instructed and anesthetized (nasal cavity and oropharynx) according to our department's protocol.[10] At the beginning of the study, laryngeal anesthesia was provided by injection through the cricothyroid membrane with 1.0 mL 10% lidocaine. Later on, we used an alternative method for laryngeal anesthesia: 2.5 mL of 4.3% lidocaine was dripped on the larynx through an epidural catheter (Perifix, B. Braun Medical Inc., Bethlehem, PA) that was passed through the working channel of the flexible laryngoscope (VNL-1570STK or VNL-J10, Pentax Medical, Uithoorn, The Netherlands).

A CO_2 laser (AcuPulse DUO, Lumenis, Yokneam, Israel) with flexible laser fiber (FiberLase Endure, Lumenis, Yokneam, Israel) and matching protection cover were used to perform all office-based procedures. Prior to the start of the procedure, a laser safety check was performed (i.e., no reflecting objects in the room, windows blinded, doors closed, laser fiber and settings checked, proper smoke evacuation of CO_2 fumes, patient, surgeons and nurses wearing laser safety glasses, and surgeons and nurses wearing laser masks). Patients were treated while sitting in an upright position. Whereas one clinician performed laryngoscopy and controlled the laser, the other controlled the laser fiber. The laser settings were superpulse, continuous wave mode and 6-watt energy delivery. Pathology on the right true vocal cord was preferably accessed through the left nasal cavity and on the left vocal cord through the right in order to guarantee maximum visibility of the laryngeal lesion.

After the procedure, surgeons kept on their masks for 10 minutes in order to clear the fumes from the surgical room. Patients were advised no oral intake for 1 hour and to obtain voice rest for 3 days. Furthermore, patients were asked to complete the Voice Handicap Index (VHI) prior to the procedure and 2 and 6 months after the procedure during outpatient clinic visits.[11] This validated questionnaire contains 30 items that score the patients' voice quality on an emotional, functional, and physical level. A VHI score below 20 corresponds with a normal voice, whereas a score above 60 means that patients experience their decreased voice quality as a handicap.[11] Standard follow-up after office-based laser surgery was performed with a consultation by telephone 2 weeks after the procedure, and outpatient clinic visits were performed 2 and 6 months after the procedure. In some cases, patients were also examined 1 year after the procedure.

Analysis

Statistical analysis was performed using IBM Statistical Package for Social Sciences Statistics 25 (released 2017; IBM Corp., Armonk, NY) and IBM SPSS Statistics for Windows 25.0 (IBM Corp.). A paired t test was used to calculate the statistical significance for VHI scores. A P value of <0.05 was considered statistically significant.

RESULTS

Since the start of inclusion in June 2016, the target of 30 procedures for benign and premalignant laryngeal pathology was reached in August 2018. Patient characteristics are displayed in Table I. Leukoplakia and vocal cord polyp were the main clinical indications to perform office-based CO_2 laser surgery. Histology revealed vocal cord polyp and hyperplasia in most cases. In four procedures, no histology was obtained (3 patients with suspicion of recurrent leukoplakia and 1 patient with suspicion of recurrent laryngeal papilloma). Twenty-nine (97%) procedures were

TABLE I.
Patient Characteristics.

Characteristics	Laser Surgery	%
Procedures	30	100
Patients (n)	27	
Sex (males)	24	80
Age (range)	62 (43–93)	
Locations		
Right true vocal cord	13	43
Left true vocal cord	12	40
Anterior commissure	5	17
Indications		
Leukoplakia	14	47
Polyp	9	30
Papilloma	3	10
Hyperkeratosis	2	7
Cyst	1	3
Anterior laryngeal web	1	3
Histology		
Polyp	8	27
Hyperplasia	6	20
Unknown*	4	13
Low grade dysplasia	3	10
Chronic inflammation	3	10
Papilloma	2	7
Hyperkeratosis	1	3
Matching laryngeal web (fibrosis)	1	3
Cyst	1	3
Masson's tumor	1	3
Completed procedures	29	97
Complications	0	0
No recurrent disease	19	66
Follow-up months (range)	9 (2–15)	
Voice Handicap Index (average)		
Prior (n)	44 (23)	
2 months postprocedure (n)	28 (21)	
6 months postprocedure (n)	14 (21)	

*Three patients had recurrent leukoplakia with a history of mild dysplasia, and one patient had suspicion of recurrent laryngeal papilloma.

TABLE II.
Patients With Residual/Recurrent Disease.

Patient	Age	Indication	Histology	Follow-up*	Examination	Management
Male	77 years	Leukoplakia	Chronic inflammation	7 months	Dysphonia: no FL: recurrent	Follow-up 4 months: complaints and FL unaltered, wait and see
Male	63 years	Leukoplakia	Hyperkeratosis	2 months	Dysphonia: no FL: residual	Follow-up 4 months: complaints and FL unaltered, wait and see
Male	75 years	Leukoplakia	Hyperplasia	7 months	Dysphonia: yes FL: recurrent	MLS laser: moderate dysplasia[†] Follow-up 10 months: no recurrence, wait and see
Male	63 years	Leukoplakia	No biopsy performed	4 months	Dysphonia: yes FL: residual	FEB + OBL: moderate dysplasia[†] Follow-up 8 months: recurrence FEB: lesion completely removed,[‡] improved voice, wait and see
Male	82 years	Leukoplakia	No biopsy performed	2 months	Dysphonia: yes FL: residual	MLS laser: moderate dysplasia[†] Follow-up 10 months: no recurrence, wait and see
Male	62 years	Papilloma	No biopsy performed	2 months	Dysphonia: yes FL: residual	FEB + OBL: papilloma Follow-up 5 months: residual Planned OBL (KTP)
Male	82 years	Leukoplakia	Hyperplasia	2 months	Dysphonia: yes FL: residual	Follow-up 2 months: improved voice Patient wishes no further follow-up

*Duration of follow-up upon which residual or recurrent pathology was detected.
[†]These histological outcomes are separated and thus not reported Table I.
[‡]This patient underwent FEB 3 days in advance, and on the initial day of OBL the lesion was not detectable during FL. Together with the patient, it was decided not to perform OBL and maintain a wait-and-see policy.
FEB = flexible endoscopic biopsy; FL = flexible laryngoscopy; KTP = Potassium-titanyl-phosphate laser; OBL = office-based laser.

fully completed. One male patient with suspicion of a polyp on the left true vocal cord developed a severe gag reflex after FEB. Even after additional laryngeal topical anesthesia, laser surgery could not be performed. Histology revealed a polyp. This patient was contacted 2 months after FEB and had an improved voice quality. Although suggested, the patient declined follow-up with flexible laryngoscopy in the outpatient clinic.

No complications occurred in 29 procedures. The VHI scores prior to the procedures were available in 23 of 29 patients and revealed a mean score of 44. Two months after the procedure, the mean VHI decreased to 28, which was statistically significant ($P = 0.032$). After 6-month follow-up, the mean VHI decreased to 14, which was also statistically significant compared to the VHI prior to office-based CO_2 laser surgery ($P < 0.001$). The difference in mean VHI score between 2 and 6 months postprocedural was not statistically significant ($P = 0.091$).

Nineteen patients (66%) had no residual or recurrent disease after a mean follow-up of 9 months (range 2–15 months). In seven patients, additional treatment was required due to residual or recurrent disease. Three patients had residual disease (histology showed chronic inflammation, hyperkeratosis, and hyperplasia, respectively) with minor or no complaints after a 2-month follow-up and were further observed with flexible laryngoscopy during regular visits. Two patients showed residual disease (histology was not obtained due to suspicion of recurrent disease) and were again treated in the office setting. Additional histology was performed prior the second office-based laser surgery treatment and revealed moderate dysplasia and laryngeal papilloma, respectively. Two patients had residual (no biopsy performed) and recurrent (histology showed hyperplasia) disease and were treated under general anesthesia. Both biopsies that were taken under general anesthesia revealed moderate dysplasia, and afterward patients underwent regular follow-up in the outpatient clinic. Table II displays each patient and their subsequent management.

DISCUSSION

Office-based laryngeal procedures in general have shown to be feasible, safe, and well tolerated by patients. They result in decreased time intervals to diagnosis and treatment and also reduce healthcare costs.[2,3,10,12–17] In patients with benign laryngeal pathology and a contraindication for general anesthesia or with a lesion inaccessible by rigid endoscopy (e.g., patients with limited neck extension or dental limitations), office-based CO_2 laser surgery is a minimally invasive therapeutic alternative. Additionally, in patients who have a strong preference for undergoing a procedure under topical anesthesia, office-based CO_2 laser surgery offers a valuable alternative. This study showed that office-based CO_2 laser surgery is feasible in almost all patients. Furthermore, it is a safe procedure, leads to subjective voice-quality improvement, and was successful in two-thirds of our study population.

A CO_2 laser operates on a wavelength of 10.6 μm and is well absorbed by tissues containing water. It therefore can be used to ablate and dissect tissue.[1] A possible consequence of the use of CO_2 laser surgery on vocal cords is thermal injury to the mucosa, which could have a negative influence on voice outcome. With the upcoming of office-based procedures, several other lasers have been investigated, such as the pulsed dye laser, KTP, and thulium laser.[3] However, studies on the application of the CO_2 laser in this setting are currently limited, although the application as such has been available for some time now.[6–8] In the evaluation of office-based CO_2 laser surgery, the effect on voice quality is important to investigate because worsening

of voice could negatively influence applicability of the procedure. To our knowledge, there is only one recent available prospective study in a small study population reporting on office-based CO_2 laser surgery.[9] Araki et al. prospectively investigated feasibility in 13 patients with benign and malignant laryngeal pathology. In 18 procedures that were performed, disease control was achieved in all except three patients with recurrent respiratory papilloma. The authors reported 100% completion rate, although two procedures were less successful due to a difficult accessible lesion and severe gag reflex. No complications occurred, and thus the authors concluded that the procedure was feasible. Furthermore, we found only one retrospective study that reported on voice outcome after office-based CO_2 laser surgery.[7] In 2017, Hu et al. concluded that office-based CO_2 laser surgery was feasible for benign laryngeal pathology. The authors described similar procedural completion rates (96%), residual disease in 12% of patients, and only one complication (mild vocal cord stiffness). Also, voice quality significantly improved, with decreasing VHI-10 and improving mean phonation time, jitter, and shimmer. These combined data demonstrate that office-based CO_2 laser surgery has a high procedural completion rate, holds few risks, and results in voice-quality improvement.

One of our goals was to provide a clear insight in patients with residual or recurrent disease. When reviewing the literature on office-based laser surgery, some studies reported results as a percentage of decrease of the pathology.[18–21] However, the goal of treatment, except for laryngeal papillomatosis, should be complete removal of pathology to avoid additional treatment and to be a valid alternative to surgery in the operating room. Our study demonstrated that two-thirds of the treated patients did not have residual or recurrent disease after 9-month follow-up. These patients were spared general anesthesia and day admission in the ward, with all its associated advantages. When there is doubt concerning histology of residual or recurrent disease, office-based FEB can be performed. In case of residual disease with complaints, office-based CO_2 laser surgery can be repeated or a treatment under general anesthesia can be performed. Conversely, in case of residual or recurrent disease without complaints, close follow-up is a viable alternative. Especially in case of laryngeal papillomatosis, for which patients usually require frequent treatment due to recurrent disease, office-based laser surgery is a suitable alternative to frequent laser treatments in the operating room under general anesthesia.

Limitations of this study were the selection bias that occurred after FEB. Because our goal was to study the feasibility of office-based CO_2 laser surgery, patients with malignant pathology were considered not suitable as a study population to start with and thus were excluded from this study. Furthermore, the VHI scores were missing in a portion of the study group. Although the VHI already significantly improved after office-based CO_2 laser surgery, an even more specific image could be obtained on voice-quality improvement if all VHI scores were available. No bias could be found as to why certain VHI scores were missing. No objective measurements on voice quality were performed. Thus, the possibility exists that these could differ from the subjective voice-quality improvement, although the patients' perspective on voice quality, and therefore a subjective measurement with, for example, the VHI score, is the most important outcome for the patient. A minimal follow-up of 6 months can be debated to be insufficient. We have no information on the duration of possible scar formation on the vocal cords after laser surgery, which could influence voice quality on a longer term.

Flaws in our study were a change of policy for topical anesthesia administration and timing of biopsy. In the first phase of the study, we used the injection technique through the cricothyroid membrane. Patients reported that this technique was uncomfortable, especially the brief feeling of severe dyspnoea that occurs directly after injection of the local anesthetic while the needle is being retracted from the larynx. Therefore, we chose a less invasive technique during the course of the study, which is described above. Our experience was that this technique is less uncomfortable for the patient and resulted in a more properly anesthetized larynx; therefore, it is currently our standard method of laryngeal anesthesia for office-based procedures. The procedure is usually well tolerated. In this study, there was one procedure that failed due to extensive coughing, which occurred in a patient anesthetized with the newer technique. Another change in policy during the study was the timing of performing FEB. During the starting phase of the study, FEB was performed just prior to CO_2 laser surgery in the same session. After FEB, minor bleeding occurs, which results in less optimal tissue penetration of the CO_2 laser. Therefore, during the course of the study the patients underwent FEB 3 days in advance. Although this resulted in more patient inconvenience because an extra outpatient clinic visit was required, CO_2 laser surgery was easier to perform, and histology was known prior to treatment.

To our knowledge, this is the largest prospective study and the only one prospectively investigating voice quality on office-based CO_2 laser surgery for benign and premalignant laryngeal lesions. Our findings are comparable to the results of other authors; together, these studies offer significant insight in how to perform office-based CO_2 laser surgery and hopefully will motivate other clinicians to start performing this procedure. In the nearby future, comparison between microlaryngoscopic and office-based CO_2 laser surgery with regard to effectiveness, costs, and patient experience should be investigated. Furthermore, in patients with small malignant glottic laryngeal carcinoma (i.e., T1a) with severe comorbidity or an inaccessible lesion during rigid microlaryngoscopy, office-based CO_2 laser surgery could be an alternative. Although this is a delicate study population, the usual alternative treatment modality is radiotherapy. Future studies should evaluate the value of office-based CO_2 laser surgery in this group of patients.

CONCLUSION

Office-based CO_2 laser surgery for benign and premalignant laryngeal lesions is a feasible and safe procedure that leads to significant voice-quality improvement. This procedure is an effective alternative treatment method, especially for patients in whom general anesthesia is

contraindicated and who have an inaccessible lesion during microlaryngoscopy or a strong preference for a procedure under topical anesthesia. Two-thirds of the patients did not require further treatment.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1983 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

BIBLIOGRAPHY

1. Zeitels SM, Burns JA. Laser applications in laryngology: past, present, and future. *Otolaryngol Clin North Am* 2006;39:159–172.
2. Wellenstein DJ, Schutte HW, Marres HAM, et al. Office-based procedures for diagnosis and treatment of esophageal pathology. *Head Neck* 2017;39:1910–1919.
3. Wellenstein DJ, Schutte HW, Takes RP, et al. Office-based procedures for the diagnosis and treatment of laryngeal pathology. *J Voice* 2018;32:502–513.
4. Devaiah AK, Shapshay SM, Desai U, et al. Surgical utility of a new carbon dioxide laser fiber: functional and histological study. *Laryngoscope* 2005; 115:1463–1468.
5. Zeitels SM, Kobler JB, Heaton JT, Faquin W. Carbon dioxide laser fiber for laryngeal cancer surgery. *Ann Otol Rhinol Laryngol* 2006;115:535–541.
6. Koufman JA, Rees CJ, Frazier WD, et al. Office-based laryngeal laser surgery: a review of 443 cases using three wavelengths. *Otolaryngol Head Neck Surg* 2007;137:146–151.
7. Hu HC, Lin SY, Hung YT, Chang SY. Feasibility and associated limitations of office-based laryngeal surgery using carbon dioxide lasers. *JAMA Otolaryngol Head Neck Surg* 2017;143:485–491.
8. Halum SL, Moberly AC. Patient tolerance of the flexible CO2 laser for office-based laryngeal surgery. *J Voice* 2010;24:750–754.
9. Araki K, Tomifuji M, Uno K, et al. Feasibility of transnasal flexible carbon dioxide laser surgery for laryngopharyngeal lesions. *Auris Nasus Larynx* 2019;46:772–778.
10. Wellenstein DJ, de Witt JK, Schutte HW, et al. Safety of flexible endoscopic biopsy of the pharynx and larynx under topical anesthesia. *Eur Arch Otorhinolaryngol* 2017;274:3471–3476.
11. Jacobson BH, Johnson A, Grywalski, et al., The Voice Handicap Index (VHI). *Am J Speech Lang Pathol* 1997;6:66–70.
12. Naidu H, Noordzij JP, Samim A, Jalisi S, Grillone GA. Comparison of efficacy, safety, and cost-effectiveness of in-office cup forcep biopsies versus operating room biopsies for laryngopharyngeal tumors. *J Voice* 2012;26:604–606.
13. Schutte HW, Takes RP, Slootweg PJ, et al. Digital video laryngoscopy and flexible endoscopic biopsies as an alternative diagnostic workup in laryngopharyngeal cancer: a prospective clinical study. *Ann Otol Rhinol Laryngol* 2018;127:770–776.
14. Lippert D, Hoffman MR, Dang P, McCulloch TM, Hartig GK, Dailey SH. In-office biopsy of upper airway lesions: safety, tolerance, and effect on time to treatment. *Laryngoscope* 2015;125:919–923.
15. Castillo Farias F, Cobeta I, Souviron R, et al. In-office cup biopsy and laryngeal cytology versus operating room biopsy for the diagnosis of pharyngolaryngeal tumors: efficacy and cost-effectiveness. *Head Neck* 2015;37:1483–1487.
16. 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.
17. Wellenstein DJ, Honings J, Schutte HW, et al. Cost analysis of office-based transnasal esophagoscopy. *Eur Arch Otorhinolaryngol* 2019;276:1457–1463.
18. Zeitels SM, Akst LM, Burns JA, Hillman RE, Broadhurst MS, Anderson RR. Office-based 532-nm pulsed KTP laser treatment of glottal papillomatosis and dysplasia. *Ann Otol Rhinol Laryngol* 2006;115:679–685.
19. 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.
20. Franco RA Jr. Aminolevulinic acid 585 nm pulsed dye laser photodynamic treatment of laryngeal keratosis with atypia. *Otolaryngol Head Neck Surg* 2007;136:882–887.
21. Sheu M, Sridharan S, Kuhn M, et al. Multi-institutional experience with the in-office potassium titanyl phosphate laser for laryngeal lesions. *J Voice* 2012;26:806–810.