Surgical and Voice Outcomes of Office-Based Vocal Fold Dysplasia and Leukoplakia Surgery: A Systematic Review☆

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SUMMARY: Objective. To investigate the surgical and voice quality outcomes of office-based laryngeal surgery for patients with laryngeal dysplasia and leukoplakia.

Data Sources. PubMed, Google scholar, and Cochrane databases.

Review Methods. Three independent investigator search databases for studies reporting surgical or voice quality outcomes of patients treated with office-based surgery for vocal fold dysplasia or leukoplakia. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were considered. Primary outcomes included patient tolerance, lesion regression, complications, number of interventions, and subjective and objective voice quality assessments. The bias analysis was carried out with the Methodological Index for Non-Randomized Studies (MINORS).

Results. Fourteen studies were included, accounting for 186 patients with vocal fold leukoplakia and 72 patients with dysplasia. Potassium-Titanyl-Phosphate (KTP), Pulsed Dye Laser (PDL), and Blue Laser were the most used lasers. Office-based leukoplakia and dysplasia surgery was associated with a cumulative complication rate of 2.3% and 1%, respectively and a high patient tolerance level. Repeat treatment was needed in 12%-58.7% of patients for persistent disease noted at the first follow-up; overall, 39% of patients required more than one procedure. Subjective voice quality and some acoustic measurements demonstrated significant pretreatment to post treatment improvements but only one study considered multidimensional voice quality evaluation. There was substantial heterogeneity across studies for inclusion criteria, surgical, and voice quality outcomes.

Conclusion. Office-based laser surgery is a safe and effective treatment for vocal fold dysplasia and leukoplakia leading to complete or partial disease regression in most cases. Future investigations should consider multidimensional voice quality assessment protocols to evaluate longitudinal voice quality outcomes. Heterogeneity among included studies and limited reporting of procedural approach represent the primary limitations of this review.

Key Words: Voice–Otolaryngology Head Neck Surgery–Otorhinolaryngology–Dysplasia–Leukoplakia–Laser.

INTRODUCTION

Leukoplakia of the vocal folds is a common condition in otolaryngology—head and neck surgery, ranging in prevalence between 2.1 and 10.2 per 100 000 persons.[1] In a cohort that included 2019 patients with voice disorders, leukoplakia accounted for 3.12% of the study population.[2] One of the main concerns in vocal fold leukoplakia is the risk of dysplasia or malignant transformation. Based on a review of 208 leukoplakia biopsies, Isenberg *et al* noted dysplastic changes in approximately 50% of the cases.[3] Dysplasia and leukoplakia represent significant therapeutic challenges. These conditions necessitate careful surgical evaluation, as overly aggressive resection carries substantial risk of compromising postoperative vocal function and quality—a critical consideration given the premalignant rather than invasive neoplastic nature of these lesions.[4,5] According to previous research results, the malignant risks of vocal fold leukoplakia in patients with a pathological diagnosis of mild, moderate, and severe dysplasia reached 11%, 33%, and 57% of cases, respectively.[6] To date, the treatment ranges from a conservative approach (surveillance), including strict voice rest, smoking and alcohol cessation, inhaled glucocorticoid therapy, and anti-reflux therapy, to cold or laser laryngeal microsurgery.[4,7] With the advent of office-based laser technologies, an increasing number of investigations have been conducted to evaluate the safety and feasibility of in-office surgical treatment for laryngeal leukoplakia and dysplasia, reporting both surgical and functional outcomes.

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The aim of this systematic review was to investigate surgical and voice quality outcomes of office-based laryngeal surgery management protocols for patients with laryngeal dysplasia and leukoplakia.

METHODS

Three independent investigators conducted the systematic review and data collection (M.M., J.R.L., and S.H.) following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[8] The criteria for study inclusion and exclusion were based on the population, intervention, comparison, outcome, timing, and setting (PICOTS) framework.[9]

Types of studies

Retrospective case series, uncontrolled and controlled prospective studies published between January 2000 and January 2025 were considered if they investigated surgical or voice quality outcomes of office-based laser procedures for vocal fold leukoplakia and dysplasia. Included studies were published in English or French in peer-reviewed journals. The following lasers were considered: photoangiolytic lasers [Potassium-Titanyl-Phosphate (KTP), Pulsed Dye Laser (PDL), and true blue laser] and cutting lasers [Carbon Dioxide Laser (CO_2)].

Populations, inclusion, and exclusion criteria

Populations consisted of adults with a diagnosis of vocal fold leukoplakia or dysplasia confirmed by videolaryngostroboscopy or histopathological examination. Studies were required to report inclusion/exclusion criteria, patient demographics, diagnostic criteria for leukoplakia or dysplasia, eligibility criteria, laser parameters and surgical technique, and outcome measures. Studies involving pediatric populations or malignant lesions were excluded from this review.

Outcomes

The following general outcomes were reviewed: study design, number of patients, and demographics (eg, mean/median age, gender, and body mass index). Primary outcomes included surgical and voice quality evaluations. Surgical outcomes consisted of safety, number of interventions, partial or total lesion regression, complications, laser setting, tolerance, and pain. Based on the European consensus guidelines for voice quality assessment,[10] voice quality outcomes included self-reported voice quality questionnaires (eg, Voice Handicap Index (VHI),[11] VHI-10[12]), perceptual evaluations (eg, Grade of dysphonia, Roughness, Breathiness, Asthenia, Strain (GRBAS),[13] Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V)[14]), stroboscopic evaluation of the vocal folds, aerodynamics (eg, maximum phonation time (MPT), phonatory quotient), and acoustic measurements [eg, fundamental frequency F0, percent jitter, percent shimmer, noise-to-harmonic ratio (NHR), and Voice Turbulence Index (VTI)].[10] For acoustic and aerodynamic assessments, the method for determining the outcomes was investigated (eg, types of sustained vowels, number of sustained vowels, and part of the vowel where the acoustic parameters were measured).

Intervention and comparison

The investigators considered only studies reporting findings of office-based laser surgery for vocal fold leukoplakia or dysplasia. The data of controlled study comparing office-based laser surgery versus transoral laser microlaryngeal surgery were considered.

Timing and setting

There were no criteria for specific stage or timing in the “disease process” of the study population.

Search strategy

The search was conducted through PubMed, Google Scholar, and Cochrane databases to identify studies evaluating surgical and voice quality outcomes of office-based laser surgery for vocal fold leukoplakia and dysplasia. The keywords included: “blue laser,” “KTP,” “PDL,” “office-based,” “in-office,” “laryngeal lesion,” “voice,” “procedure,” “dysplasia,” “leukoplakia,” “keratosis,” and “premalignant.” Results of the search strategy were reviewed for relevance and the reference lists of these articles were examined for additional pertinent studies. Each selected study was reviewed to exclude overlapping publications through the analysis of the following parameters: study design, number of patients, gender distribution, age (mean/median), lesion characteristics, and reported outcomes.

Bias analysis

The bias analysis was carried out with the Methodological Index for Non-Randomized Studies (MINORS) tool, which is a validated instrument designed for assessing the quality of nonrandomized surgical studies, whether comparative or noncomparative.[15] The MINORS consists of 12 items related to the analysis of methodological points of comparative and non-comparative studies. The items were scored 0 if absent; 1 when reported but inadequate; and 2 when reported and adequate. The aim of the study was rated as clearly stated (2), unclear (1), or absent (0). The inclusion of patients was evaluated in terms of consecutive inclusion (0 or 2), while the prospective data collection was rated as perfectly prospective (2), retrospective analysis of prospective recruited patients (1), or absent (0). The quality of endpoints was judged as high (2) when authors evaluated both subjective and objective outcomes, stroboscopy, and surgical outcomes. The evaluation of surgical outcome only, or partial evaluation of voice quality, was judged as incomplete (1). According to the time of tissue healing and the timing of occurrence of early and delayed complications related to procedures and the risk of recurrence, a

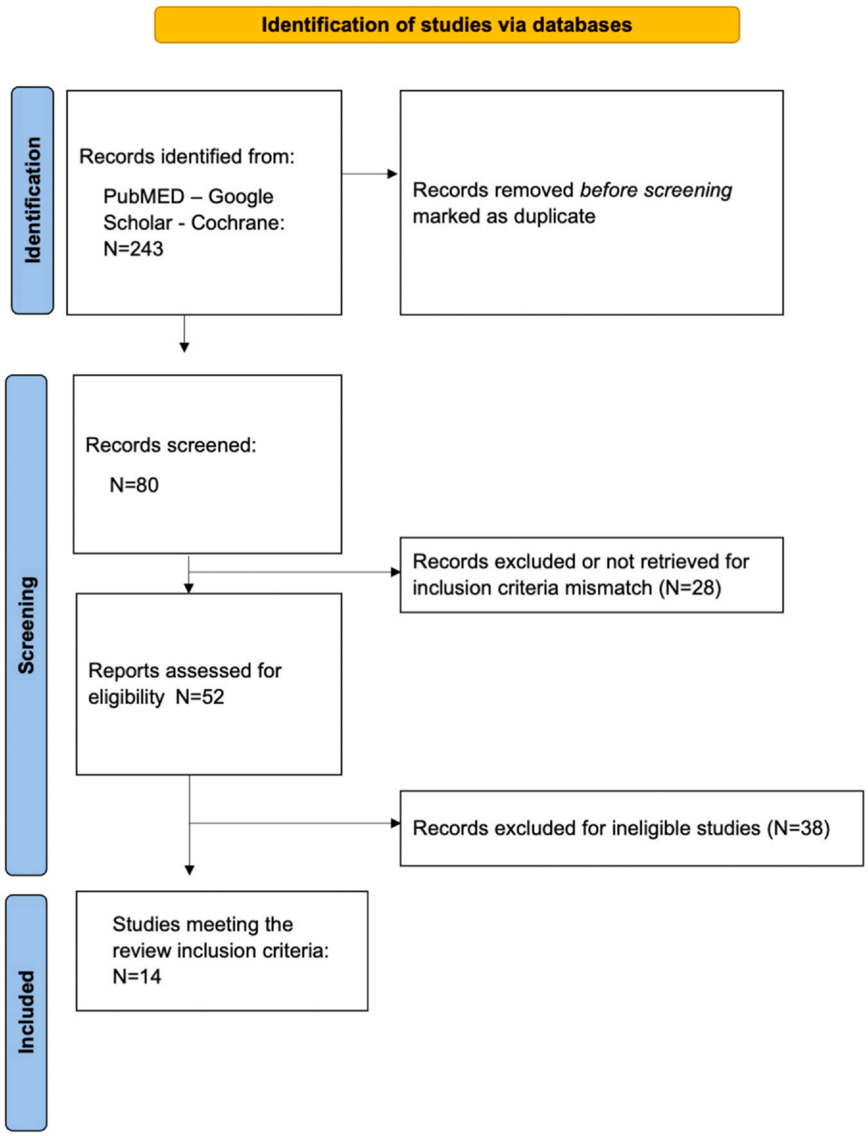

FIGURE 1. Flow chart.

follow-up period of 3 months was considered as adequate. Finally, the 5% rate of lost-to-follow-up patients was considered as the threshold in the MINORS. The ideal MINORS score was 16 for noncomparative studies and 24 for comparative studies.[15]

RESULTS

Of the 243 retrieved publications, 14 studies met the inclusion criteria (Figure 1). There were 10 retrospective,[16–25] one controlled prospective,[26] and three uncontrolled prospective studies (Table 1).[27-29] Leukoplakia and dysplasia data were extracted from studies reporting multiple vocal fold lesion findings in eleven studies (905 patients).[17-20,22,27,28] Surgical or voice quality findings were reported for 149 patients with vocal fold leukoplakia and 105 patients with dysplasia (Table 2). The majority of subjects were male, with mean ages ranging from 48.9 to 70.7 years (Table 2). KTP (n = 6), PDL (n = 5), and Blue Laser (n = 4) were the most used lasers in office-based procedures (Table 3).

Surgical outcomes

Surgical outcomes were reported in most studies, primarily consisting of postoperative partial or total lesion regression,[16,19-26,28,29] influence of anxiety and depression on office-based procedures,[27] and patient tolerance (Table 4).[17,18,26,27] Hamdan et al investigated the anxiety and depression in patients selected for office-based procedure. They found no significant association between patient tolerance and vital sign parameters, although there was a significant increase in mean heart rate, systolic and diastolic blood pressures, and a significant decrease in oxygen saturation during the office-based procedure.[27] The level of patient tolerance during the office-based procedure was evaluated with visual analog scale

TABLE 1.
Study Features

References	Design	Disease	Patients (N)	M/F	Age (y)	Laser	Setting	Interventions (N)	Outcomes	Results	Follow-Up
Hamdan et al, 2024[27]	Uncontrolled	Multiple VF	45	25/20	48.9	Blue laser	NP	NP	HR, ST, and DT	OB > post-op	5 minutes
	Prospective	Lesions	8 LE			(445 nm)			GAD-7/PHQ-9—vital signs	No correlation	
Hamdan et al, 2023[16]	Retrospective	Leukoplakia	10 (12 VF)	7/3	64.8	Blue laser	10 W	Single: $n = 9$	VHI-10, GRBAS, and VLS	pre > post	9 months
						(445 nm)	30-ms pulse	Two: $n = 3$	Jitter and shimmer	pre > post	
							300-ms I-pulse		Maximum phonation time	post > pre	
Hamdan et al, 2023[17]	Retrospective	Multiple VF	48	26/22	54.0	Blue laser	NP	Single: $n = 10$	IOWA anesthesia tolerance score	no-SMO > SMO	NP
		Lesions	10 LE			(445 nm)				Cyst > polyps; BLVF = LE	
									Tolerance =-swallowing VAS, VFM	Negatively correlated	
Zheng et al, 2021[18]	Retrospective	Multiple VF	56	42/14	61.0	KTP 532 nm	NP	NP	Tolerance (VAS)	PL > NPL—SM-O > no-SMO polyp/ cyst > RRP > RE- > DY	NP
		Lesions	9 DY								
Hamdan and Ghanem, 2021[19]	Retrospective	Multiple VF	11	8/3	55.2	Blue laser	10 W	Single: $n = 2$	Complete/ partial regression	50-50%	1.75 months
		Lesions	1 LE, 1 DY			(445 nm)			VHI-10—VAS voice quality	pre > post	
									Complicati-on rate	0%	

TABLE 1 (*Continued*)

References	Design	Disease	Patients (N)	M/F	Age (y)	Laser	Setting	Interventions (N)	Outcomes	Results	Follow-Up
Hu et al, 2017[20]	Retrospective	Multiple VF	40	28/12	56.0	CO_2 laser	5-10 W—0.05 second	1 or 2 N > 1: 3/16	VLS lesion regression	n = 9/11	10 months
		Lesions	1 LE 8 DY				on/0.01 second off-t				
Koss et al, 2017[21]	Retrospective	Leukoplakia	46	45/1	70.7	KTP or PDL	KTP: 32.5 W	Med: 2	Complete regression	41.3%	19.6 months
							15.0 ms	N > 1: 12/46	OB, OR, and RT failure trt	26-28.3-4.3%	
									VHI-10	pre > post	
Del Signore et al, 2016[22]	Retrospective	Multiple VF	255	145/110	49.0	KTP or PDL	NP	Single = 73%	Complication rate	4.3%	10 months
		Lesions	33 LE					Two = 27% 39% -> OR	Lesion regression	61%	
Sheu et al, 2012[23]	Retrospective	Multiple VF	102	NP	56.0	KTP 532 nm	NP	NP	VLS lesion reduction	+	2.0-4.9 months
		Lesions	37 LE						Mucosal wave/glottic closure	> 90%	
Mallur et al, 2011[24]	Retrospective	Multiple VF	32	NP	NP	KTP 532 nm	25-W	Two: n = 7	Lesion regression	+(1 mo)	12 months
		Lesions	1 LE				pulse: 20 ms				
Halum and Moberly, 2010[26]	Controlled	Multiple VF	10	6/4	57.2	CO_2 laser vs	CO_2: 4-W co	1	VLS lesion regression	n = 1/2 (50%)	1 months
	Prospective	Lesions	2 LE			PDL			Tolerance (pain/burning-/10)	CO_2 = PDL (2 vs 3/10)	
Koufman et al, 2007[25]	Retrospective	Multiple VF	151	NP	PDL: 55	PDL (n = 406)	NP	Mean = 3.2 5/25-> OR	Complication rate (PDL)	0.9%	16 months
		Lesions	25 DY			CO_2 (n = 10)			Total lesion regression	80% (DY)	
						Tm:YAG (n = 27)			VHI reduction	n = 20/25	

TABLE 1 (*Continued*)

References	Design	Disease	Patients (N)	M/F	Age (y)	Laser	Setting	Interventions (N)	Outcomes	Results	Follow-Up
Zeitels et al, 2006[28]	Uncontrolled Prospective	Multiple VF Lesions	48 28 DY	NP	NP	KTP 532 nm	NP	NP	VLS lesion regression (%) (DY only)	>75%: 62% 50-75%: 24% 25-50%: 14%	4-8 weeks
Zeitels et al, 2004[29]	Uncontrolled Prospective	Dysplasia	51 34 DY	NP	NP	PDL 585 nm	NP	NP	VLS lesion regression (%)	>50%: 88% 25-50%: 12%	4-8 weeks

Abbreviations: BLVF, benign lesion of the vocal folds; co, continuous; DT, diastolic tension; DY, dysplasia; HR, heart rate (mean); I-pulse, interpulse; LE, leukoplakia; Med, median; mo, month(s); NP, not provided; NPL, nonposterior lesions; OB, office-based; off-t, off-timing; OR, operating room; PL, posterior lesions; pro, procedure; RE, Reinke edema; RRP, recurrent respiratory papillomatosis; RT, radiotherapy; SMO, smokers; ST, systolic tension; trt, treatment; VAS, visual analog scale; VF, vocal folds; VFM, vocal fold movements; W, watts.

TABLE 2.
Study Demographic and Laser Outcomes

Outcomes	Number	Studies
Number of patients (%)		
Vocal fold lesions (total number)	905	
Leukoplakia	149	
Dysplasia	105	
Gender		
Females/males	189/332	
Unspecified	384	
Mean age (years)	48.9-70.7	
Types of lasers		
KTP (532 nm)	6	19,22,23,24,25,28
PDL (585 nm)	5	22,23,26,27,29
Blue laser (455 nm)	4	16,17,18,20
CO_2	3	21,26,27
Tm:YAG	1	27

Abbreviations: KTP, potassium-titanyl-phosphate (532 nm); PDL, pulsed dye laser (585 nm); Blue laser (455 nm); CO_2, carbon dioxide; Tm:YAG, thulium: yttrium aluminum garnet.

(VAS) in two studies,[18,26] which reported high tolerance of patients undergoing CO_2 or PDL lesion resection (Table 4).

Hamdan et al demonstrated that patients with leukoplakia and Reinke's edema exhibited lower tolerance to treatment, though no statistically significant differences were observed when compared with other benign vocal fold lesions.[17] Conversely, Zheng et al reported that dysplastic lesions were associated with the poorest tolerance among all vocal fold pathologies studied, with further decreased tolerance observed in smokers and patients with posterior laryngeal lesions.[18]

Laser parameters varied considerably across studies (Table 3). For leukoplakia, blue laser (445 nm) was used in four studies with average energy delivery of 131.53 J at 10 W.[16,17,19,27] PDL laser (585 nm) delivered an average energy of 201.25 J,[21,22] while KTP laser (532 nm) was employed at 25-32.5 W,[21,24] with total energy estimated at 183.5 J in two studies.[21,22] CO2 laser power ranged from 4 to 10 W.[20,26] For dysplasia treatment, blue laser (445 nm) was set at 10 W,[19] PDL (585 nm) delivered 0.6-1 J/pulse,[25,29] and KTP (532 nm) delivered a mean energy of 525-750 mJ/pulse in one study.[28]

The complications related to the office-based procedures were described in 11 studies (Table 5).[16,19-23,25-29] The cumulative complication rate for office-based procedures treating leukoplakia and dysplasia was 2.3% and 1%, respectively. The 17 reported complications included prolonged hyperemia ($n = 7$ patients), vocal fold wound stiffness ($n = 2$ patients), vocal fold atrophy ($n = 2$ patients), swallowing or inhalation of laser fiber fragments ($n = 2$ patients), vocal fold hemorrhage ($n = 2$ patients), and epistaxis ($n = 2$ patients).

Voice quality outcomes

Voice quality outcomes are reported in Tables 1 and 2. Practitioner stroboscopic evaluation (unblinded) from pretreatment to post treatment was the most reported

TABLE 3.
Laser Parameters and Surgical Technique

Study	Laser Type	Patients (*N*)	Setting	Energy Delivered	Comments
Hamdan et al, 2024[27]	Blue laser	45 8 LE	NP	-	-
Hamdan et al, 2023[16]	Blue laser	10 (12 VF LE)	10 W 30-ms pulse 300-ms I-pulse	147.2 J	Near-contact and contact modes
Hamdan et al, 2023[17]	Blue laser	48 10 LE	NP	Mean 115.86 J ± 82.5 J For 29/48 patients	Mean total duration: 10.38 ± 4.8 minutes
Zheng et al, 2021[18]	KTP	56 9 DY	NP	-	-
Hamdan and Ghanem, 2021[19]	Blue laser	11 1 LE 1 DY	10 W 30-ms pulse 300-ms I-pulse	-	Contact mode
Hu et al, 2017[20]	CO_2	40 1 LE 8 DY	5-10 W—0.05 seconds ON/ 0.01 seconds OFF	-	Lesions on the free edge of VF →3 W. Use of a saliva ejector
Koss et al, 2017[21]	KTP/PDL	46 LE	KTP: 32.5 W, 15-ms pulse	KTP: 124 J PDL: 159.5 J	-
Del Signore et al, 2016[22]	KTP/PDL	255 37 LE	-	Responders: 243 J Failures: 337 J	Pulse-stacking technique→ photothermolysis Direct thermal effect for LE
Sheu et al, 2012[23]	KTP	102 37 LE	NP	-	-
Mallur et al, 2011[24]	KTP	32 1 LE	25 W 20 ms ON 2 pulse/sec	-	-
Halum and Moberly, 2010[26]	CO_2, PDL	10 2 LE	CO2: 4-W co PDL: 1 J/pulse	-	Lesions on phonatory surface of the VF: CO_2 → 2 W and PDL → 0.75 J/pulse Lesions off the free edge of the VF→ CO_2 laser was ↑ (range 4-16 W).
Koufman et al, 2007[25]	PDL (406) CO_2 (10), Tm:YAG (27)	151 25 DY	PDL: mean 1 J/pulse	Mean 117 ± 68 J	-
Zeitels et al, 2006[28]	KTP	48 28 DY	15 ms ON 2 Hz	525-750 mJ/pulse	-
Zeitels et al, 2004[29]	PDL 585 nm	51 34 DY	450 μs ON 2 Hz	600-800 mJ/pulse	*Photocoagulation mode. *Area treated: lesion ± 5-mm margins *Contact mode and ± 2-mm distance *Endpoints: photocoagulation, visible blanching, and/or separation of the epithelial lesion

Abbreviations: Blue laser (455 nm), CO_2, carbon dioxide; DY, dysplasia; J, joule; KTP, potassium titanyl phosphate (532 nm); LE, leucoplakia; NP, not provided; PDL, pulsed dye laser (585 nm); VF, vocal fold; W, watt; Tm:YAG, thulium:yttrium aluminum garnet.

TABLE 4.
Surgical and Voice Quality Outcomes

Outcomes	Number of Studies	References	Overall Trends
Voice outcomes			
Subjective voice quality			
VHI-10	3	[16,19,21]	Pre > post treatment
VHI	1	[25]	Pre > post treatment
GRBAS	1	[16]	Pre > post treatment
VAS	2	[19]	Better postoperative voice quality
Objective voice quality			
Percent jitter	1	[16]	Pre > post treatment
Percent shimmer	1	[16]	Pre > post treatment
NHR	1	[16]	Pre = post treatment
VTI	1	[16]	Pre = post treatment
MPT	1	[16]	Post > pretreatment
Stroboscopy evaluation			
Unspecified VLS lesion evaluation	11	[16,19-24,26,25,28,29]	Postoperative partial or total regression
Mucosal wave	1	[23]	Higher postoperative amplitude
Glottic closure	1	[23]	Better postoperative closure
Perioperative and tolerance outcomes			
GAD-7-PHQ-9	1	[27]	Not associated with surgical outcomes
Vital signs (HR, ST, and DT)	1	[27]	Increased during office-based procedures
IOWA anesthesia tolerance score	1	[17]	Better in nonsmokers and when treating cysts
Swallowing tolerance	1	[17]	Negatively associated with IOWA score
Tolerance (pain/burn—VAS)	2	[18,26]	Comparable between CO_2 and PDL

Abbreviations: CO_2, carbon dioxide; DT, diastolic tension; GAD-7, Generalized Anxiety Disorder 7-item scale; GRBAS, Grade, Roughness, Breathiness, Asthenia, Strain scale; HR, heart rate; IOWA, Iowa Satisfaction with Anesthesia Scale; MPT, maximum phonation time; NHR, noise-to-harmonic ratio; PDL, pulsed dye laser; PHQ-9, Patient Health Questionnaire 9-item scale; ST, systolic tension; VAS, visual analog scale; VHI, Voice Handicap Index; VHI-10, Voice Handicap Index 10-item version; VLS, videolaryngostroboscopy; VTI, Voice Turbulence Index.

TABLE 5.
Complications

Study	Complication Rate	Sample Size	Laser Type	Types of Complications
Hamdan et al, 2024[27]	0% (0/45)	45 patients	Blue laser	-
Hamdan et al, 2023[16]	0% (0/10)	10 patients	Blue laser	-
Hamdan et al, 2023[17]	NP	48 patients	Blue laser	NP
Zheng et al, 2021[18]	NP	56 patients	KTP	NP
Hamdan and Ghanem, 2021[19]	0% (0/11)	11 patients	Blue laser	-
Hu et al, 2017[20]	2% (1/49 procedures)	40 patients (49 procedures)	CO_2	Mild vocal fold wound stiffness
Koss et al, 2017[21]	0% (0/46)	46 patients	KTP/PDL	-
Del Signore et al, 2016[22]	4.3% (11/255)	255 patients	KTP/PDL	Stiffness ($n=1$), atrophy ($n=2$), transient but prolonged hyperemia ($n=7$), and swallowed piece of glass ($n=1$)
Sheu et al, 2012[23]	0% (0/102)	102 patients	KTP	-
Mallur et al, 2011[24]	NP	32 patients (47 procedures)	KTP	NP
Halum and Moberly 2010[26]	0% (0/10)	10 patients	CO_2, PDL	-
Koufman et al, 2007[25]	0.67% (3/443)	443 procedures	PDL (406)	Vocal fold hemorrhages ($n=2$)
			CO_2 (10), Tm:YAG (27)	PDL fiber tip broke off in the trachea ($n=1$)
Zeitels et al, 2006[28]	0%	36 dysplasia cases	KTP	-
Zeitels et al, 2004[29]	3.9% (2/51)	51 patients	PDL 585 nm	Epistaxis ($n=2$)

Abbreviations: KTP, potassium titanyl phosphate (532 nm); NP, not provided; PDL, pulsed dye laser (585 nm); Blue laser (455 nm); CO_2, carbon dioxide; YAG, yttrium aluminum garnet.

outcome measure ($n = 11$ studies),[16,19-26,28,29] with varying definitions of partial and complete lesion regression. Studies suggested that lesion regression can be observed at 1 month post treatment. Re-intervention rates varied considerably between studies and lesion types. Among patients with leukoplakia, two studies[16,21] reported a rate of in-office re-intervention of 25% and 26%, respectively. Subsequent operating room intervention was required in 28.3% to 39% of leukoplakia patients.[21,22] For dysplastic lesions, one study reported that 20% of patients required additional operating room procedures.[25] Hu et al reported an overall re-intervention rate of 18.75% without distinguishing between leukoplakia and dysplasia groups.[20] The available data suggest that fewer than 39% of patients required multiple treatment sessions[16,20–22,25] (Table 1).

Other stroboscopic findings included assessment of vocal fold wave and glottic closure.[23] Subjective voice quality was evaluated in four studies, reporting significant improvements of VHI, VHI-10, GRBAS, and VAS.[16,19,21,25] Objective voice quality was evaluated from pretreatment to post treatment in one study.[16] Hamdan et al demonstrated significant improvements of percent jitter, percent shimmer, and MPT 9 months postprocedure.[16] This was the only study that considered both subjective and objective voice quality evaluations (Table 4).

Bias analysis

The mean MINORS was 7.1 ± 1.6, suggesting low-to-moderate quality of studies (Table 6). The inclusion and exclusion criteria were specifically provided in only five studies.[16,21,23,24,26] Comorbidities potentially influencing both surgical and voice quality outcomes were reported in only a few studies. Specifically, patients with smoking history were documented in six studies,[17-19,21,26,27] while reflux disease was reported in only two studies without use of objective diagnostic approach (hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring).[17,27] Similarly, postoperative care, including anti-reflux therapy, was not specified in studies. No study evaluated patients' voice abuse patterns or voice behavior from pretreatment to post treatment. Additionally, none of the studies reported recommendations for postoperative speech therapy. Because of retrospective design, most studies did not consider prospective inclusion of consecutive patients, which substantially influence the MINORS. Some studies excluded patients if their follow-up was incomplete or insufficient.[21,24] The low mean MINORS score was primarily attributable to insufficient reporting of lost-to-follow-up patient percentages and biased endpoint assessment methodologies in most studies. Specifically, studies failed to implement blinded stroboscopic evaluations and did not consider both subjective and objective voice quality assessment measures. Finally, there was no study reporting sample size calculation, although some acknowledged the small sample size as a limitation that affected the generalizability of their results. According to the standardized adequate MINORS score of 16 for noncomparative

TABLE 6.
Bias Analysis

References	Clearly Stated Aim	Inclusion of Consecutive Patients	Prospective Data Collection	Endpoints Appropriate to Study	Unbiased Endpoint Assessment	Follow-Up Adequate Period	<5% of Lost to Follow-Up	Sample Size Calculation	Total MINORS Score
Hamdan et al, 2023[17]	2	0	0	2	1	2	0	0	7
Hamdan et al, 2024[27]	2	2	2	2	1	1	0	0	10
Koss et al, 2017[21]	2	0	0	2	1	2	0	0	7
Hamdan et al, 2023[16]	2	0	0	2	2	0	0	0	6
Del Signore et al, 2016[22]	2	0	0	2	1	2	0	0	7
Hamdan and Ghanem, 2021[19]	2	0	0	2	1	1	0	0	6
Koufman et al, 2007[25]	2	0	0	2	1	2	2	0	9
Halum and Moberly, 2010[26]	2	0	1	2	1	1	0	0	7
Hu et al, 2017[20]	2	0	0	2	1	2	2	0	9
Zeitels et al, 2004[29]	0	0	1	2	1	1	0	0	5
Zheng et al, 2021[18]	2	0	0	2	1	0	0	0	5
Sheu et al, 2012[23]	2	0	0	2	1	2	0	0	7
Mallur et al, 2011[24]	2	0	0	2	1	1	0	0	6
Zeitels et al, 2006[28]	2	0	1	2	1	1	2	0	9

Abbreviations: Methodological Index for Non-Randomized Studies.

studies, the current bias analysis reports that there is no high-quality study conducted in the office-based management of vocal fold leukoplakia and dysplasia. Finally, it is important to note that the patient cohorts in the two publications by Hamdan et al[16,17] are indeed independent even if dates of treatment may overlap. Specifically, the 10 patients included in Hamdan et al[16] were not previously reported or included in any prior publication—including Hamdan et al[17]—as explicitly stated by the authors.

DISCUSSION

Office-based laser therapy is currently considered a reliable and cost-effective surgical approach for epithelial and premalignant lesions of the vocal fold, avoiding general anesthesia-associated risks (eg, cardiopulmonary complications, postoperative nausea/vomiting, and cognitive dysfunction) while reducing healthcare expenditures, minimizing procedural duration, and accelerating patient recovery.[30,31] The surgical management of vocal fold leukoplakia and dysplasia requires adequate ablation and/or resection with margin assessment regarding the risk of malignancies, which increases with the grade of dysplasia. Consequently, these procedures have historically been conducted in operating room rather than ambulatory clinical settings.

The primary findings of this systematic review support that office-based laser surgery represents a safe and effective treatment modality for vocal fold leukoplakia and dysplasia leading to disease regression and improvement in voice outcome measures. However, the generalizability of these findings remains limited by significant methodological biases identified in the current literature.

First, for patients with vocal fold leukoplakia, some studies[17,19,22-24,27] did not specify whether a prior histopathological examination was conducted to confirm the diagnosis. Consequently, it is not possible to ascertain if patients with a clinical diagnosis of leukoplakia had underlying dysplasia in the absence of biopsy confirmation. In the context of our systematic review, prior histopathological examination would have been preferable to differentiate leukoplakia and dysplasia, as their respective outcomes were analyzed separately in this study. However, to date, no studies have specifically investigated the use of in-office laser surgery in in situ glottic carcinoma nor defined clear selection criteria for the office-based management of malignant vocal fold lesions. In clinical practice, when there is diagnostic uncertainty, the operating room resection or the in-office biopsy prior to proceeding with in-office laser surgery may be recommended, with treatment modality adapted according to the histopathological findings. Previous studies have demonstrated a reasonable concordance between histological diagnoses obtained through office-based biopsy and those obtained via direct microlaryngoscopy under general anesthesia.[32–34]

Second, although most authors have demonstrated partial or total regression of leukoplakia and dysplasia in the months following office-based laser procedures, predictors of incomplete lesion regression and subsequent need for further treatment remain unidentified. Some of these may relate to incomplete treatment in the office setting; however, even with complete treatment in the office or operating room, it is known that these pathologies often recur—the recurrence rate of leukoplakia ranges from 9.5% to 46.4%—[35]and that serial evaluation and repeat treatment are often needed over time.[36] Tobacco consumption and laryngopharyngeal reflux disease (LPRD) have been established etiological factors for leukoplakia, dysplasia, and related recurrences,[37–39] but studies provide minimal information regarding the prevalence and management of these conditions from preoperative through postoperative care. Tobacco and LPRD can influence surgical and voice quality outcomes of office-based surgery through multiple mechanisms. Tobacco consumption exhibits similar deleterious effects on vocal fold healing and likely constitutes an important factor with adverse effects on office-based laser laryngeal surgery for vocal fold dysplasia and leukoplakia cases.[39] Hamdan et al[17] and Zheng et al[18] demonstrated that smokers exhibited significantly lower procedural tolerance than nonsmokers, potentially compromising the efficacy of surgery and treatment outcome. From a voice quality perspective, refluxate exposure of upper aerodigestive tract mucosa is associated with epithelial injury, inflammation, significant reduction of epithelial defense mechanisms, and impaired healing processes.[40] In both operating room and office-based benign vocal fold lesion procedures, postoperative voice quality is therefore undoubtedly influenced by LPRD management—information frequently unreported in most studies.

Third, detail on treatment approach and technique description is lacking or absent in the reviewed studies (Table 3). When KTP laser is being used, no study reported the tissue interaction targeted using the KTP laser effect Mallur Classification System.[41]

Moreover, the methodology for assessing postoperative voice quality represents a significant area requiring improvement in future investigations. In most studies, clinicians evaluated vocal fold lesion regression in the postprocedure weeks through nonblinded assessments, while they did not use multidimensional subjective and objective voice quality outcome measurements. Current consensus statements and expert papers recommend using a multidimensional approach to reliably evaluate presurgical to postsurgical voice quality outcomes, including both subjective and objective assessment modalities.[10,40]

The implementation of short- to long-term multidimensional voice quality evaluation protocols could yield valuable insights regarding the efficacy of office-based leukoplakia/dysplasia surgery and its comparative performance against operating room procedures. Among the multidimensional voice quality assessment, practitioners commonly assess the patient vocal habits as phonotraumatic habits (vocal abuse) can be contributing factors to vocal fold microtrauma and subsequent development of some benign vocal fold lesions.[42] Phonotraumatic behaviors and related risk of impaired vocal fold mucosa healing can be addressed through preoperative and postoperative voice and speech therapy interventions,[43] though recommendations regarding such therapeutic management represent another lacking information in the current literature.

On the other hand, the absence of controlled randomized studies comparing office-based versus operating room procedures for vocal fold leukoplakia and dysplasia surgery is a significant methodological limitation. Demonstrating the added value of office-based surgery despite its limitations compared with operating room procedures remains important. Indeed, the comparative cost profiles of both surgical settings warrant careful consideration within the context of diminishing governmental healthcare expenditures.

Rees et al[43] estimated cost savings of approximately $5000 per case when selecting office-based settings. Similarly, Miller and Gardner[44] documented a cost differential approaching $9000 between office-based procedures and their operating room counterparts. However, these financial advantages were partially offset by the increased frequency requirement for office-based interventions—approximately three times more frequent than operating room procedures. In patients with recurrent respiratory papillomatosis, Filauro et al[45] identified a cost difference of 1392 euros favoring office-based management over operating room approaches.

The heterogeneity across studies regarding inclusion criteria, types of laser and related settings, surgical and voice quality outcome parameters, and follow-up protocols constitutes the primary limitation of the present review, limiting the drawing of valid conclusion. The relatively small sample sizes in reported case series represent an additional methodological limitation.

CONCLUSION

Office-based laser surgery is a safe and effective treatment for vocal fold dysplasia and leukoplakia leading to complete or partial disease regression. Future investigations should incorporate multidimensional voice quality assessment protocols to evaluate longitudinal short- to long-term voice quality outcomes and related recurrence factors. Heterogeneity among included studies and limited reporting of procedural approach represent the primary limitations of this review.

Author Contributions

Meryem Miri: design, final approval, and accountability for the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. **Abdul-Latif Hamdan, Clemence Forges, Robin Baudouin, Tiffany Rigal, Kathy Huet, Veronique Delvaux, and Stephane Hans:** final approval, and accountability for the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. **Lee M. Akst**: final approval, and accountability for the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. **Jerome R. Lechien**: design, acquisition of data, final approval, and accountability for the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of Competing Interest

The authors have no financial interest in the subject under discussion. All authors have read and approved the paper. Would you be so kind to consider the present paper and send us the reviewer's comments.

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