



REVIEW

# Vocal fold leukoplakia: Diagnostic approaches, risk stratification, and management of laryngeal premalignant lesions

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## ABSTRACT

**Background:** Vocal cord leukoplakia is a diverse epithelial condition with indeterminate biological characteristics, resulting in ongoing conflict between early oncological intervention and voice preservation. To integrate current knowledge about diagnostic methodologies, risk classification, and the management of vocal cord leukoplakia and associated laryngeal precancerous lesions.

**Method:** This narrative literature review focused on English-language journal papers published from 2016 to April 2026, with the final selection restricted to studies published in Scopus-indexed publications. Primary cohort studies, diagnostic investigations, systematic reviews, meta-analyses, and a 2021 position document from the European Laryngological Society were given top priority.

**Results:** The most consistent message from recent research is that combining white-light laryngoscopy with stroboscopy, narrowband imaging, and histopathology makes diagnosis more accurate. Lesions that are rough, thick, hyperemic, and non-vibrating and have an unusual vascular pattern are more likely to lead to severe dysplasia or cancer. Histologic grade, on the other hand, is still the most important factor in determining whether a tumor will turn malignant over time. Conservative treatment seems best for certain modest lesions. On the other hand, suspicious, persistent, recurrent, or histologically progressed lesions usually need a biopsy or excision.

**Conclusion:** Contemporary management options for vocal cord leukoplakia must be multimodal, risk-adapted, and explicitly associated with longitudinal surveillance. Future research should concentrate on standardized scoring systems, external validation of optical biopsy instruments, and biomarker-driven predictive models.

**Keywords:** vocal cord leukoplakia, laryngeal dysplasia, narrowband imaging, precancerous laryngeal lesions, risk stratification, transoral laser microsurgery

## Introduction

Vocal fold leukoplakia denotes white epithelial plaques affecting the mucosa of the true vocal folds, yet the term does not delineate the histology. This semantic limitation is significant because lesions can vary from non-dysplastic keratosis to different levels of dysplasia, carcinoma in situ, or invasive carcinoma, making biological interpretation impossible based solely on nomenclature.<sup>1,2</sup>

This topic remains clinically critical as undertreatment may delay cancer diagnosis, while overtreatment may cause permanent damage to vibrating function, scarring, and preventable dysphonia. Consequently, recent reviews characterize vocal cord leukoplakia as an issue of informed decision-making rather than mere lesion excision.<sup>3,4</sup>

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The current research is abundant yet disjointed. Certain investigations prioritize gross morphology observed under white light, whilst others concentrate on narrowband imaging, videostroboscopy, histological grading, recurrence patterns, biomarkers, or machine-learning help. These various techniques are not consistently amalgamated into a singular, therapeutically relevant synthesis. This gap is important because histopathological assessment gives prognostic information but is not perfect, and translational research shows more and more that lesions with similar microscopic grades may still behave differently over time.<sup>5,6</sup>

Therefore, this review aims to provide a clinically oriented narrative synthesis of the current evidence regarding the diagnostic evaluation, precancerous risk stratification, and management strategies for vocal fold leukoplakia, with particular attention to studies that are likely to influence current laryngology practice.<sup>2,4</sup>

## Method

This article is designed as a narrative literature review because the available evidence encompasses heterogeneous study designs, including retrospective surgical cohorts, diagnostic accuracy studies, translational biomarker analyses, systematic reviews, meta-analyses, and consensus-based position papers.

A structured search strategy was developed based on recurring concepts used in recent papers defining the topic, including “vocal fold leukoplakia,” “vocal cord leukoplakia,” “laryngeal dysplasia,” “laryngeal premalignant lesions,” “narrowband imaging,” “videostroboscopy,” “risk stratification,” “malignant transformation,” “laser surgery,” “optical biopsy,” “artificial intelligence,” and “optical coherence tomography.” Publications from January to April 2026 were considered, and only English-language articles published in Scopus-indexed journals were retained. Priority was given to primary studies, systematic reviews, meta-analyses, and formal position papers. In contrast, non-journal publications, outdated sources, articles outside the laryngeal precancer spectrum, and studies not materially relevant to diagnosis, risk assessment, or management were excluded from the final manuscript.

This final narrative synthesis intentionally prioritizes clinically actionable evidence: how endoscopic appearances relate to pathology, which features predict the risk of malignancy or recurrence, which patients can be managed conservatively, and how newer adjunctive technologies may alter future outcomes.

## Result and Discussion

### Clinical and pathological spectrum

The first principle in interpreting vocal fold leukoplakia is that the visual phenotype is descriptive, not diagnostic. White plaques arise from epithelial keratinization, but the underlying pathology spans a continuum from non-dysplastic hyperkeratosis to severe dysplasia and invasive carcinoma. Therefore, leukoplakia should be approached as a surface sign of varying biological risk rather than as a single disease entity.<sup>1,2</sup>

The pathological framework remains a key concern. Recent laryngeal dysplasia literature, including the ELS position paper, emphasizes that determining the stage of dysplasia remains the cornerstone of prognosis and management. However, diagnostic uncertainty remains because sampling may miss the most advanced foci, and histological interpretation, particularly at the lower end of the dysplasia spectrum, is not fully reproducible. Transcriptomic studies have reinforced these concerns by demonstrating that lesions with similar histological labels can still have distinct biological trajectories.<sup>1,3,6</sup>

The strongest longitudinal evidence currently supports histology as the most robust risk predictor. In a 2024 meta-analysis by Horton and colleagues, the combined malignant transformation rate increased gradually from 4.5% in non-dysplastic lesions to 10.9% in mild dysplasia, 23.3% in moderate dysplasia, and 30.5% in severe dysplasia, with an overall median time to transformation of 28.8 months. These figures do not eliminate uncertainty but strongly justify increasing follow-up intensity with histologic severity.<sup>7</sup>

### Diagnostic approach

White-light laryngoscopy remains the starting point for diagnosis, and recent studies continue to demonstrate the importance of morphology. Fang et al.<sup>8</sup> developed a clinical assessment approach for preoperative stratification. At the same time, Zhang et al.<sup>9</sup> demonstrated that coarser, more prominent leukoplakia patterns correlate more closely with adverse pathology than flat, smooth lesions. Li et al.<sup>10</sup> subsequently extended this morphological logic into a treatment-guided classification, reinforcing the practical value of systematically documenting surface contours and masses.

Videostroboscopy adds functional information that cannot be inferred from static morphology alone. In vocal cord leukoplakia, disruption or absence of the mucosal waveform indicates deeper epithelial or subepithelial disorders and is therefore clinically useful in deciding whether conservative observation is warranted. Rzepakowska et al.<sup>11</sup> and Leduchowska et al.<sup>12</sup> found that combining morphology with vibration assessment and vascular findings improved the prediction of malignancy compared with surface appearance alone.

Narrowband imaging has become the most important optical tool for risk enrichment. Klimza et al.<sup>13</sup> highlighted the "umbrella effect," in which thick keratin can obscure the most informative blood vessels on the plaque surface, making examination of the surrounding mucosa crucial. Ni et al.<sup>14</sup> subsequently proposed a narrowband imaging classification specific to vocal cord leukoplakia, and Lu et al.<sup>15</sup> further supported the diagnostic value of Ni's framework in leukoplakia and early-stage glottic cancer. Across studies, a common lesson learned is that an abnormal, perpendicular, or irregular intrapapillary capillary loop pattern substantially increases the suspicion of high-grade disease.

Meta-analytic evidence now supports this clinical impression. Chen et al.<sup>16</sup> concluded in 2023 that narrowband imaging has useful overall accuracy for detecting malignant transformation in vocal cord leukoplakia, strengthening the argument that vascular assessment should be integrated into routine clinical evaluation whenever equipment and expertise are available.

Despite this, histopathology remains the reference standard. The ELS diagnostic framework continues to place endoscopy and biopsy at the center of decision-making. Recent clinician-based biopsy data by Hosri et al.<sup>17</sup> suggest that laryngeal endoscopic findings can be highly sensitive for identifying high-grade dysplasia or carcinoma but are not definitive enough to replace tissue confirmation when clinical suspicion is high or management would change significantly based on severity.

A further development is the emergence of digital optical biopsy. Deep learning models trained on white-light and narrowband images have demonstrated promising classification performance, and a multicenter study by Tie et al.<sup>18</sup> suggests that such systems may be particularly useful for less experienced laryngologists. Handheld optical coherence tomography combined with machine learning has also demonstrated feasibility for rapid intraoperative classification, pointing to future image-based decision-making support rather than direct replacement of histology.<sup>19,20</sup>

#### Risk stratification of laryngeal premalignant lesions

The most clinically valuable risk stratification models currently are multimodal. Recent studies have repeatedly identified lesion thickness, roughness, hyperemia, suspicious vascular patterns, vibration disturbances, and anterior commissure involvement as high-risk features, especially when all are clustered within the same lesion. Li et al.<sup>21</sup> found that thickness and hyperemia were independent predictors of higher-risk disease, while Pietruszewska et al.<sup>5</sup> showed that combined white-light and narrowband classification outperformed white-light description alone; Klimza et al.<sup>13</sup> also showed that suspicious narrowband vascular findings significantly increased the probability of invasive cancer occult within plaques appearing leukoplakic.

Formal scoring systems have begun to transform these observations into bedside tools. Ni et al.<sup>22</sup> proposed a five-point laryngoscopy-based score ranging from 0 to 10, with a 6-point threshold, that yielded 93.8% sensitivity, 83.6% specificity, and 86.0% overall accuracy for differentiating benign from malignant vocal fold leukoplakia. These results are clinically important because they demonstrate that white-light morphology itself can be systematized in situations where advanced imaging is unavailable or inconsistently used.

However, longitudinal risk is not limited to predicting early malignancy. Among 207 patients with primary vocal cord leukoplakia, Klimza et al.<sup>13</sup> reported a 19.8% recurrence rate, with Ni types IV–VI associated with a greater risk. In a separate two-year cohort of 344 cases, Yin et al.<sup>23</sup> found that lesion size, light-white morphology stage, surgical method, and pathological type independently influenced recurrence. At the same time, the pathological type also provided information on the risk of malignant transformation. Therefore, clinicopathological follow-up studies such as those by Cui et al.<sup>24</sup> and Yang et al.<sup>25</sup> remain relevant because recurrence is not a trivial event; it is part of the natural history of precancerous lesions and should influence the intensity of surveillance.

Molecular risk stratification remains promising but is not yet ready for routine practice. Wan et al.<sup>26</sup> reviewed candidate biomarkers for malignant potential and concluded that the field remains exploratory, with no single molecular marker sufficiently validated for clinical decision-making. Maffini et al.<sup>6</sup> extended

this discussion by demonstrating transcriptional alterations in innate immune pathways that appear to separate progressive from non-progressive dysplasia, suggesting a biologically meaningful layer of risk not fully captured by routine histology.

Because evidence regarding vocal cord leukoplakia has emerged from heterogeneous observational cohorts, diagnostic accuracy studies, translational analyses, and consensus-based frameworks, a comparative synthesis is needed to clarify how current understanding has evolved from descriptive morphology to integrated risk-based management. Table 1 summarizes the key studies included in this review according to design, focus, major findings, and relevance to contemporary clinical interpretation.<sup>7,8,18</sup>

Table 1. Comparative summary of studies related to vocal cord leukoplakia: diagnostic approach, risk stratification, and management of precancerous lesions of the laryngeal

Study	Country/setting	Study design/population	Diagnostic or research focus	Main findings	Relevance to the review topic	Implication for clinical practice or future research
Fang et al. (2016) <sup>8</sup>	Single-centre tertiary voice practice	Retrospective clinicopathological correlation	White-light clinical scoring	Morphological scoring correlated with pathological severity	Foundational evidence that structured white-light assessment is informative	Encourages systematic recording of macroscopic features at first visit
Klimza et al. (2017) <sup>13</sup>	Tertiary laryngology service	Diagnostic cohort of vocal fold leukoplakia	Narrow-band imaging and the "umbrella effect"	Peri-lesional vascular assessment improved suspicion despite keratin masking	Clarified how NBI should be interpreted in leukoplakia	Clinicians should inspect surrounding mucosa, not only the plaque surface
Chen et al. (2017) <sup>16</sup>	Single-centre observational cohort	178 patients managed conservatively	Nonsurgical treatment by lesion subtype	Smooth lesions responded substantially better than rough lesions	Key conservative-management evidence	Supports selective observation/medical therapy in low-risk smooth lesions
Lim et al. (2018) <sup>27</sup>	Single-centre surgical cohort	70 surgically treated patients	Angiolytic laser stripping versus CO <sub>2</sub> microflap excision	Comparable disease control, with better voice preservation after angiolytic stripping	Important comparative management study	Suggests function-preserving laser choice matters in appropriate lesions
Ni et al. (2019) <sup>14</sup>	Diagnostic endoscopy cohort	Retrospective classification study	Novel NBI classification for leukoplakia	NBI classification improved differentiation of benign and malignant lesions	Standardised vascular-pattern interpretation	Strengthens routine use of NBI in office laryngology
Rzepakowska et al. (2020) <sup>11</sup>	Tertiary laryngology unit	Cohort study	Morphology, mucosal wave and vascular pattern	Combined vibratory and vascular findings improved malignancy prediction	Demonstrates value of multimodal office assessment	Videostroboscopy adds clinically relevant information beyond static imaging
Pietruszewska et al. (2021) <sup>5</sup>	Tertiary oncology setting	Comparative classification analysis	White-light and NBI frameworks; diagnostic algorithm	Combined classifications outperformed white-light assessment alone	Integrative risk-stratification paper	Useful for triage and follow-up planning
Leduchowska et al. (2022) <sup>12</sup>	Tertiary referral centre	Retrospective cohort	Videolaryngoendoscopic and stroboscopic predictors	Suspicious videolaryngoscopic patterns and impaired vibration associated with malignant histology	Refines functional risk assessment	Supports lower biopsy threshold when mucosal wave is reduced or absent
Horton et al. (2024) <sup>7</sup>	Systematic review and meta-analysis	18 retrospective cohorts; 3243 participants	Malignant transformation by dysplasia grade	Transformation risk increased stepwise with histological grade; mean time to progression about 29 months	Strongest contemporary synthesis of natural history	Histological grade should guide follow-up intensity and counselling
Ni et al. (2024) <sup>22</sup>	Retrospective image cohort	200 cases	Laryngoscopy-based scoring system	Five-item score with good sensitivity and	Operational bedside risk tool	Potentially useful where NBI is

				specificity for malignancy prediction		unavailable or equivocal
Tie et al. (2024) <sup>18</sup>	Multicentre image-based study	White-light and NBI datasets	Multi-instance learning for benign versus malignant leukoplakia	AI model showed effective classification performance, especially for junior raters	Emerging digital decision-support evidence	Needs external validation before incorporation into routine clinical pathways
Li et al. (2025) <sup>19</sup>	Intraoperative translational study	Handheld OCT with machine-learning assistance	Real-time intraoperative classification	Rapid optical classification was feasible during surgery	Important "optical biopsy" advance	May support margin selection and real-time decision-making after validation

In these studies, the same high-risk groups recurred: coarse or thick morphology, abnormal vascularity on narrowband imaging, disrupted mucosal waves, high-grade histology, and recurrence after treatment. It is important to note that newer AI and OCT systems do not introduce entirely different biological logic; rather, they attempt to formalize and enhance the same visual and structural cues that have been identified in human-centered clinical studies.<sup>7,8,14,19</sup>

### Management strategies

Management should be risk-specific, not uniform. Contemporary reviews consistently argue that smooth, low-risk lesions without compelling vascular or functional alarm features can be managed initially with close surveillance, risk factor modification, and medical optimization. In contrast, coarse, thick, hyperemic, or recurrent lesions should not be overlooked. The key principle is to intervene neither too late for oncological safety nor too early to prevent unnecessary phonatory injury.<sup>2,4,16</sup>

A conservative approach is directly supported by Chen et al., whose analysis of 178 cases showed that smooth lesions were significantly more likely to respond to nonsurgical treatment than rough lesions. While this study does not eliminate the need for vigilance, it does support a practical distinction between low-risk morphology suitable for structured observation and high-risk morphology that should prompt biopsy or excision.<sup>16</sup>

When procedural treatment is indicated, transoral laser approaches remain the focus. In Yang et al.'s<sup>25</sup> surgical series, carbon dioxide laser excision was effective for dysplastic lesions confined to the vocal cords. However, postoperative recurrence still occurred in 22.7%, and gastroesophageal reflux disease independently predicted recurrence. Lim et al.<sup>27</sup> subsequently demonstrated that angiolytic laser stripping and CO<sub>2</sub> microflap excision achieved similar long-term disease control, with angiolytic stripping offering superior voice preservation. Together, these findings support surgery that is explicitly oncological in intent but sensitive to function in its implementation.

The indication for biopsy or excision is strongest when there is a suspicious vascular pattern, diminished mucosal wave, anterior commissure involvement, recurrence, or histologically advanced disease. This position is consistent with the ELS framework and with subsequent algorithmic studies showing that combined white light and narrowband findings improve preoperative triage but do not eliminate the need for tissue diagnosis when management relies on accurate assessment.<sup>3,5,13</sup>

Follow-up is not optional and should be considered later. A 2024 meta-analysis by Horton et al.<sup>7</sup> showed that even mild dysplasia carries a non-zero risk of transformation, and recurrence models suggest that disease recurrence is common enough to justify longitudinal surveillance after seemingly adequate primary treatment. In practice, recurrence, worsening morphology, new vascular abnormalities, or loss of vibratory function should trigger a renewed diagnostic workup rather than passive waiting and observation.<sup>13,23</sup>

### Clinical and research implications

The clinical implication of current evidence is that vocal fold leukoplakia should be assessed as an integrated risk issue rather than a binary operative/non-operative issue. White light examination remains indispensable, but diagnostic yield improves significantly when complemented by videostroboscopy, narrowband imaging, and timely histopathology, ideally interpreted in a manner that explicitly documents lesion surface, thickness, vascularity, vibratory function, and previous recurrence status.<sup>3-5</sup>



Function is as important as pathology in treatment planning because the vocal cords are not a generic mucosal site. Comparative laser studies have shown that oncological adequacy and voice preservation can be balanced, but not at the expense of tissue biomechanics. Consequently, clinicians should strive for the least damaging intervention compatible with a reliable diagnosis and oncological safety, rather than reflexively adopting an aggressive or conservative approach.<sup>2,27</sup>

#### Research gaps and future directions

Several gaps remain. First, preoperative risk models are improving but are still not fully standardized across centers. Different groups emphasize different combinations of white-light morphology, vascular patterns, commissural involvement, and vibration features, and even the most promising scoring systems still require extensive external validation in prospective practice settings.<sup>17,21,22</sup>

Second, translational risk prediction remains immature. A 2021 biomarker review concluded that no molecular candidates have yet passed the threshold for routine decision-making, while a 2024 transcriptomic analysis revealed biologically meaningful dysplasia subtypes not captured by current morphology-pathology models. This represents an important direction for future work, but prospective correlation with recurrence, progression, and treatment response is still needed before biomarker-based management can be recommended.<sup>6,26</sup>

Third, the next generation of optical biopsy tools is promising but not yet definitive. AI systems and handheld OCT may improve reproducibility, shorten the intraoperative decision-making cycle, and support less experienced clinicians, but current data are best interpreted as proof of concept or initial multicenter validation rather than evidence for direct replacement of biopsy-based pathways.<sup>18–20</sup>

A further practical research need is a better link between oncological outcomes and voice outcomes. Studies that report progression or recurrence without robust phonation endpoints, or vice versa, only partially address important clinical questions for patients. Therefore, future prospective studies should integrate histology, advanced imaging, recurrence trajectories, and validated voice outcome measures within the same protocol.<sup>2,25,27</sup>

#### Conclusion

The current literature supports a coherent view of vocal cord leukoplakia as a heterogeneous, precancerous epithelium that cannot be safely managed based solely on visual impression. The most viable strategy currently is multimodal and risk-adapted: structured white-light assessment, additional narrowband imaging and stroboscopy if available, histopathologic confirmation for clinically significant lesions, and surveillance intensity based on histologic grade, endoscopic risk features, and history of recurrence. A conservative approach remains appropriate for selected subtle, low-risk lesions, while suspicious or recurrent lesions generally require tissue diagnosis or definitive excision. AI, OCT, and molecular profiling may ultimately refine this approach but for now should be viewed as promising adjuncts rather than substitutes for integrated clinical and histologic assessment.

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