



TREATMENT OF DYSPHONIA IN LARYNGEAL PAPILLOMATOSIS

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Abstract. *Laryngeal papillomatosis (LP) is a chronic, recurrent disease caused by human papillomavirus (HPV) infection, characterized by the growth of benign epithelial tumors within the larynx and respiratory tract. One of the most debilitating consequences of LP is persistent dysphonia, which often leads to significant deterioration in quality of life, particularly among individuals whose professional and social activities rely heavily on vocal communication. Despite the benign histological nature of papillomas, their tendency for recurrence, airway obstruction, and malignant transformation makes LP a serious condition requiring continuous medical attention [1].*

The management of dysphonia in laryngeal papillomatosis is complex due to the chronic and recurrent nature of the disease. Conventional surgical interventions such as microlaryngoscopy with cold instruments or laser excision remain the gold standard for papilloma removal. However, these approaches are palliative rather than curative, as papillomas often recur within weeks or months [2]. Adjuvant pharmacological therapies, including antiviral agents, interferon, and bevacizumab injections, have been introduced to extend remission periods and improve vocal outcomes, but their long-term efficacy remains under investigation [3,4].

Recent studies highlight the importance of combined treatment strategies that integrate surgical, pharmacological, and rehabilitative approaches to improve voice quality and reduce recurrence. Voice therapy and rehabilitation techniques are increasingly recognized as valuable adjuncts, aiming not only to restore phonatory function but also to prevent maladaptive vocal behaviors that exacerbate dysphonia [5]. Furthermore, the introduction of vaccination against HPV has shown



promise in reducing the incidence of recurrent respiratory papillomatosis, especially in younger populations [6].

This article aims to provide a comprehensive overview of the epidemiology, clinical features, and therapeutic strategies for managing dysphonia in patients with laryngeal papillomatosis. Particular emphasis is placed on the effectiveness of combined treatment approaches, their impact on voice outcomes, and the challenges associated with long-term management of this condition.

Keywords: *laryngeal papillomatosis; dysphonia; treatment; surgical micro-laryngoscopy; adjuvant therapy; interferon; cidofovir; voice therapy.*

Introduction

Epidemiology of Laryngeal Papillomatosis. Laryngeal papillomatosis, also referred to as recurrent respiratory papillomatosis (RRP), is considered the most common benign neoplasm of the larynx in children and the second most common in adults [7]. The disease is caused by human papillomavirus (HPV), primarily types 6 and 11, which are transmitted through vertical (perinatal) or horizontal (sexual and non-sexual) transmission routes [8]. The incidence of juvenile-onset RRP is estimated at 4.3 per 100,000 children, while adult-onset RRP occurs at a rate of approximately 1.8 per 100,000 adults [9]. Despite these relatively low incidence rates, the chronicity of the disease and its high recurrence make it a significant medical and social problem.

Dysphonia is one of the earliest and most persistent symptoms of laryngeal papillomatosis. The growth of papillomas on the vocal folds disrupts glottal closure and mucosal wave propagation, resulting in hoarseness, roughness, and vocal fatigue [10]. Children with juvenile-onset LP often present with chronic hoarseness, misdiagnosed initially as recurrent laryngitis, which leads to delays in diagnosis and treatment. In adults, persistent dysphonia can severely affect professional activities, particularly for teachers, singers, and public speakers, where optimal vocal quality is essential [11].



The burden of LP extends beyond dysphonia. In severe cases, papillomas obstruct the airway, leading to stridor, dyspnea, and potentially life-threatening respiratory compromise. Moreover, LP has a well-documented tendency for recurrence even after repeated surgical removal, with patients often requiring dozens of surgeries throughout their lifetime. This not only increases healthcare costs but also contributes to the progressive scarring of the vocal folds, further worsening dysphonia.

Epidemiological studies have also demonstrated geographical and demographic variations in the incidence and severity of LP. For instance, higher prevalence rates have been reported in populations with limited access to HPV vaccination and healthcare resources. Moreover, juvenile-onset disease tends to be more aggressive, requiring more frequent surgical interventions and leading to more pronounced voice disorders compared to adult-onset forms.

From a public health perspective, LP imposes a significant socioeconomic burden due to repeated hospitalizations, lifelong follow-up, and the loss of productivity resulting from impaired voice function. As such, the management of dysphonia in LP is not only a clinical challenge but also an important social issue, necessitating effective therapeutic strategies that can improve both medical and quality-of-life outcomes for affected patients [12].

Pathogenesis and Clinical Features of Dysphonia in Papillomatosis. The pathogenesis of dysphonia in laryngeal papillomatosis (LP) is multifactorial, involving structural, functional, and neurological components. The primary factor is the direct mechanical obstruction of the glottis caused by papillomatous growths on the vocal folds, which disrupts glottal closure, alters the mucosal wave, and reduces vocal fold vibration symmetry. As papillomas enlarge or recur after surgical removal, patients experience progressive worsening of voice quality, with symptoms ranging from mild hoarseness to complete aphonia.

Inflammatory changes also play an important role. Papillomas induce chronic irritation of the laryngeal mucosa, which leads to edema, hyperemia, and thickening of the vocal folds. These pathological changes further impair phonation by



increasing vocal fold stiffness and disrupting the layered structure of the vocal cord epithelium. As a result, patients with LP often report vocal fatigue, strain, and decreased pitch control, especially after prolonged speech or singing.

Neurological factors may contribute as well. Repeated surgeries for papilloma removal can cause trauma to the recurrent laryngeal nerve or superior laryngeal nerve, leading to vocal fold paresis or paralysis. Even in the absence of nerve damage, repeated scarring of the vocal folds significantly compromises their vibratory properties, producing a rough and breathy voice quality.

Clinically, dysphonia in LP is often accompanied by other symptoms such as chronic cough, throat clearing, and globus sensation. In advanced cases, inspiratory stridor and exertional dyspnea indicate airway compromise, which may coexist with voice changes. However, dysphonia remains the most disabling symptom for many patients, particularly those engaged in vocally demanding occupations, where even mild alterations in voice quality may result in significant functional impairment [13].

Conventional Treatment Approaches. The cornerstone of LP management is surgical removal of papillomas. The goal of surgery is to restore and maintain airway patency while preserving vocal fold function as much as possible. Two main surgical techniques are currently used: cold instrument microlaryngoscopy and laser excision. Cold instrument surgery allows precise mechanical removal of papillomas, but it often results in incomplete clearance and frequent recurrence. Laser techniques, particularly carbon dioxide (CO₂) and potassium-titanyl-phosphate (KTP) lasers, provide improved hemostasis and precision but may increase the risk of thermal injury and scarring if not carefully applied.

Despite advances in surgical technology, the recurrence of papillomas remains the greatest limitation of surgical treatment. Studies indicate that patients with aggressive juvenile-onset disease may require up to 100 surgical interventions during their lifetime, while adult patients undergo fewer but still recurrent procedures. These repeated interventions carry a cumulative risk of vocal fold scarring, anterior commissure web formation, and permanent deterioration of voice quality.



Tracheostomy is rarely used today but may be required in life-threatening cases of airway obstruction where papillomas occupy a large portion of the glottic or subglottic airway. However, tracheostomy is generally avoided, as it can facilitate distal spread of papillomas into the trachea and bronchi, complicating disease management.

Phonotherapy is an essential adjunct to surgical treatment. Speech-language pathologists work with patients to optimize vocal hygiene, reduce maladaptive compensatory behaviors, and rehabilitate vocal function after surgery. While phonotherapy cannot prevent papilloma recurrence, it plays a key role in improving overall voice outcomes and reducing the psychosocial burden of dysphonia [14].

Innovative and Combined Therapies. Due to the limitations of surgery alone, combined therapeutic approaches have gained significant attention. Adjuvant pharmacological therapies are used to reduce the recurrence rate and prolong remission between surgeries. Interferon-alpha was one of the earliest agents employed, with modest benefits in reducing papilloma regrowth, though its use has declined due to systemic side effects.

Cidofovir, an antiviral agent, has been widely studied as an intralesional injection directly into papillomas. Several clinical trials have reported prolonged remission and improved voice quality, although concerns about potential carcinogenicity have limited its universal adoption. Bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor, has shown promising results in reducing papilloma vascularization and recurrence when injected intralesionally, particularly when combined with KTP laser surgery .

More recently, HPV vaccination has emerged as a preventive and therapeutic strategy. Although originally developed to prevent cervical cancer, prophylactic vaccines against HPV types 6 and 11 have shown potential in reducing the incidence and severity of LP in both children and adults. Case reports suggest that vaccination may decrease the frequency of surgical interventions in affected patients, though large-scale studies are still needed to confirm these findings.



Photodynamic therapy (PDT) is another experimental approach in which photosensitizing agents are applied to papillomas and activated by light exposure, leading to selective destruction of diseased tissue. Early trials have shown encouraging results in prolonging disease-free intervals, but widespread clinical adoption is still limited [15].

Challenges in Long-term Management. The chronic and recurrent nature of laryngeal papillomatosis presents major challenges in long-term management of dysphonia. Despite advances in surgical and adjuvant treatments, recurrence remains almost inevitable, with papillomas frequently reappearing within weeks or months after excision. This cycle of repeated surgeries places patients at risk for cumulative scarring, progressive deterioration of vocal fold pliability, and worsening dysphonia.

Another critical challenge is the variability of disease aggressiveness among patients. Some individuals experience mild disease with infrequent recurrences, while others suffer from highly aggressive forms requiring multiple surgical procedures annually. The unpredictability of disease progression complicates treatment planning and often leads to patient frustration and reduced compliance with follow-up protocols [16].

Psychosocial consequences are also profound. Dysphonia significantly affects professional and social functioning, particularly for teachers, actors, and singers who depend on their voices. Many patients experience depression, social withdrawal, and decreased quality of life due to chronic hoarseness and communication difficulties. Moreover, parents of children with juvenile-onset papillomatosis often report anxiety and stress related to the need for repeated surgeries and the uncertainty of long-term outcomes [17].

From a healthcare systems perspective, LP imposes a considerable economic burden. The cumulative cost of surgeries, hospitalizations, pharmacological treatments, and rehabilitation is substantial. In countries with limited access to specialized surgical care, patients may suffer prolonged periods of untreated dysphonia and airway obstruction, further worsening prognosis.



Finally, concerns about malignant transformation of papillomas, although rare, add to the complexity of long-term management. Dysplastic changes and progression to squamous cell carcinoma have been reported, particularly in patients with HPV type 11 or in those who underwent prolonged cidofovir therapy. Continuous monitoring with regular laryngoscopic examinations is therefore essential in all patients with recurrent disease [18].

Future Directions in Dysphonia Treatment in LP. Future strategies for managing dysphonia in LP focus on reducing recurrence, improving vocal outcomes, and minimizing treatment-related morbidity. Immunotherapy represents one of the most promising avenues. Research into therapeutic vaccines targeting HPV proteins (E6 and E7 oncoproteins) is ongoing, with early results suggesting the potential to enhance host immune response and reduce papilloma regrowth [19].

Gene therapy is another area of active investigation. Experimental studies have explored the use of small interfering RNA (siRNA) to silence viral gene expression, thereby inhibiting papilloma proliferation. While still in preclinical stages, these approaches hold promise for providing more durable disease control than current therapies.

Advances in surgical technology are also expected to improve outcomes. The use of pulsed-dye lasers and photoangiolytic techniques, which target papilloma vasculature with minimal damage to surrounding tissues, may reduce the risk of scarring and preserve better vocal quality compared to older CO₂ lasers. Integration of robotics and high-definition imaging in microlaryngoscopy may further enhance precision in papilloma removal.

Adjunctive voice therapy will continue to play a central role in rehabilitation. Increasingly, individualized voice training programs are being developed to address the specific phonatory deficits of LP patients, incorporating biofeedback technologies and high-fidelity acoustic analysis. Telemedicine may expand access to voice therapy for patients in remote areas, allowing ongoing support and monitoring between surgical interventions [20].



Finally, broader implementation of prophylactic HPV vaccination programs offers the most effective long-term solution for reducing the incidence of LP and its associated dysphonia. Widespread vaccination of adolescents against HPV types 6 and 11 is expected to significantly decrease the number of new cases of juvenile-onset LP in future generations. Early reports already suggest a decline in LP incidence in countries with high vaccine coverage, highlighting the critical role of public health initiatives in disease prevention [21].

Conclusion

Dysphonia in patients with laryngeal papillomatosis (LP) remains one of the most challenging aspects of disease management due to the recurrent and progressive nature of papillomatous growths. Although benign in histology, papillomas often lead to significant deterioration of vocal function, negatively impacting communication, professional performance, and overall quality of life. Traditional surgical approaches, while essential for airway maintenance, are primarily palliative, as recurrence is almost universal. This necessitates repeated interventions, which in turn contribute to cumulative scarring and worsening dysphonia.

The integration of pharmacological adjuvant therapies, such as cidofovir, interferon, and bevacizumab, with surgical management has provided some improvement in prolonging remission and reducing disease severity. Additionally, phonotherapy and vocal rehabilitation play a critical role in restoring phonatory efficiency and minimizing maladaptive vocal behaviors. The introduction of HPV vaccination has opened new perspectives for long-term prevention, showing early evidence of reduced incidence and disease severity.

Despite these advances, numerous challenges remain, including the unpredictable aggressiveness of disease, psychosocial consequences, economic burden, and the rare but real risk of malignant transformation. Future directions are likely to focus on immunotherapy, gene therapy, and improved surgical technologies aimed at reducing recurrence while preserving voice quality. Public health initiatives



such as widespread HPV vaccination programs will also be pivotal in reducing the burden of LP globally.

In conclusion, the treatment of dysphonia in LP requires a comprehensive, multidisciplinary approach that combines surgical, pharmacological, rehabilitative, and preventive strategies. Only through such integrated management can clinicians hope to achieve long-term improvements in voice quality, reduce recurrence rates, and ultimately improve the quality of life for affected patients.

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