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Photodynamic therapy for treatment and prevention of recurrent respiratory papillomas: A systematic review and meta-analysis

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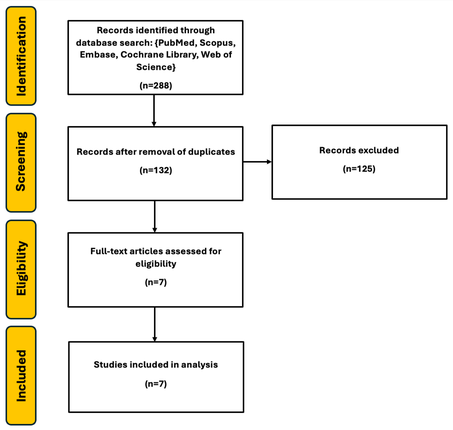
Introduction

Respiratory papillomas (RP) are most commonly benign epithelial growths associated with exposure to human papillomaviruses 6 and 11 (HPV6/11). RP generally appears in the larynx, known as laryngeal papillomatosis, and can occur as a single or recurring event in those affected.[1,2] In individuals with RP or recurrent respiratory papillomatosis (RRP), the location of disease involvement, such as nasopharynx, subglottic, and tracheal extension, can cause significant morbidity and mortality.[3,4] With uncertainty about acquiring the disease and no current definitive cure, treatment for RP focuses on maintaining airway patency and voice quality.[5]

Despite its relatively low prevalence, the high economic burden, particularly in individuals with RRP and risk of malignant transformation, makes finding efficacious treatment modalities critical to reducing the financial costs and improving healthcare outcomes.[2,6-8] The current mainstay treatment for RP includes surgical excision and laser therapy, commonly potassium titanyl phosphate (KTP) lasers, for debulking papillomas.

Treatment with photodynamic therapy has also been explored because of its potential to treat RP through a minimally invasive procedure with greater sensitivity against tumors and the possibility of preventing repeated debridement.[9,10] Photodynamic therapy utilizes the application of a light-sensitizing substance that, when activated by specific wavelengths of light, generates reactive oxygen species that lead to the death of the target tissue.[9-11]

Methods



Results

We conducted a single-proportion meta-analysis under the random-effects model using mean modified Kashima indices to assess the effectiveness of photodynamic therapy at reducing the growth rate of respiratory papillomas. Another single-proportion meta-analysis was conducted under the random-effects model using tumor recurrence rates to assess the effectiveness of PDT at preventing recurrence of respiratory papillomas.

Reduction in Disease Severity:
Across 4 articles, 124 patients received treatment with PDT and 54 received carbon dioxide laser surgery as a control. The effect size for tumor growth rate in the PDT group was -0.73 which was statistically significant (p = 0.03). The effect size for the control group was -0.13 and was not statistically significant (p = 0.37). The overall effect size showed a 0.57 reduction in tumor growth rate that was statistically significant (p = 0.03).

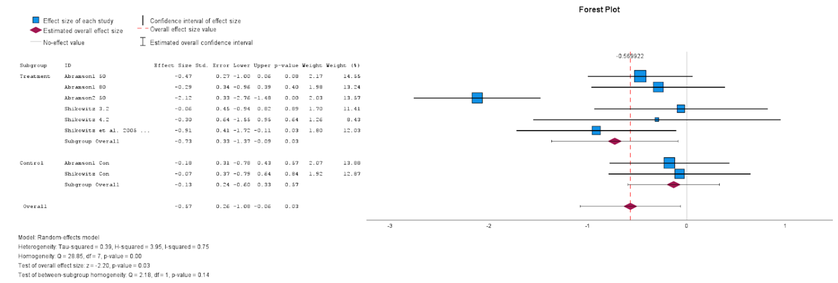


Table 1: Analysis of reduction in disease severity

Disease Recurrence Rate:
Across 3 articles, data from 31 patients were utilized in the analysis of disease recurrence; recurrence rate following PDT was determined to be 79% (CI [65%, 93%], P=0.54).

Study	Events	Total	Weight (common)	Weight (random)	IV, Fixed + Random, 95% CI
Liang et al. 2019	11	13	50.8%	50.8%	0.85 [0.55; 0.98]
Yoshida et al. 1995	8	10	31.8%	31.8%	0.80 [0.44; 0.97]
Glisinski et al. 2020	5	8	17.4%	17.4%	0.62 [0.24; 0.91]
Total (common effect, 95% CI)		**31**	**100.0%**	.	**0.79 [0.65; 0.93]**
Total (random effect, 95% CI)			.	**100.0%**	**0.79 [0.65; 0.93]**

Heterogeneity: $Tau^2 = 0$; $Chi^2 = 1.25$, df = 2 (P = 0.54); $I^2 = 0\%$

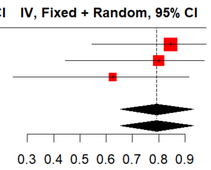


Table 2: Analysis of disease recurrence rate

Discussion and Conclusion

The subgroup analysis indicates that PDT has a stronger effect on reducing tumor growth rate compared to control, with a statistically significant effect size in the treatment group (d = -0.73, *p* = 0.03) but not in the control group (d = -0.13, *p* = .574). Notably, the confidence interval for the PDT group was relatively narrow, suggesting a more consistent treatment effect across studies. However, the wide 95% prediction intervals, particularly for the treatment group (–2.84 to 1.39), point to substantial variability in expected outcomes, which may reflect heterogeneity in patient populations, treatment protocols, or study designs. These findings highlight the importance of considering between-study variability.

Effect Size Estimates for Subgroup Analysis

	Effect Size	Std. Error	Z	Sig. (2-tailed)	95% Confidence Interval Lower	95% Confidence Interval Upper	95% Prediction Interval[a] Lower	95% Prediction Interval[a] Upper
Treatment	-.727	.3258	-2.232	.026	-1.366	-.089	-2.840	1.386
Control	-.133	.2360	-.562	.574	-.595	.330	.	.
Overall	-.570	.2587	-2.203	.028	-1.077	-.063	-2.218	1.078

a. Based on t-distribution.

Table 3: Effect Sizes for Subgroup Analysis

The purpose of this study was to evaluate the efficacy of photodynamic therapy for the treatment of recurrent respiratory papillomas. There was determined to be a statistically significant reduction in the growth rate of RP following treatment with PDT. The limited effect of PDT on tumor recurrence highlights the need for continued exploration of adjunctive therapies to enhance the long-term efficacy of PDT.

References/Contact Info