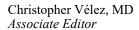
EVIDENCE-BASED GI AN ACG PUBLICATION



Can Tacrolimus Tame Esophageal Lichen Planus?







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This summary reviews Kukreja K, Kumar A, Camisa C, Jacobs J, Richter JE. Esophageal lichen planus: The efficacy and safety of tacrolimus in reducing inflammation and need for dilation. *Clin Trans Gastroenterol.* 2024; 15(12): e00752.

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STRUCTURED ABSTRACT

Question: Can low-dose oral tacrolimus effectively and safely reduce inflammation and the need for esophageal dilation in patients with esophageal lichen planus (ELP)?

Design: A retrospective cohort study.

Setting: Single tertiary care academic medical center: the University of South Florida and its affiliated Joy McCann Culverhouse Center for Swallowing Disorders.

Patients: Adults with confirmed ELP who underwent esophagogastroduodenoscopy (EGD) between 2011 and 2020 were included. All EGDs were performed by 1 of 2 esophagologists. Patients were identified via *International Classification of Diseases* and Current Procedural Terminology code review. Clinical, treatment, and endoscopic data were extracted from the electronic medical record.

Interventions: Patients were stratified into 2 cohorts: those treated with oral tacroli-

mus (1–2 mg twice daily) and those receiving alternative therapies (e.g., steroids, cyclosporine, or no treatment). Tacrolimus was prescribed by a dermatologist when standard treatments failed. All patients underwent baseline EGD with biopsy and bougie dilation, with repeat procedures as needed. Disease severity was assessed using the Esophageal Lichen Planus Severity Score (ELPSS), a novel endoscopic scoring tool capturing both inflammatory and fibrostenotic features (**Figure 1**).

Outcomes: The primary outcome was change in ELPSS. Secondary outcomes included clinical response, frequency of dilations, and safety. The tacrolimus group showed a significant reduction in ELPSS (mean decrease of 2.2 points vs 0.3 in controls; P = 0.02) and a higher clinical response rate (89% vs 30%; P = 0.04). Both groups reached a maximal dilation diameter of 16 mm, though tacrolimus-treated patients required fewer dilations over time, a difference that did not reach statistical significance.

Data Analysis: Descriptive statistics summarized baseline characteristics. Group comparisons used the Mann-Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables. Treatment effects were reported as mean differences with 95% confidence intervals. Kaplan-Meier analysis with log-rank testing compared response rates; dilation frequency was analyzed as a ratio over follow-up time. Significance was set at P < 0.05. Analyses were performed using SPSS v25 (IBM, Armonk, NY).

Funding: No external funding was reported.

Results: Twenty-two patients were included, evenly divided between tacrolimus (TAC) and non-tacrolimus (No-TAC) treatment groups. Baseline demographics and disease severity were comparable between groups. Tacrolimus therapy resulted in a significant reduction in disease severity, with mean ELPSS scores improving from 5.8 to 3.6, compared to a minimal change in the No-TAC group (5.9 to 5.6; P = 0.02). Clinical response was significantly higher in the TAC group (89% vs 30%; P = 0.04), and Kaplan-Meier analysis confirmed faster time-to-response (**Figure 2**).

All patients underwent bougie dilation, with a maximum diameter of 16 mm achieved in both groups. Although TAC-treated patients required fewer dilations over time, the difference was not statistically significant. Tacrolimus was generally well tolerated; 2 patients discontinued due to mild lab abnormalities. Minor procedural adverse events occurred in 1 patient per group.

These findings suggest that low-dose oral tacrolimus improves clinical and endoscopic outcomes in ELP with an acceptable safety profile.

	ELP Sev	erity Score	
Inflammation (Max 6)		Fibrostenosis (Max 4)	
Pale, edematous, or lacy appearance (1)		None (0)	
Sloughing or peeling (2)		Single stricture traversed with 10 mm scope (1)	
Exudate (1-mild, 2-moderate, and 3-severe)		Multiple strictures or narrowing (2)	
		**Additional points if narrowing required	
		downsize to 5 mm scope (2)	
Score range: 1-10. Interpretation: Mild	(1-2), Moderate	(3-4), Moderate-Seve	ere (5-7), Severe (8-10)
	FLDCC		
\$4!L! /4 3\	ELPSS Examples Moderate (4-5)		C (7.0)
Mild (1-2)	IVIOUE	:Tate (4-5)	Severe (7-9)

Figure 1. Illustration of the mild (left), moderate (middle), and severe (right) ELPSS. In the inflammatory component, sloughing or peeling occurs spontaneously or with the passage of scope only—not after dilatation. Exudate classification: mild—scattered punctate exudates; moderate—short serpiginous plaques; and severe—long, thick, serpiginous plaques. Within the fibrostenosis component, "multiple narrowing" describes more than one stricture or general narrowing involving more than one location in the esophagus. Adapted from ref. (1). ELP, esophageal lichen planus; ELPSS, Esophageal Lichen Planus Severity Score.

COMMENTARY

Why Is This Important?

ELP is a rare and under-recognized condition that presents significant diagnostic and therapeutic challenges, especially for gastroenterologists who often encounter these patients first. There is no consensus on diagnostic criteria or standard treatment, and existing histologic scoring systems are often impractical for routine use due to variability and nonspecific findings. This study introduces a visually based severity score (ELPSS) tailored for endoscopic use similar to scoring tools in eosinophilic esophagitis—and highlights the potential of low-dose oral tacrolimus as a safe and effective treatment option for patients with moderate to severe ELP. Addressing this unmet need improve disease recognition and longterm management.

Key Study Findings

Low-dose oral tacrolimus (1–2 mg twice daily) significantly reduced disease severity in ELP, as measured by ELPSS, compared to alternative therapies.

Patients treated with tacrolimus had a higher response rate (89% vs 30%) and required fewer dilations over time, suggesting both anti-inflammatory and antifibrotic benefits.

Tacrolimus was well tolerated, with only 2 discontinuations due to mild, manageable side effects.

The ELPSS showed good inter-rater reliability and may serve as a practical

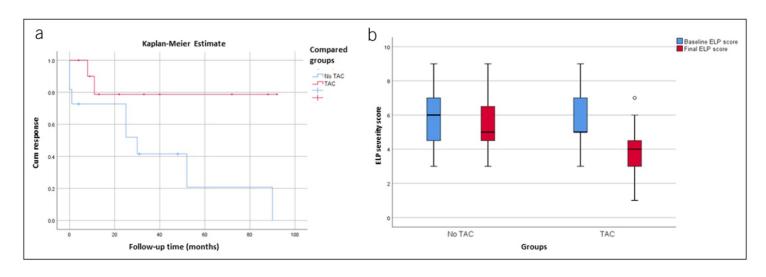


Figure 2. (a) Kaplan-Meier plot of response over time in patients undergoing tacrolimus treatment (TAC) vs no treatment; (b) box plot illustrating pre-post Esophageal Lichen Planus Severity Score in the TAC vs no-TAC group. The horizontal black lines denote median values, and the boxes extend from the 25th to the 75th percentile. The vertical extending lines represent adjacent values, and the dots represent the outliers. ELP, esophageal lichen planus.

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tool for clinicians to assess and monitor ELP severity in real time.

Caution

The principal causes for concern when interpreting this study include its design and sample size. Namely, while the authors did their best to standardize assessment of efficacy and rely upon reasonably objective metrics for success such as dilation practices, the sample size is too small to be definitive. Additionally, there could be long term risks for tacrolimus usage, particularly concerning immune suppression and potential nephrotoxicity (presumably less of a risk with the small doses needed to topical control). Shared decision making is critical prior to electing tacrolimus.

My Practice

Periodically when the EBGI Associate Editors convene, we review which recently published deserve to be summarized for our readership. This article spoke to me because it validated the care I offer a dear patient who I treat, who had been referred to me from a community practice for management of lichenoid esophagitis. Her thoughtful gastroenterologist had tried the usual immune suppressing regimens to no avail, and with good intention recommended gastrostomy tube placement to ensure nutritional status. Ever the spitfire, the patient decided that this was not how she wanted to spend her golden years and sought my opinion. I was initially flummoxed. Faced with dilations every 8-12 weeks with swallowed

proton pump inhibitors combined with swallowed steroids, this was sustainable for either of us. My colleague recommended tacrolimus; as a neuromotilist, I called upon my hepatology colleagues to help with dosing. We settled on a slurry of tacrolimus. Dilations are now spaced to every 6-months, with bougie dilation with a Savary. No more impactions and able to continue a generally normal per os intake, the patient is thankful. This article justifies my approach. Tacrolimus is not a first line agent I reach to, as people can be nervous about the immune suppression and the potential for tacrolimus-induced neurotoxicity and nephrotoxicity. But, with refractory strictures that are characteristic of this condition, I certainly would choose tacrolimus over a gastrostomy tube.

For Future Research

Fundamentally, this study is retrospective and small, making it unclear if the devised scoring system will be of utility. A larger data set would be needed for validation. Longer term data examining for possible sequelae of chronic tacrolimus use would be helpful, along with assessment for optimal formulation and dosing. Yet, given that this is a relatively rare condition, I doubt that such a study would be feasible. This study likely will be the best guess as to the role tacrolimus can play in successful management for this disease.

Conflicts of Interest

Dr. Syed reports and Dr. Vélez report no relevant conflicts.

Abbreviations

EGD, esophagogastroduodenoscopy; ELP, esophageal lichen planus; ELPSS, Esophageal Lichen Planus Severity Score; TAC, tacrolimus.

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1. Jacobs JW Jr, Kukreja K, Camisa C, Richter JE. Demystifying esophageal lichen planus: A comprehensive review of a rare disease you will see in practice. *Am J Gastroenterol*. 2022 Jan 1;117(1):70-77. Erratum in: *Am J Gastroenterol*. 2022 Jun 1;117 (6):1016-1017.