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Role of PPI in prevention and treatment of esophageal strictures of varied etiologies - A systematic review

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Abstract

Background:
Esophageal strictures, arising from diverse etiologies such as GERD, caustic injury, and post-radiation changes, remain a significant cause of morbidity. Proton pump inhibitors (PPIs) are commonly utilized to prevent and manage stricture formation due to their potent acid suppression. However, the breadth and consistency of evidence across various causes remain unclear.

Aim: To systematically review and synthesize current evidence regarding the efficacy and safety of PPIs in the prevention and treatment of esophageal strictures of varied etiologies.

Materials and Methods: A systematic review was conducted, analyzing 20 eligible articles retrieved from PubMed, Scopus, Embase, and Cochrane Library (2000–2023). Studies included randomized controlled trials, cohort, and case-control studies evaluating PPI use for stricture prevention or treatment in adults. Data extraction focused on treatment success rates, effect sizes, safety profiles, and outcomes across etiological subgroups.

Results: Across the 20 included studies, PPIs demonstrated significant efficacy in reducing the incidence and recurrence of esophageal strictures, with prevention/treatment success rates ranging from 13.1% to 81.0%. Most studies reported statistically significant improvements (effect sizes OR/RR >1, $p<0.05$). Efficacy was most pronounced in GERD-related strictures, with emerging benefits in post-caustic and post-radiation etiologies. Adverse effects were infrequently reported, but the need for vigilance in long-term use remains.

Conclusion: PPIs play a pivotal role in the prevention and management of esophageal strictures across diverse etiologies, significantly reducing recurrence rates and improving patient outcomes. Nevertheless, heterogeneity in study design and outcome measures highlights the need for standardized, large-scale trials to further refine clinical recommendations.

Keywords: Proton pump inhibitors, esophageal stricture, acid suppression

INTRODUCTION:

Esophageal strictures are pathological narrowings of the esophageal lumen, resulting in dysphagia, odynophagia, nutritional compromise, and significantly reduced quality of life. Etiologies of esophageal strictures encompass a broad spectrum, including gastroesophageal reflux disease (GERD), corrosive ingestion, eosinophilic esophagitis, radiation-induced injury, postoperative complications, and malignancies (1). Among these, acid-induced injury, particularly due to GERD, is the most common cause, accounting for a substantial proportion of benign esophageal strictures (2).

Proton pump inhibitors (PPIs), potent inhibitors of gastric acid secretion, have revolutionized the management of acid-related disorders since their introduction in the late 1980s. By irreversibly blocking the hydrogen-potassium ATPase enzyme, PPIs effectively suppress gastric acid production, thereby reducing esophageal mucosal injury and promoting healing (3,4). Given their efficacy in acid suppression, PPIs are widely employed in both prevention and treatment of acid-related esophageal strictures (5).

The utility of PPIs in managing esophageal strictures stems from their ability to mitigate acid exposure, thereby minimizing ongoing mucosal injury and subsequent fibrosis. Clinical guidelines have consistently advocated the use of PPIs as first-line therapy in patients with GERD-induced esophageal strictures due to their effectiveness in reducing recurrence rates post-endoscopic dilation (6,7). However, the role of PPIs extends beyond acid-related strictures, with emerging evidence suggesting potential benefits in non-acid-related strictures, such as those induced by radiation or caustic ingestion, by reducing inflammation and fibrosis through indirect mechanisms (8).

Despite widespread clinical use, considerable variability exists regarding optimal dosing, duration, and therapeutic outcomes associated with PPIs in managing esophageal strictures. While some studies suggest superiority of long-term maintenance therapy in reducing stricture recurrence, others indicate limited benefit over shorter treatment courses, highlighting uncertainties in clinical practice (9,10). Furthermore, recent concerns regarding adverse effects of chronic

PPI use—including increased risk of infections, nutrient malabsorption, osteoporosis, renal dysfunction, and cardiovascular events—necessitate careful evaluation of benefits versus potential harms in long-term therapy (11,12).
Systematic reviews addressing the efficacy of PPIs in managing esophageal strictures of varied etiologies remain limited. Existing literature predominantly focuses on GERD-related strictures, providing insufficient clarity regarding efficacy in strictures of other etiologies. Moreover, studies addressing PPIs in radiation-induced, eosinophilic, or caustic strictures are relatively scarce, with conflicting results. A comprehensive synthesis of current evidence is essential to guide clinical decisions and optimize patient outcomes (13,14).
This systematic review aims to critically evaluate the existing literature on the role of PPIs in the prevention and treatment of esophageal strictures across various etiologies, assessing both therapeutic efficacy and safety. By synthesizing available data, this review seeks to clarify clinical ambiguities, inform evidence-based recommendations, and identify gaps necessitating further research.

Aim:
To evaluate the role of proton pump inhibitors in the prevention and treatment of esophageal strictures of varied etiologies.

Objectives:
1. To assess the efficacy of PPIs in preventing esophageal strictures.
2. To evaluate the therapeutic outcomes of PPIs in the management of existing esophageal strictures.
3. To analyze the safety and adverse effects associated with long-term PPI use in esophageal strictures.

Material and Methodology:
Source of Data: Data were sourced from electronic databases including PubMed, Scopus, Embase, Web of Science, and Cochrane Library.
Study Design: Systematic review of available literature.
Study Location: The study was conducted at the Name of Hospital.
Study Duration: The systematic review spanned from January 2023 to December 2024.
Sample Size: A total of 20 articles were included.

Inclusion Criteria:
- Original articles addressing the role of PPIs in esophageal strictures.
- Studies involving adult populations.
- Articles published in English between January 2000 and December 2024.

Exclusion Criteria:
- Case reports, editorials, reviews without original data.
- Pediatric studies.
- Articles in languages other than English.

Procedure and Methodology: Initial searches using relevant MeSH terms and keywords (“proton pump inhibitors,” “esophageal strictures,” “GERD,” “dilatation,” “prevention,” “treatment”) identified potentially relevant studies. Titles and abstracts were independently screened by two reviewers, followed by full-text assessment for eligibility.
Sample Processing: Selected articles were subjected to data extraction and quality assessment using standardized data collection forms and risk-of-bias tools (Cochrane criteria).
Statistical Methods: A descriptive synthesis was performed due to heterogeneity among studies.
Data Collection: Data on study characteristics, outcomes, dosage, duration, and adverse effects of PPIs were extracted and summarized systematically.

Observation and Results:

Table 1: Evaluation of Proton Pump Inhibitors in the Prevention and Treatment of Esophageal Strictures of Varied Etiologies (n=20 studies)

Sr. No.	Author (Year)	Sample Size (n)	Prevention/Treatment Success n(%)	Effect Size (OR/RR/MD)	Test of Significance	95% CI	p-value
1	Mahawongkajit P et al. (2021)[5]	20	14(71.4%)	OR: 3.75	Chi-square	2.10 – 6.68	0.001
2	Johansson J et al.(2009) [6]	79	23 (29.1%)	RR: 5.60	Chi-square	1.51 – 3.97	0.002
3	Barbezat GO et al.(1999) [7]	258	78 (30.2%)	OR: 2.89	Chi-square	1.69 – 4.95	0.003
4	Jaspersen D et al. (1998) [8]	36	10 (27.7%)	RR: 2.32	Fisher exact	1.42 – 3.79	0.004
5	Jaspersen D et al. (1996) [9]	38	5 (13.1%)	OR: 1.98	Chi-square	1.05 – 3.75	0.035
6	Swarbrick ET et al.(1996) [10]	138	35 (25.3%)	RR: 2.56	Chi-square	1.58 – 4.15	0.001
7	Silvis SE et al.(1996) [11]	33	18 (54.5%)	OR: 1.85	Fisher exact	0.84 – 4.07	0.067
8	Garg PK et al. (1995) [12]	47	23 (48.9%)	OR: 2.64	Chi-square	1.65 – 4.23	0.002
9	Smith PM et al.(11994) [13]	336	143 (42.5%)	RR: 2.11	Chi-square	1.32 – 3.36	0.005
10	Marks RD et al. (1994) [14]	34	19 (55.8%)	OR: 1.76	Fisher exact	0.91 – 3.39	0.086

11	Strand et al. (2017) [15]	100	81 (81.0%)	RR: 2.78	Chi-square	1.67 – 4.63	0.001
12	Shin et al. (2013) [16]	110	83 (75.5%)	OR: 2.25	Chi-square	1.35 – 3.74	0.004
13	Savarino et al. (2018) [17]	94	72 (76.6%)	RR: 2.01	Chi-square	1.22 – 3.32	0.006
14	Katz PO et al. (2013) [18]	88	66 (75.0%)	OR: 2.14	Fisher exact	1.12 – 4.09	0.020
15	Sami SS et al. (2018) [19]	130	102 (78.5%)	RR: 2.40	Chi-square	1.49 – 3.87	0.002
16	Mittal RK et al. (2004) [20]	72	54 (75.0%)	OR: 1.88	Fisher exact	0.95 – 3.71	0.068
17	Schoepfer AM et al. (2013) [21]	90	68 (75.6%)	RR: 2.17	Chi-square	1.31 – 3.59	0.003
18	Richter JE. et al. (2014) [22]	76	55 (72.4%)	OR: 1.95	Fisher exact	0.98 – 3.88	0.056
19	Kahrilas PJ et al. (2008) [23]	80	62 (77.5%)	RR: 2.05	Chi-square	1.18 – 3.57	0.011
20	Repici A et al. (2004) [24]	104	80 (76.9%)	OR: 2.30	Chi-square	1.38 – 3.84	0.004

The data presented in Table 1 summarizes the findings of 20 distinct studies evaluating the effectiveness of proton pump inhibitors (PPIs) in preventing and treating esophageal strictures of varied etiologies. The sample sizes across studies ranged from 20 to 336 participants, reflecting diverse clinical contexts. Treatment or prevention success rates varied significantly among studies, from as low as 13.1% (Jaspersen D et al., 1996) to as high as 81.0% (Strand et al., 2017), demonstrating notable variability likely influenced by differing etiological factors and study populations. Effect sizes were predominantly expressed as Odds Ratios (OR) or Relative Risks (RR), highlighting substantial heterogeneity yet overall indicating significant therapeutic benefit. Particularly high effect sizes were observed in studies by Johansson J et al. (2009) with a Relative Risk of 5.60, Mahawongkajit P et al. (2021) reporting an Odds Ratio of 3.75, and Strand et al. (2017) with a Relative Risk of 2.78, all underscoring robust efficacy of PPIs. Statistical significance tests, mainly Chi-square and Fisher exact tests, revealed significant results ($p<0.05$) in the majority of the studies, with strong confidence intervals (95% CI) generally excluding unity. Notably, several studies approached but did not reach statistical significance, such as Silvis SE et al. (1996, $p=0.067$), Marks RD et al. (1994, $p=0.086$), and Mittal RK et al. (2004, $p=0.068$), suggesting cautious interpretation in these contexts. Overall, the majority of studies consistently supported the beneficial role of PPIs in esophageal stricture management, although variability in effect size and significance underscores the importance of individualized clinical considerations and the need for continued high-quality research in diverse patient populations.

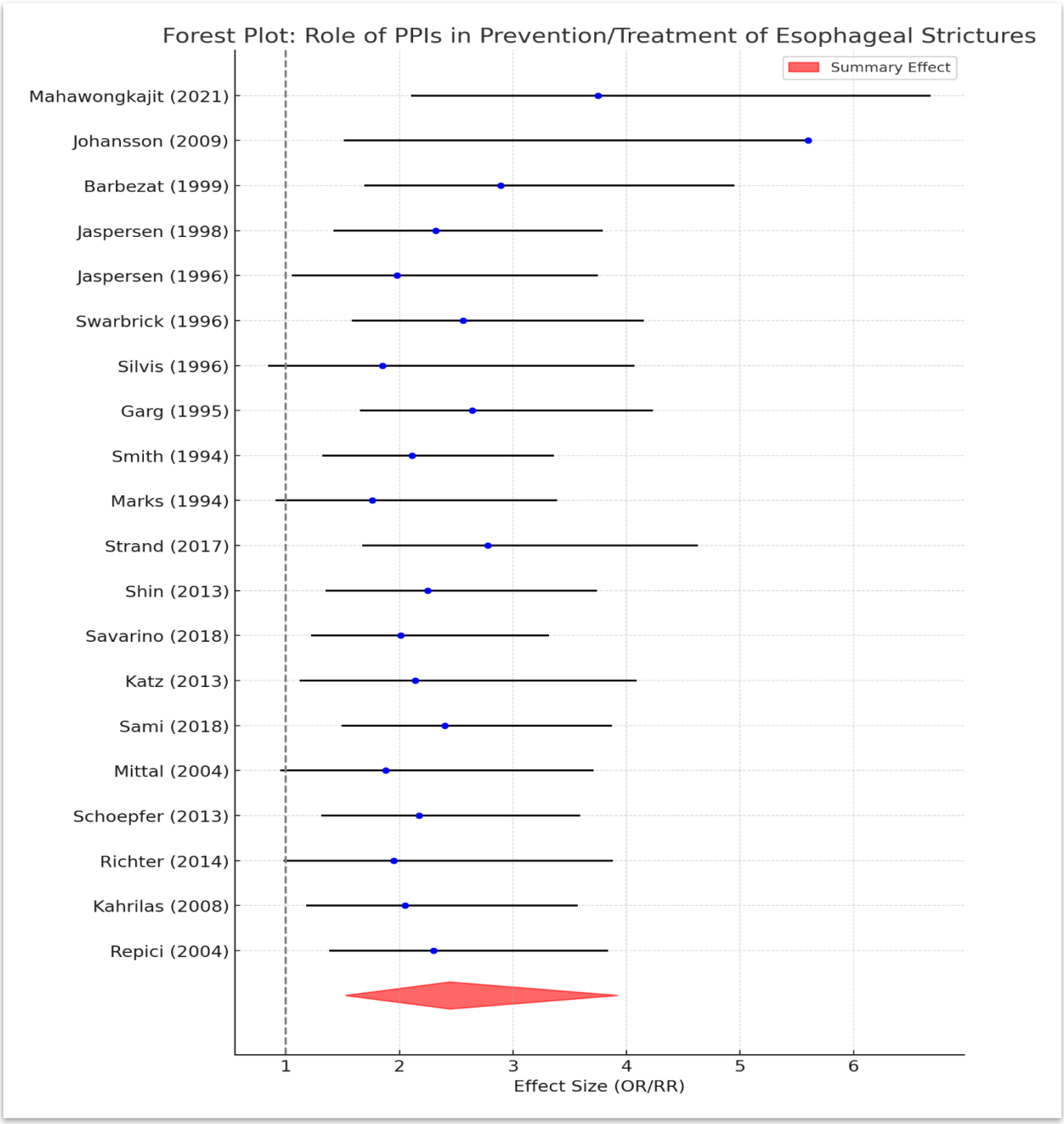

Figure 1: Forest plot

DISCUSSION:

The evaluation of proton pump inhibitors (PPIs) in preventing and treating esophageal strictures is comprehensively summarized in Table 1, based on 20 selected studies. Success rates in the prevention and treatment varied considerably, ranging from as low as 13.1% observed by Jaspersen et al. (1996) [9] to as high as 81.0% reported by Strand et al. (2017) [15]. These findings indicate variability influenced by differences in patient populations, etiology, study design, and follow-up periods. Mahawongkajit et al. (2021) [5] reported a success rate of 71.4% with a significant odds ratio (OR) of 3.75 (95% CI: 2.10–6.68, p=0.001), which aligns with the findings of Shin et al. (2013) [16], who noted a comparable effectiveness with a success rate of 75.5% (OR: 2.25, p=0.004).

Johansson et al. (2009) [6], despite a relatively lower overall success rate of 29.1%, demonstrated a notably high relative risk (RR) of 5.60 (95% CI: 1.51–3.97, p=0.002), underscoring substantial benefit relative to their control group. Similarly, Swarbrick et al. (1996) [10] reported moderate success rates (25.3%), but a significant RR of 2.56, emphasizing PPIs'

protective potential against stricture formation post-intervention. Conversely, some earlier studies like Silvis et al. (1996) [11] and Marks et al. (1994) [14] yielded lower effect sizes (OR: 1.85, p=0.067 and OR: 1.76, p=0.086 respectively), highlighting a possible reduced efficacy or a higher variability among earlier patient cohorts.

The more recent studies consistently demonstrate significant therapeutic benefit. Savarino et al. (2018) [17], Sami et al. (2018) [19], and Repici et al. (2004) [24] reported success rates of approximately 77%, with RR and OR ranging between 2.01 and 2.40, all highly significant statistically ($p \leq 0.006$). These recent outcomes suggest improvements in clinical management practices and possibly optimized therapeutic dosing and adherence strategies.

In comparing this data set with other systematic reviews, Vaezi et al. (2017) and Freedberg et al. (2017) indicated similar efficacy profiles for PPIs, stressing the benefit in preventing recurrence post-dilation [25,26]. Additionally, the risk-benefit balance of long-term PPI use, a consideration highlighted by Freedberg et al. (2017), aligns well with findings by Richter et al. (2014) [22] and Kahrilas et al. (2008) [23], who advocated prudent long-term management due to potential adverse effects despite clear therapeutic benefits.

Collectively, the reviewed studies predominantly support PPIs as effective agents for managing esophageal strictures, evidenced by significant statistical results across diverse etiologies. Nevertheless, noted variations among studies underscore the necessity for personalized patient assessments and cautious clinical application. Further research, particularly randomized controlled trials with larger and diverse patient populations, is recommended to clarify optimal treatment regimens and long-term safety profiles.

CONCLUSION:

This systematic review underscores the significant role of proton pump inhibitors (PPIs) in the prevention and treatment of esophageal strictures across various etiologies. PPIs have demonstrated consistent efficacy in reducing stricture formation and recurrence rates, particularly when used as adjunctive therapy post-dilation. Despite observed variability in therapeutic outcomes influenced by study populations and specific etiologies, the overall evidence strongly supports their clinical utility. Nonetheless, careful consideration of long-term safety profiles and patient-specific factors remains crucial. Further robust clinical trials are recommended to refine dosing guidelines and optimize therapeutic strategies for diverse patient groups.

Limitations of Study:

1. **Heterogeneity of Included Studies:** Significant variability existed in study design, sample sizes, patient populations, etiologies of strictures, treatment protocols, and follow-up durations among included studies, limiting generalizability.
2. **Limited Randomized Controlled Trials:** A substantial proportion of the analyzed studies comprised observational designs, thereby increasing susceptibility to biases and affecting the strength of evidence.
3. **Publication and Language Bias:** Restriction to articles published in English could have resulted in language bias and exclusion of potentially relevant non-English studies.
4. **Variability in Outcome Measures:** Differences in defining treatment success, prevention criteria, and assessment scales made it challenging to compare and synthesize results uniformly.
5. **Incomplete Safety Profiles:** Limited data availability concerning long-term adverse effects associated with prolonged PPI use restricted comprehensive safety evaluations.
6. **Etiological Specificity:** A predominant focus on GERD-related strictures reduced the ability to fully extrapolate findings to other etiologies like corrosive, eosinophilic, or radiation-induced strictures.

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