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2025 Focused Update of the Seoul Consensus on Gastroesophageal Reflux Disease: Evidence-based Recommendations on Acid Suppressive Therapy

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Gastroesophageal reflux disease (GERD) is a chronic and relapsing gastrointestinal disorder characterized by the reflux of gastric contents into the esophagus, leading to troublesome symptoms and/or complications. Since the publication of the 2020 Seoul Consensus on GERD, significant new evidence has emerged, particularly regarding acid-suppressive therapies and diagnostic approaches. This 2025 focused update aims to refine GERD management strategies by incorporating the latest evidence on acid suppressive therapies and regional considerations in Asian populations. This study builds on the 2020 Seoul Consensus by integrating systematic reviews, meta-analyses, and expert consensuses to offer updated recommendations for the definition and medical treatment of GERD. These guidelines incorporate recent advances in acid-suppressive therapies, particularly potassium-competitive acid blockers, and adopt updated diagnostic frameworks in accordance with the Lyon Consensus 2.0. Key clinical questions were identified and structured using the following format: Population, Intervention, Comparator, Outcome. The resulting recommendations address the initial treatment, long-term maintenance strategies, and role of personalized therapy based on disease severity, such as the grade of reflux esophagitis. Six key statements are presented: updated definition and classification of GERD (Statement 1); initial and long-term treatment strategies tailored to GERD phenotypes, such as non-erosive reflux disease, mild erosive esophagitis, and severe erosive esophagitis (Statements 2-5); and dose optimization strategies for long-term safety (Statement 6). These guidelines aim to support gastroenterologists and general healthcare providers in making individualized evidence-based decisions for GERD management.

Keywords: Definition; Gastroesophageal reflux disease; Meta-analysis; Practice guideline; Treatment

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a chronic and relapsing gastrointestinal disorder characterized by the reflux of gastric contents into the esophagus, leading to troublesome symptoms and/or complications.[1,2] This

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patient-centered definition, originally proposed by the Montreal Consensus,[3] has been widely adopted in clinical practice. However, the heterogeneous nature of GERD phenotypes and their overlap with functional disorders highlight the need for more objective diagnostic criteria. The Lyon Consensus 2.0, published in 2023, introduced a revised diagnostic framework that emphasizes objective physiologic testing and introduces the concept of "actionable GERD" to guide individualized therapy.[4]

GERD treatment is essential not only for prompt symptom relief and mucosal healing, but also to prevent chronic complications such as peptic strictures, Barrett's esophagus, and esophageal cancer.[5,6] Given the relapsing nature of GERD, effective long-term maintenance strategies are crucial for clinical decision making.

For more than 2 decades, proton pump inhibitors (PPIs) have been the cornerstone of GERD management.[7,8] However, limitations of PPIs include their requirement for proton pump activation, delayed onset of action, insufficient duration of action, and incomplete symptom relief in some patients. Another limitation is the growing concern over potential long-term adverse effects, including bone fractures, micronutrient deficiencies, pneumonia, chronic kidney disease, small intestinal bacterial overgrowth, *Clostridium difficile* infection, and hypergastrinemia.[9-16] Potassium-competitive acid blockers (P-CABs), which were first introduced in Asia, have emerged as promising alternatives with improved pharmacological profiles—such as more potent acid suppression, stability in acidic environments, rapid onset of action, and longer half-life—compared to that of PPIs.[17-21] An increasing number of randomized trials, real-world studies, and meta-analyses support the role of P-CABs in both initial and maintenance treatments of GERD, although further data are needed on their long-term safety.[22-30]

The 2020 Seoul Consensus on GERD provides region-specific recommendations for the diagnosis and treatment of GERD in Asian populations, incorporating global evidence and local practice patterns.[31] Since its publication, growing evidence comparing PPI and P-CAB therapies has emerged, along with updates in the diagnostic criteria for GERD. This 2025 focused update refines and expands the 2020 Seoul Consensus by incorporating recent data on acid-suppressive therapies and reflecting the evolving diagnosis of GERD. We present updated meta-analytic findings and expert insights to support individualized phenotype-based GERD management.

METHODS

The working group comprised gastroenterologists affiliated with the Korean Society of Neurogastroenterology and Motility (KSNM) and methodology experts. The participating committee members provided written consent on whether they had any conflicts of interest. These revised guidelines were developed using a hybrid methodology that combined systematic reviews, meta-analyses, and expert consensuses. The development process was modeled after the evidence-based methods used in the 2020 Seoul Consensus on GERD and other recent Korean clinical practice guidelines. Nine online meetings were held to develop these guidelines (started in May 2024). The guidelines were developed using a combination of de novo and adaptation methods, considering current developments in GERD management. To derive the key clinical questions, the working group reviewed existing domestic and international guidelines and selected core topics related to GERD definition and management through structured discussions. The key questions were categorized according to the definition and treatment of GERD. The working group conducted a literature search, performed quality assessments and meta-analyses, and evaluated the evidence levels and strengths of the recommendations. Key clinical questions were developed using the Population, Intervention, Comparator, Outcome format, focusing on 2 major areas: (1) initial treatment strategies for GERD based on disease severity and (2) long-term maintenance approaches, including on-demand vs continuous therapy and optimal dosing.

A systematic literature search was performed across PubMed, Embase, and the Cochrane Library to identify randomized controlled trials (RCTs) published up to December 2024. The search focused on 2 comparisons: (1) on-demand vs continuous PPI maintenance therapy and (2) P-CAB vs PPI therapy for the initial and/or maintenance treatment of GERD. The search results were complemented by a manual search. The search was completed in January 2025. Studies were included if they met the following criteria: (1) RCTs evaluating patients diagnosed with GERD, including non-erosive reflux disease (NERD), erosive reflux disease (ERD), reflux esophagitis, and endoscopy-negative reflux disease; (2) comparisons between continuous PPI maintenance therapy and on-demand PPI maintenance therapy, and comparisons between PPI and P-CAB therapy in either initial treatment or maintenance therapy; and (3) available full-text articles. The exclusion criteria were as follows: (1) abstract-only publications or unpublished studies, (2)

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Table 1. Definition of Levels of Evidence and Strength of Recommendation

Level of evidence	
High	At least 1 RCT or SR/meta-analysis with no concerns regarding study quality
Moderate	At least 1 RCT or SR/meta-analysis with minor concerns regarding study quality or, at least 1 cohort/case-control/diagnostic test design study with no concerns regarding study quality
Low	Low at least 1 cohort/case-control/diagnostic test study with minor concerns regarding study quality, or at least 1 single arm before-after study or cross-sectional study with no concerns regarding study quality
Very low	At least 1 cohort/case-control/diagnostic test design study with serious concerns regarding study quality, or at least 1 single arm before-after study or cross-sectional study with minor/severe concerns regarding study quality
Grade of recommendation	
Strong for	Strong recommendations are offered when the desirable effects of an intervention clearly outweigh the undesirable effects
Weak for	Weak recommendations are offered when trade-offs are less certain, either because of low-quality evidence or because

RCT, randomized controlled trial; SR, systematic review.

case reports and narrative reviews, (3) systematic reviews or meta-analyses, (4) conference proceedings or study protocols, and (5) studies with insufficient data on treatment outcomes. Studies were selected in two stages. First, titles and abstracts were screened to exclude irrelevant studies. Second, full-text articles were reviewed to determine eligibility based on predefined inclusion and exclusion criteria. Data extraction was performed independently by 2 reviewers (J.W.C. and C.W.H.) using a standardized data collection form. Any discrepancies were resolved through discussion with senior investigators (Y.H.Y. and K.J.L.). The strengths of the recommendations were determined using the grading of Recommendations, Assessment, Development, and Evaluation framework. The evidence level was categorized as high, moderate, low, or very low based on the study design, risk of bias, inconsistency, indirectness, imprecision, and publication bias (Table 1). The overall strength of each recommendation was determined in accordance with the assessed level of evidence.[32]

A consensus on draft recommendations was achieved using a modified Delphi method. Each recommendation statement was evaluated by a panel of experts on a 5-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = undecided, 4 = agree with reservations, and 5 = strongly agree). Consensus was defined as ≥ 80% agreement (score of 4 or 5). In the first round, 59 expert panel members agreed to participate and submitted their responses via email. All statements reached a consensus in the first round and were subsequently adopted (Table 2). All members of the working group who participated in guideline development declared any competing interests in writing. These guidelines will be uploaded to the KSNM websites and published in both English and Korean.

DEFINITION OF GASTROESOPHAGEAL REFLUX DISEASE

Statement 1

1. **Gastroesophageal reflux disease is a condition characterized by regurgitation of gastric contents into the esophagus or the mouth, resulting in troublesome symptoms or complications.**
   - Level of evidence: NA
   - Strength of recommendation: NA
   - Expert opinion: strongly agree, 86.4%; agree with reservation, 13.6%; undecided, 0.0%; disagree, 0.0%; and strongly disagree, 0.0%.

2. **Proven gastroesophageal reflux disease is defined as either (1) reflux esophagitis (Los Angeles grades B, C, and D), Barrett's esophagus, or ulceration/stricture attributable to esophagitis documented on endoscopy, or (2) pathological gastroesophageal reflux confirmed by ambulatory pH-impedance monitoring.**
   - Level of evidence: NA
   - Strength of recommendation: NA
   - Expert opinion: strongly agree, 50.9%; agree with reservation, 39.0%; undecided, 10.1%; disagree, 0.0%; and strongly disagree, 0.0%.

3. **Gastroesophageal reflux disease can be subclassified into non-erosive reflux disease and erosive reflux disease based on the presence of erosive esophagitis. Erosive esophagitis, characterized by mucosal breaks, is graded by the Los Angeles classification, with grades A and B considered mild, and grades C and D considered severe.**
   - Level of evidence: NA

Table 2. Summary of Key Statements and Recommendations in the 2025 Focused Update of the Seoul Consensus on Gastroesophageal Reflux Disease

Statements	Level of evidence	Strength of recommendation
Definition		
1.1. GERD is a condition characterized by regurgitation of gastric contents into the esophagus or the mouth, resulting in troublesome symptoms or complications	N/A	N/A
1.2 Proven GERD is defined as either (i) reflux esophagitis (LA grades B, C, and D), Barrett's esophagus, or ulceration/stricture attributable to esophagitis documented on endoscopy, or (ii) pathological gastroesophageal reflux confirmed by ambulatory pH-impedance monitoring	N/A	N/A
1.3 GERD can be subclassified into NERD and ERD based on the presence of EE. EE, characterized by mucosal breaks, is graded by the LA classification, with grades A and B considered mild, and grades C and D considered severe	N/A	N/A
Treatment		
2. The administration of a standard dose of PPIs or P-CABs once daily for 4 to 8 weeks is recommended as the initial treatment for NERD or mild EE	High	Strong
3. The administration of a standard dose of P-CABs or PPIs once daily for 8 weeks is recommended as the initial treatment for severe EE • Consideration: P-CABs may offer superior mucosal healing efficacy compared to PPIs in patients with severe EE	High	Weak
4. On-demand therapy with PPI or P-CAB is recommended for the long-term management of patients with NERD or mild EE	Moderate	Weak
5. Continuous daily therapy with PPI or P-CAB is proposed for the long-term management of patients with severe EE	Low	Weak
6. The lowest effective dose that controls symptoms and maintains mucosal healing is recommended for patients with GERD requiring long-term maintenance therapy with PPIs or P-CABs, to avoid overuse and potential risks	Low	Weak

GERD, gastroesophageal reflux disease; LA, Los Angeles classification; NERD, non-erosive reflux disease; ERD, erosive reflux disease; EE, erosive esophagitis; PPIs, proton pump inhibitos; P-CABs, potassium-competitive acid blockers; NA, not applicable.

- Strength of recommendation: NA
- Expert opinion: strongly agree, 66.1%; agree with reservation, 28.8%; undecided, 3.4%; disagree, 1.7%; and strongly disagree, 0.0%.

GERD is a clinical condition in which the reflux of gastric contents into the esophagus or beyond causes troublesome symptoms and/or complications.[3] Recently, the Lyon Consensus 2.0 proposed a revised definition to increase specificity, introducing the concept of "actionable" GERD.[4] Previous definitions based on "troublesome" symptoms alone are insufficient for a conclusive diagnosis. Therefore, actionable GERD requires conclusive evidence of reflux esophagitis (Los Angeles [LA] grades B, C, and D), Barrett's esophagus, or ulceration/stricture attributable to esophagitis documented on endoscopy and/or pathological gastroesophageal reflux confirmed by ambulatory pH-impedance monitoring. However, the thresholds for esophageal reflux testing in Asians may differ from those in Western populations, warranting further investigation. In addition, GERD can be classified into NERD and erosive esophagitis (EE), depending on the absence or presence of mucosal injury on endoscopy. LA grades A and B were categorized as mild EE, while LA grades C and D were categorized as severe EE. Although LA grade A does not meet the criteria for proven GERD according to the Lyon Consensus 2.0, it is still considered part of the EE spectrum in many clinical and research contexts. Therefore, while LA-A alone may not be sufficient to define proven GERD, it remains clinically relevant when subclassifying GERD and guiding phenotype-based treatment strategies. In alignment with recent Japanese GERD guidelines,[33] this focused update also recommends phenotype-based treatment strategies tailored to disease severity, such as the grade of reflux esophagitis, reinforcing the principle of personalized GERD management.

TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE

Statement 2. Administration of a standard dose of proton pump inhibitors or potassium-competitive acid blockers once daily for 4-8 weeks is recommended as the initial

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treatment for non-erosive reflux disease or mild erosive esophagitis.

- Level of evidence: high
- Strength of recommendation: strong
- Expert opinion: strongly agree, 70.7%; agree with reservation, 25.9%; undecided, 1.7%; disagree, 1.7%; and strongly disagree, 0.0%.

Standard-dose PPI therapy for 4-8 weeks has long been established as the first-line treatment for NERD and mild EE based on multiple international guidelines.[4,31,33-35] Recently, P-CABs have emerged as an alternative class of acid-suppressive agents that reversibly inhibit the H^+, K^+-ATPase, offering a more rapid and sustained acid suppression profile than PPIs.[11,29,36]

In the pooled analysis of 7 RCTs[18,29,37-41] comparing PPIs and P-CABs—including vonoprazan, fexuprazan, keverprazan, and zastaprazan—the healing rates of EE were comparable between the 2 groups at both 8 weeks (pooled RR = 1.00; 95% CI, 0.99-1.02; Fig. 1A) and 4 weeks in patients with mild EE (pooled RR = 1.01; 95% CI, 0.97-1.06; Fig. 2A). Subgroup analysis also showed similar results for vonoprazan (RR = 1.00; 95% CI, 0.98-1.01; Supplementary Fig. 1) and other P-CABs, including fexuprazan, keverprazan, and zastaprazan (RR = 1.01; 95% CI, 0.98-1.05; Supplementary Fig. 1). Although tegoprazan-specific data for mild EE were not available, pooled analyses across all EE grades demonstrated comparable efficacy to that of PPI at both 4 weeks and 8 weeks (pooled RR = 1.03; 95% CI, 0.97-1.10). Regarding safety, the overall incidence of treatment-emergent adverse events (TEAEs) over 8 weeks was comparable between the 2 groups (pooled RR = 1.04; 95% CI, 0.94-1.15; Supplementary Fig. 2). A flow diagram of the study selection process and a summary of the included studies are provided in Supplementary Figure 3 and Supplementary Table 1, respectively. In patients with NERD, several RCTs have demonstrated that P-CABs provide superior symptom relief compared to placebo.[18,42-44]

Based on current evidence, the use of either a standard-dose PPI (eg, lansoprazole 30 mg, esomeprazole 40 mg, pantoprazole 40 mg, etc) or P-CAB (eg, tegoprazan 50 mg, fexuprazan 40 mg, zastaprazan 20 mg, vonoprazan 20 mg, etc) for 4-8 weeks is recommended as the initial treatment for NERD or mild EE.

Statement 3. Administration of a standard dose of potassium-competitive acid blockers or proton pump inhibitors once daily for 8 weeks is recommended as the initial treatment for severe erosive esophagitis.

- Level of evidence: high
- Strength of recommendation: weak

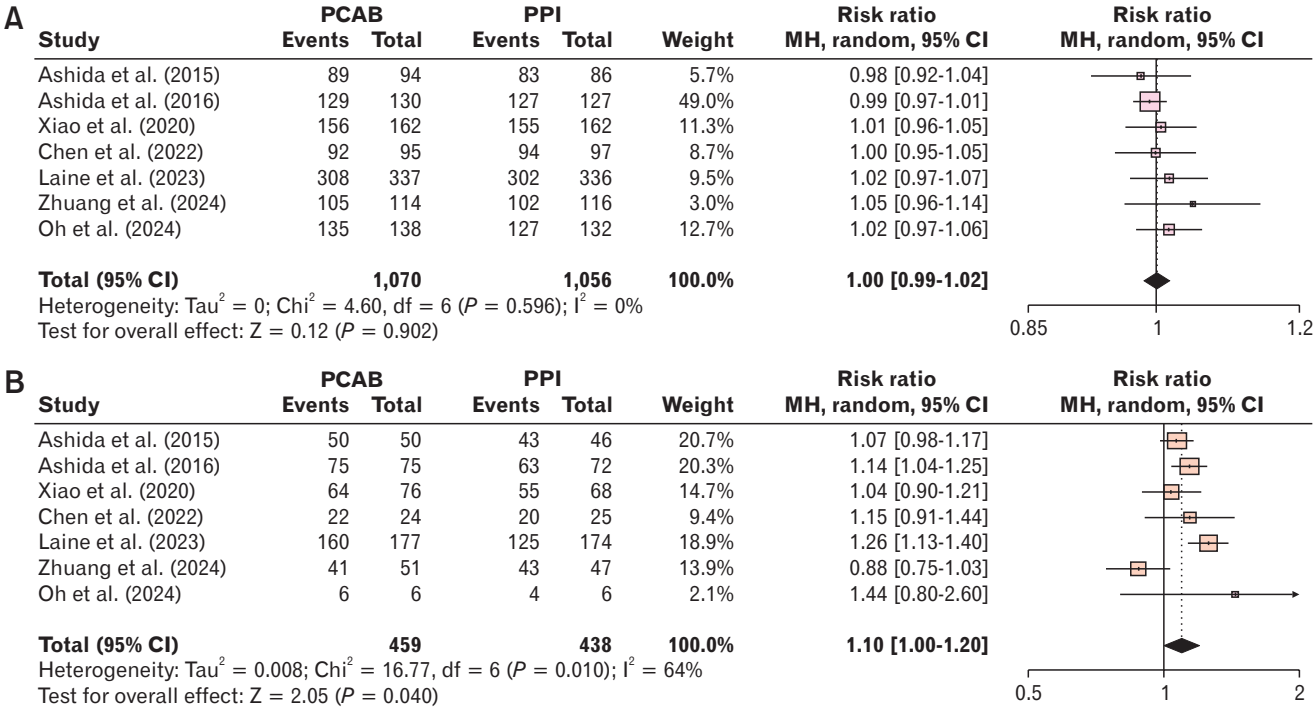

Figure 1. Pooled analysis of healing rates at 8 weeks in patients with erosive esophagitis (EE). (A) Pooled analysis of healing rates at 8 weeks in patients with mild EE: proton pump inhibitors (PPI) vs potassium-competitive acid blockers (P-CABs); (B) pooled analysis of healing rates at 8 weeks in patients with severe EE: PPI vs P-CABs. MH, Mantel-Haenszel.

- Expert opinion: strongly agree, 50.0%; agree with reservation, 37.9%; undecided, 5.2%; disagree, 6.9%; and strongly disagree, 0.0%.

Consideration

- P-CABs may offer superior mucosal healing efficacy compared to PPIs in patients with severe EE.

In the pooled analysis of 7 RCTs[18,29,37-41] comparing PPIs and P-CABs—including vonoprazan, fexuprazan, keverprazan, and zastaprazan—the healing rates of esophagitis were superior with P-CABs at both 8 weeks (pooled RR = 1.10; 95% CI, 1.00-1.20; Fig. 1B) and 4 weeks in patients with severe EE (pooled RR = 1.14; 95% CI, 1.03-1.26; Fig. 2B). In subgroup analyses, vonoprazan showed superior efficacy compared to PPIs (RR = 1.13; 95% CI, 1.04-1.23; Supplementary Fig. 4), while other P-CABs—including fexuprazan, keverprazan, and zastaprazan—demonstrated comparable efficacy (RR = 1.04; 95% CI, 0.81-1.34; Supplementary Fig. 4). Although tegoprazan-specific data for severe EE were not available, pooled analyses across all EE grades demonstrated comparable efficacy to PPI at both 4 weeks and 8 weeks (pooled RR = 1.03; 95% CI, 0.97-1.10). In addition, a pooled analysis of treatment failure rates, defined as the failure to heal EE, showed significantly lower failure rates with P-CABs than with PPIs (P-CABs, 8.9% vs PPI, 19.4%; $P < 0.001$; Fig. 3). In terms of safety, the overall incidence of TEAEs over 8 weeks was comparable between the 2 groups (pooled RR = 1.04; 95% CI, 0.94-1.15; Supplementary Fig. 3).

Based on current evidence, an 8-week course of standard-dose P-CAB or PPI is recommended as the initial treatment option for patients with severe EE. However, P-CABs may be preferred over PPIs owing to their superior healing efficacy in severe EE and comparable safety profiles.

Statement 4. On-demand therapy with proton pump inhibitor or potassium-competitive acid blocker is recommended for the long-term management of patients with non-erosive reflux disease or mild erosive esophagitis.

- Level of evidence: moderate
- Strength of recommendation: weak
- Expert opinion: strongly agree, 63.8%; agree with reservation, 29.4%; undecided, 3.4%; disagree, 3.4%; and strongly disagree, 0.0%.

Long-term maintenance therapy is essential in managing GERD, as both NERD and EE have high relapse rates

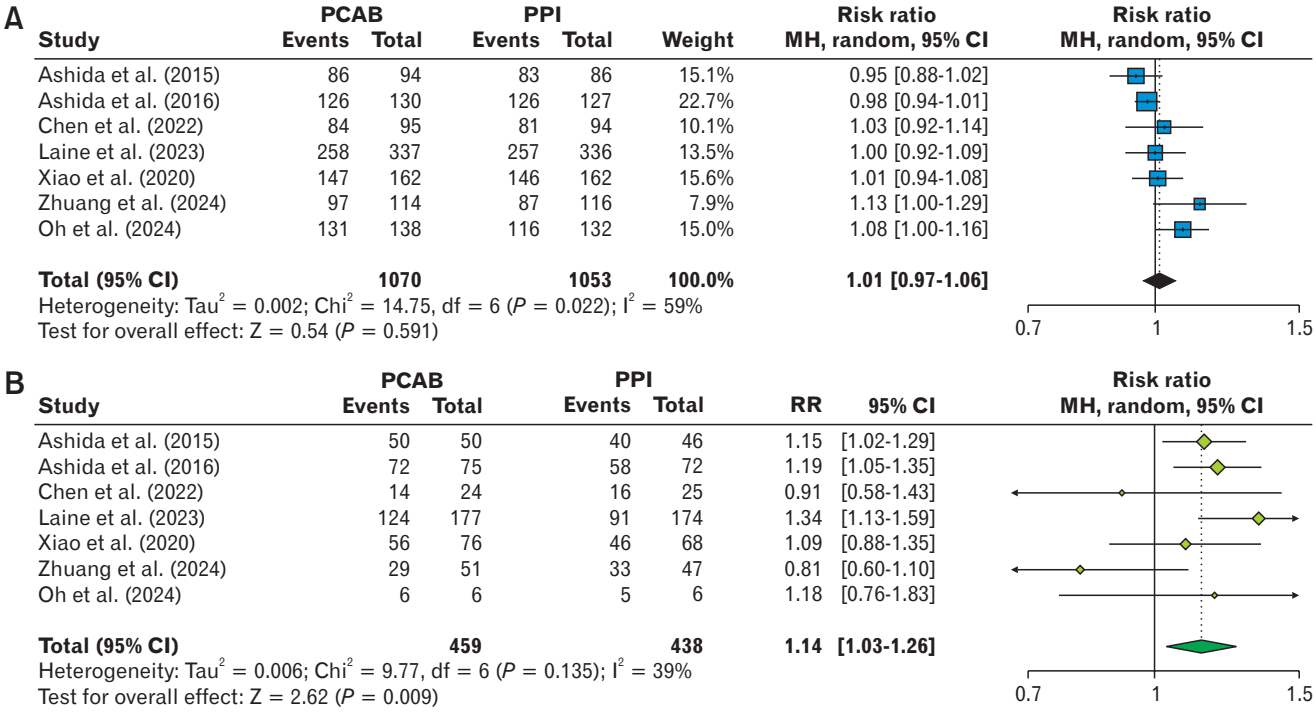

Figure 2. Pooled analysis of healing rates at 4 weeks in patients with erosive esophagitis (EE). (A) Pooled analysis of healing rates at 4 weeks in patients with mild EE: proton pump inhibitor (PPI) vs potassium-competitive acid blockers (P-CABs); (B) pooled analysis of healing rates at 4 weeks in patients with severe EE: PPI vs P-CABs. MH, Mantel-Haenszel.

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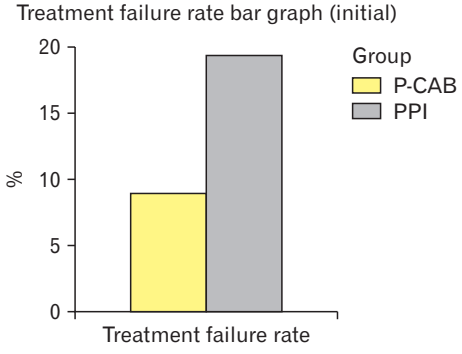
following cessation of acid-suppressive therapy.[45,46] Therefore, effective long-term strategies are required to maintain symptom control and prevent the recurrence of EE. Several maintenance strategies have been explored for the long-term management of GERD, including continuous, on-demand, intermittent, and threshold therapies. Continuous therapy involves taking PPIs daily, regardless of the presence of symptoms, whereas on-demand therapy refers to taking PPIs only when symptoms occur. Intermittent and threshold therapies are less commonly adopted and involve short treatment courses during symptom relapse and gradual extension of dosing intervals based on symptom control, respectively. Among them, continuous and on-demand therapies are the most widely adopted in clinical practice.

In the pooled analysis of 6 RCTs[2,47-51] in patients with NERD or mild EE, on-demand and continuous PPI therapies showed comparable rates of treatment failure (pooled RR = 1.17; 95% CI, 0.65-2.13; Fig. 4), which was defined as premature discontinuation of the allocated maintenance therapy. The incidence of adverse events was similar between groups (RR = 0.98; 95% CI, 0.89-1.09; Supplementary Fig. 5). Pill burden was significantly lower with on-demand therapy as shown in Supplementary Figure 6 (risk difference = −0.52; 95% CI, −0.62 to −0.42). A flow diagram of the study selection process and a summary of the included studies are provided in Supplementary Figure 7 and Supplementary Table 2, respectively.



	P-CAB	PPI	*P*-value
Treatment failure	41	85	< 0.001
N	459	438	

Figure 3. Comparison of treatment failure rates at 8 weeks in patients with severe erosive esophagitis: proton pump inhibitor (PPI) vs potassium-competitive acid blocker (P-CAB).

Although evidence on on-demand P-CAB therapy for the long-term maintenance of GERD remains limited, some studies have suggested its effectiveness in patients with NERD or mild EE.[52,53] Furthermore, a pooled analysis of four RCTs[20,54-56] in patients with mild EE showed that long-term P-CAB therapy was superior to PPI therapy in preventing EE recurrence over 24 weeks (pooled RR = 0.60; 95% CI, 0.38-0.94; Fig. 5A). A flow diagram of the study selection process and a summary of the included studies are provided in Supplementary Figure 8 and Supplementary Table 3, respectively. Although robust evidence on long-term on-demand P-CAB therapy remains scarce, its clinical usefulness in patients with NERD or mild EE is supported by findings from individual studies, results from meta-analyses, and the superior pharmacological properties of P-CABs, such as rapid onset of action and long-lasting effects.

Therefore, based on current evidence, on-demand therapy with PPI or P-CAB is recommended for the long-term management of patients with NERD or mild EE.

Statement 5. Continuous daily therapy with potassium-competitive acid blocker or proton pump inhibitor is proposed for the long-term management of patients with severe erosive esophagitis.

• Level of evidence: low

Study	On-demand Events	On-demand Total	Continuous Events	Continuous Total	Weight	Risk ratio MH, random, 95% CI
Tsai et al. (2004)	19	311	41	311	17.3%	0.46 [0.28-0.78]
Janssen et al. (2005)	13	215	17	217	15.6%	0.77 [0.38-1.55]
Sjostedt et al. (2005)	54	183	16	184	17.3%	3.39 [2.02-5.70]
van der Velden et al. (2010)	34	141	5	62	13.8%	2.99 [1.23-7.28]
Bayerdorffer et al. (2016)	19	301	29	297	17.0%	0.65 [0.37-1.13]
Jung et al. (2023)	67	146	53	147	19.1%	1.27 [0.96-1.68]
Total (95% CI)		**1,297**		**1,218**	**100.0%**	**1.17 [0.65-2.13]**

Heterogeneity: Tau^2 = 0.461; Chi^2 = 38.70, df = 5 (P < 0.001); I^2 = 87%
Test for overall effect: Z = 0.53 (P = 0.596)

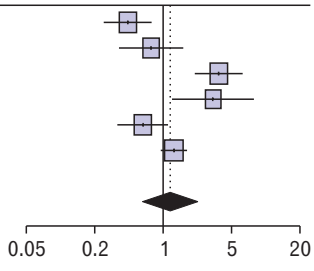


Figure 4. Pooled analysis of treatment failure rates during maintenance therapy in patients with non-erosive reflux disease or mild erosive esophagitis: proton pump inhibitor on-demand therapy vs continuous. MH, Mantel-Haenszel.

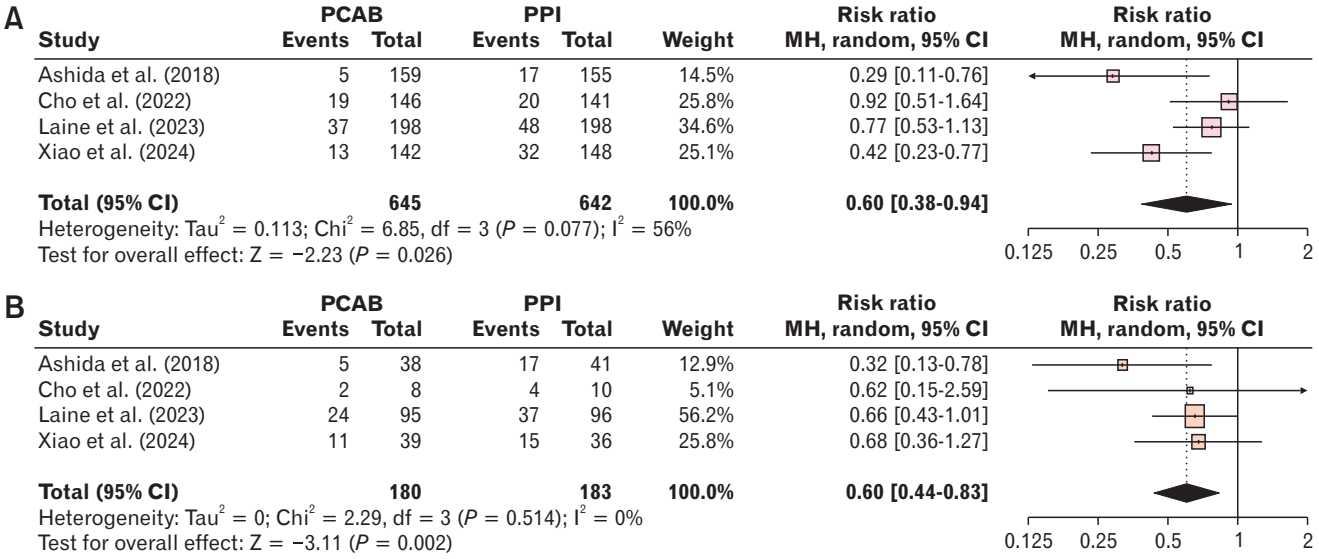
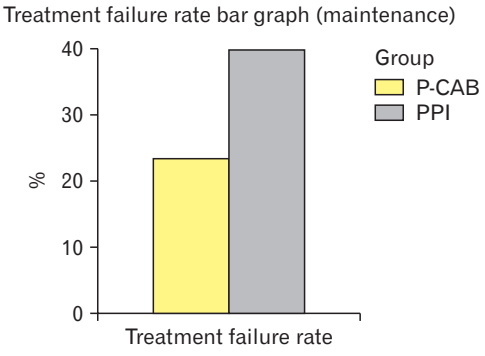


Figure 5. Pooled analysis of recurrence rate of erosive esophagitis (EE) at 24 weeks. (A) Pooled analysis of recurrence rate of EE at 24 weeks in patients with mild EE: proton pump inhibitor (PPI) vs potassium-competitive acid blocker (P-CAB); (B) pooled analysis of recurrence rate at 24 weeks in patients with severe EE: PPI vs P-CAB. MH, Mantel-Haenszel.



	P-CAB	PPI	*P*-value
Treatment failure	42	73	0.001
N	180	183	

Figure 6. Comparison of treatment failure rate during maintenance therapy in patients with severe erosive esophagitis: proton pump inhibitor (PPI) vs potassium-competitive acid blocker (P-CAB).

- Strength of recommendation: weak
- Expert opinion: strongly agree, 46.6%; agree with reservation, 37.9%; undecided, 10.3%; disagree, 5.2%; and strongly disagree, 0.0%.

Limited evidence suggests that continuous PPI therapy may be more effective than on-demand therapy for the long-term maintenance of patients with severe EE. A previous RCT reported significantly higher relapse rates in the on-demand treatment group than in the continuous treatment group, particularly in patients with severe EE.[48] Similarly, a recent meta-analysis demonstrated that continuous maintenance therapy was more effective than on-demand therapy in patients with severe EE in terms of treatment failure and symptom relief.[1]

Furthermore, a pooled analysis of four RCTs[20,54-56] in patients with severe EE showed that long-term P-CAB therapy was superior to PPI therapy in preventing EE recurrence over 24 weeks (pooled RR = 0.60; 95% CI, 0.44-0.83; Fig. 5B). Similarly, a pooled analysis of treatment failure rates, defined as the endoscopic recurrence of EE, revealed significantly lower failure rates with P-CABs than with PPIs (23.3% vs 39.9%; *P* = 0.001; Fig. 6).

Although sufficient evidence remains limited, continuous maintenance therapy is considered appropriate for patients with severe EE, given the elevated risk of complications, such as Barrett's esophagus, peptic strictures, esophageal cancer, and a high rate of symptomatic and endoscopic relapse following treatment discontinuation.[57-60] This rationale is reflected in most international guidelines that recommend continuous maintenance therapy for patients with severe EE.[33-35,61]

Given the current evidence, continuous daily therapy with P-CABs or PPIs is proposed for the long-term management of patients with severe EE. Although P-CABs have shown superior efficacy compared to PPIs, further studies are required to establish their long-term safety profiles.

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Statement 6. The lowest effective dose that controls symptoms and maintains mucosal healing is recommended for patients with gastroesophageal reflux disease requiring long-term maintenance therapy with proton pump inhibitors or potassium-competitive acid blockers, to avoid overuse and potential risks.

- Level of evidence: low
- Strength of recommendation: weak
- Expert opinion: strongly agree, 83.1%; agree with reservation, 15.2%; undecided, 1.7%; disagree, 0.0%; and strongly disagree, 0.0%.

PPIs have been widely used for acid suppression, with well-established efficacy for long-term use. However, concerns have emerged regarding the potential adverse events associated with its long-term use, including increased risks of enteric infection, kidney dysfunction, nutrient malabsorption, cardiovascular events, dementia, gastric malignancy, hypomagnesemia, vitamin B12 deficiency, and bone fracture.[14-16,62-66] Recent long-term data on P-CABs suggest a safety profile comparable to that of PPIs; however, the increasing use of P-CABs has raised concerns regarding potential risks such as hypergastrinemia,[21,67] gastric malignancy,[68] and kidney dysfunction.[69] Further research is required to clarify the long-term safety of PPIs and P-CABs, particularly P-CABs, given their relatively recent clinical adoption.

Several international guidelines emphasize the importance of periodic reassessment of therapeutic indications, doses, and durations of therapy. For example, the Japanese guidelines recommend minimizing the dose and duration while allowing for long-term maintenance when clearly indicated.[33] The American Gastroenterological Association expert review advises reassessing both appropriateness and dosing within 12 months, ideally through endoscopic and reflux monitoring.[35] Similarly, the American College of Gastroenterology clinical guidelines state that although PPIs are generally safe, their potential risks should be considered for long-term use.[34]

Given the potential concerns related to their long-term use, PPIs and P-CABs should be administered at the lowest effective dose for the appropriate duration. Long-term maintenance therapy should be periodically reassessed and adjusted according to individual clinical responses, risk factors, and evolving indications.

CONCLUSION AND PERSPECTIVES

This 2025 focused update of the Seoul Consensus on GERD provides an evidence-based approach for the diagnosis and management of GERD, emphasizing recent advances in acid-suppressive therapy and the evolving definition of GERD. These guidelines highlight the integration of recent data on P-CABs with established evidence for PPI therapy. The updated recommendations are stratified according to disease severity such as the grade of reflux esophagitis, including NERD, mild EE, and severe EE, and offer recommendations for both initial and long-term maintenance therapies. As new diagnostic modalities and therapeutic agents continue to emerge, ongoing research, particularly on the long-term safety of P-CABs, is essential. In addition, further studies are warranted to establish evidence-based strategies for pediatric GERD and extraesophageal manifestations of the disease. These guidelines will be periodically revised in accordance with accumulating evidence to ensure optimal clinical outcomes across diverse patient populations.

SUPPLEMENTARY MATERIALS

Note: To access the supplementary tables and figures mentioned in this article, visit the online version of *Journal of Neurogastroenterology and Motility* at http://www.jnmjournal.org/, and at http://dx.doi.org/10.5056/jnm25128.

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