



## What is proton pump inhibitors unresponsiveness in gastroesophageal reflux disease? How should these cases be managed?

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### ABSTRACT

Proton pump inhibitors become the most potent therapeutic option in gastroesophageal reflux disease. Unresponsiveness to this treatment is not uncommon in clinical practice. We reviewed the definition of PPI unresponsiveness and the management of this situation.

**Anahtar Kelimeler:** Proton pump inhibitors, drug therapy, gastroesophageal reflux disease

### WHAT IS PPI UNRESPONSIVENESS IN GASTROESOPHAGEAL REFLUX DISEASE (GERD)?

By conducting a search using the terms “gastroesophageal reflux/drug therapy” (MeSH Terms) AND “proton pump inhibitors (MeSH Terms),” we aimed to find articles that were related to the definitions of PPI unresponsiveness and to create an expert opinion on the approach proposals related to unresponsive patients.

By scanning the summaries of 342 articles that were found in the literature, full texts of 16 articles involving PPI-refractory GERD patients were obtained. Because no description was made about the PPI refractoriness in 6 of these articles, they were excluded from the evaluation. The remaining 10 articles were used to create an expert opinion.

Seven articles containing the duration, dose, and response criteria that are taken into consideration in PPI unresponsiveness in GERD are tabulated. Fass et al. (1) and Fass and Sifrim (2) defined the PPI unresponsiveness in GERD as the failure to achieve adequate symptomatic relief and/or complete esophageal healing with a single daily dose of PPI without providing any duration. Richter et al. (3) defined the symptoms that do not respond to 4–8 weeks of double-dose PPI therapy, and Dellon and Shaheen (4) defined the symptoms that do not respond to a double-dose PPI therapy without spe-

cifying any duration. Kohata et al. (5) and Ribolsi et al. (6) defined the failure to receive an adequate symptomatic response to a 4-week double-dose PPI therapy as PPI unresponsiveness. Sifrim and Zerbib (7) defined the PPI unresponsiveness as inadequate response with a 12-week double-dose PPI therapy in patients with typical reflux symptoms.

As a result, the PPI unresponsiveness has been defined in the literature as the failure to obtain an adequate clinical response to 4-12-week single- or double-dose treatment.

### HOW SHOULD THE PPI-UNRESPONSIVE GERD PATIENTS BE MANAGED?

The treatment approach schema to PPI-unresponsive GERD was made by the consensus group, using the prior study references (Figure 1) (4,7-10).

### RECOMMENDATION

- If there is no response to a 4-week 1×1 PPI treatment in patients without alarm symptoms, it is recommended to increase the dose to 2×1 and the treatment to be completed within 8 weeks. Less than 50% recovery in typical reflux symptoms is considered to be unresponsiveness to PPI (Level of evidence: 5).

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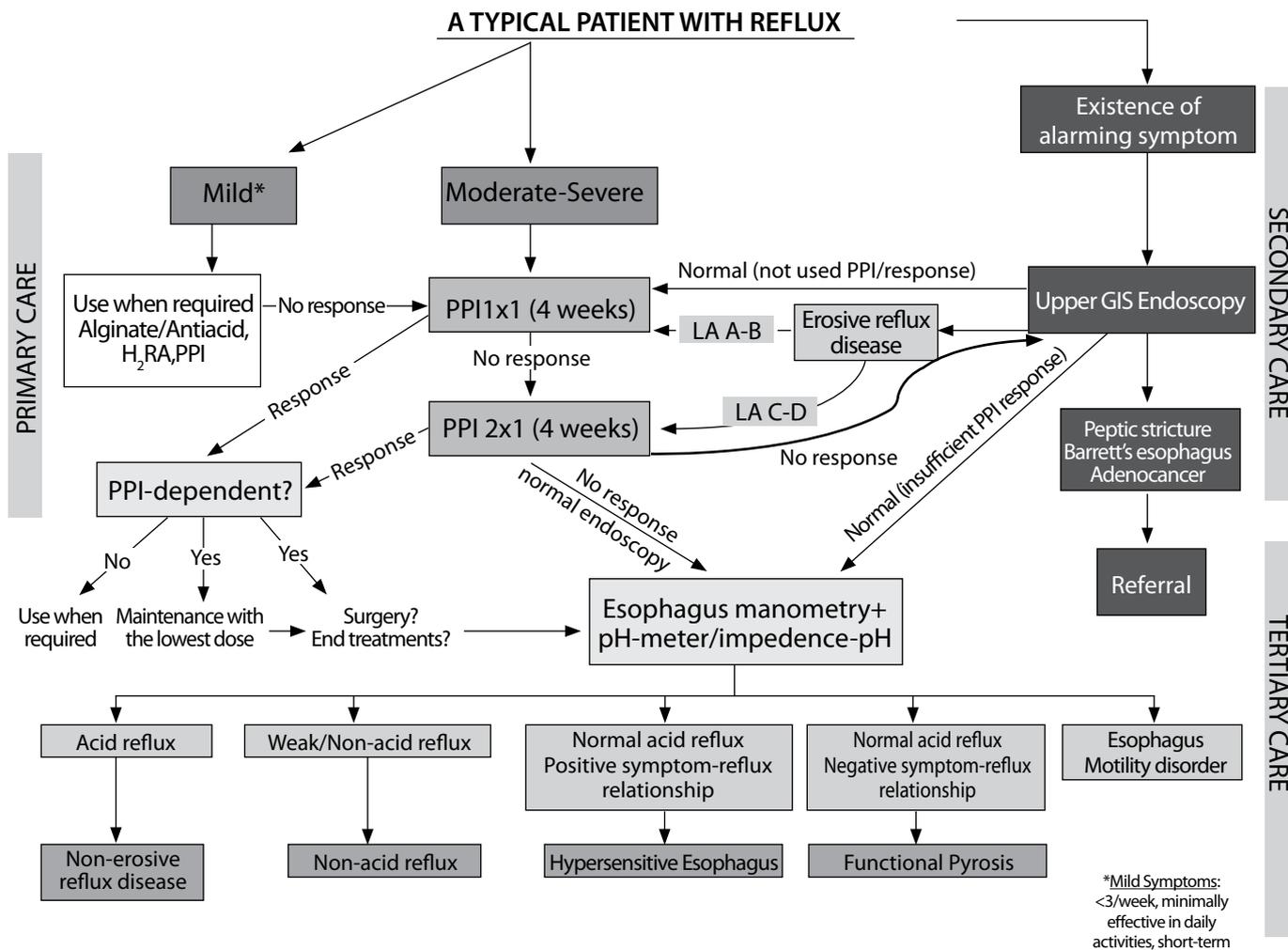


Figure 1. Patient with typical reflux symptom

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**REFERENCES**

1. Fass R, Shapiro M, Dekel R, Sewel J. Systematic review: proton-pump inhibitor failure in gastro-oesophageal reflux disease - where next? *Aliment Pharmacol Ther* 2005; 22: 79-94. [CrossRef]
2. Fass R, Sifrim D. Management of heartburn not responding to proton pump inhibitors. *Gut* 2009; 58: 295-309. [CrossRef]
3. Richter JE. The patient with refractory gastroesophageal reflux disease. *Dis Esophagus* 2006; 19: 443-7. [CrossRef]
4. Dellon ES, Shaheen HJ. Persistent reflux symptoms in the proton pump inhibitor era: The changing face of gastroesophageal reflux disease. *Gastroenterology* 2010; 139: 7-13. [CrossRef]
5. Kohata Y, Fujiwara Y, Machida H, et al. Pathogenesis of proton pump inhibitor refractory non-erosive reflux disease according to

6. Ribolsi M, Emerenziani S, Borrelli O, et al. Impedance baseline and reflux perception in responder and non-responder non-erosive reflux disease patients. *Scan J Gastroenterol* 2012; 47: 1266-73. [CrossRef]
7. Sifrim D, Zerbib F. Diagnosis and management of patients with reflux symptoms refractory to proton pump inhibitors. *Gut* 2012; 61: 1340-54. [CrossRef]
8. Hershcovici T, Fass R. Management of gastroesophageal reflux disease that does not respond well to proton pump inhibitors. *Curr Opin Gastroenterol* 2010; 26: 367-78. [CrossRef]
9. Hershcovici T, Fass R. Step by step management refractory gastroesophageal reflux disease. *Dis Esophagus* 2013; 26: 27-36. [CrossRef]
10. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol* 2013; 108: 308-28. [CrossRef]