

National Consensus on the Management of Gastroesophageal Reflux Disease in Indonesia

The Indonesian Society of Gastroenterology

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ABSTRAK

Penyakit refluks gastroesofageal atau gastroesophageal reflux disease (GERD) merupakan suatu gangguan dimana isi lambung mengalami refluks secara berulang ke dalam esofagus, yang menyebabkan terjadinya gejala dan/atau komplikasi yang mengganggu. Berbagai penelitian epidemiologi menunjukkan adanya perbedaan secara regional dari segi prevalensi dan manifestasi klinik. Data regional juga menunjukkan peningkatan angka kejadian komplikasi seperti Barret's Esophagus dan adenokarsinoma. Menanggapi situasi tersebut, pada tahun 2004, para ahli GERD di Asia Pasifik termasuk Indonesia telah mengeluarkan suatu konsensus bersama untuk tatalaksana kelainan ini, kemudian direvisi pada tahun 2008.

Kemajuan teknologi kedokteran, khususnya teknik endoskopi gastrointestinal dan perangkat diagnostik lainnya seperti pH-metri 24 jam dan manometri, telah meningkatkan kemampuan penatalaksanaan GERD. Di sisi lain, pengetahuan dan kemampuan para dokter, baik dokter umum maupun spesialis penyakit dalam di negara kita dalam penatalaksanaan GERD yang adekuat, dirasakan belum merata. Begitu pula penyediaan sarana penunjang diagnostik dan terapeutik yang tidak sama antara satu daerah dengan yang lainnya. Pengurus Besar Perkumpulan Gastroenterologi Indonesia (PB PGI) memandang perlu untuk merevisi Konsensus Nasional Penatalaksanaan GERD di Indonesia tahun 2004, yang diharapkan akan menjadi suatu pedoman penatalaksanaan GERD.

Kata kunci: Barret's esophagus, diagnosis, endoskopi, GERD, manometri, pH-metri.

ABSTRACT

Gastroesophageal reflux disease (GERD) is a disorder, which gastric content repeatedly reflux into the esophagus causing disturbing symptoms and/or complications. Various epidemiological studies show that there is regional difference on the aspect of prevalence and clinical manifestation. Regional data also demonstrates increased incidence of complications such as the Barret's Esophagus and adenocarcinoma. In response to the situation, the Asia-Pacific GERD experts, including Indonesia, had published a consensus on the management of GERD in 2004, which was subsequently revised in 2008.

Advances in medical technology, especially on gastrointestinal endoscopy technique and other diagnostic instruments such as 24-hour pH-metry and manometry, have improved the capacity of management of GERD. On the other hand, we feel that adequate knowledge and skills of doctors, both for general physicians and specialists of internal medicine in our country are not well-distributed. Moreover, the availability of instruments for diagnostic and therapeutical supports differs from one region to the others. The Organizing Committee of Indonesian Society of Gastroenterology or Pengurus Besar Perkumpulan Gastroenterologi Indonesia (PB PGI) considers that it is important to revise the National Consensus on the Management of GERD in Indonesia 2004, which is expected to be the guideline of GERD management.

Key words: Barret's esophagus, diagnosis, endoscopy, GERD, manometry, pH-metry.

INTRODUCTION

In recent years, attention of the experts on gastroesophageal reflux disease (GERD) is increasing, either on the aspect of endeavors evaluating the pathogenesis, establishing diagnosis or on the aspect of management. Various epidemiological studies show that there is regional difference on the aspect of prevalence and clinical manifestation. In addition, regional data also demonstrates increased incidence of complications such as the Barrett's Esophagus and adenocarcinoma. In response to the abovementioned situation, the Asia-Pacific GERD experts, including Indonesia, had published a consensus on the management of GERD in 2004, which was subsequently revised in 2008.

Gastroesophageal reflux disease (GERD) is defined as a disorder, which gastric content repeatedly reflux into the esophagus causing disturbing symptoms and/or complications. The statement was proposed by the Asia-Pacific Consensus on the Management of GERD in 2008 that stressing the word of "disturbing", as it characterized the disturbance on quality of life and as an extraction of general opinion, which says that if esophageal reflux should be stated as a disease, it must affect the patients' quality of life.¹

GERD may also be regarded as a disorder that causes the reflux of gastric fluid and its various contents into the esophagus, causing typical symptoms such as heartburn (a burning sensation in chest, which is sometime accompanied with painful and stinging sensation) and other symptoms such as regurgitation (sour and bitter taste in mouth), epigastric pain, dysphagia and odynophagia.² There are two groups of GERD patients, i.e. patients with erosive esophagitis, who are characterized by damages on esophageal mucosa as shown by endoscopic examination (the Erosive Esophagitis/ERD) and another group is patients with disturbing reflux symptom, but the endoscopic examination shows no damage on esophageal mucosa (Non-Erosive Reflux Disease/NERD).¹

Advances in medical technology, especially on gastrointestinal endoscopy technique and other diagnostic instruments such as 24-hour pH-metry and manometry, have improved the

capacity of management of GERD. On the other hand, we feel that adequate knowledge and skills of doctors, both for general physicians and specialists of internal medicine in our country are not well-distributed. Moreover, the availability of instruments for diagnostic and therapeutical supports differs from one region to the others. The Organizing Committee of Indonesian Society of Gastroenterology or Pengurus Besar Perkumpulan Gastroenterologi Indonesia (PB PGI) considers that it is important to revise the National Consensus on the Management of GERD in Indonesia 2004, which is expected to be the guideline of GERD management. During the process of compiling the consensus, the committee refers to various similar consensus issued by various centers worldwide, which are generally based on the evidence-based medicine.

EPIDEMIOLOGY

GERD prevalence and complications in Asian countries, including Indonesia, is generally lower than the western countries; however, recent data shows that the prevalence is increasing. It is caused by changes of lifestyle that may increase the risk of GERD, such as smoking and obesity.¹

Epidemiological data in USA demonstrates that one of five adults has esophageal reflux symptom (heartburn) and/or acid regurgitation once in a week and more than 40% of them have the symptoms at least once in a month.³ The prevalence of esophagitis in western countries shows a mean value ranges between 10-20%; while in Asia, the prevalence ranges between 3-5% with an exception in Japan and Taiwan with a range between 13-15% and 15%. A recent study on the prevalence in Japan reveals a mean value of 11.5% and GERD is defined as the sensation of burning in the chest of at least twice a week.^{4,5}

Until now, Indonesia has no complete epidemiological data on this condition. The available data is a report from a study conducted by Lelosutan SAR et al in Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo Hospital, Jakarta (FKUI/RSCM-Jakarta), which demonstrates that of 127 study subjects who underwent upper gastrointestinal endoscopy, 22.8% (30 subjects of them) had esophagitis.⁶ Another study conducted by Syam AF et al.⁷,

which is also from RSCM/FKUI-Jakarta, shows that of 1718 patients who underwent upper gastrointestinal endoscopy on indication of dyspepsia for 5 years (1997-2002), there is an increased prevalence of esophagitis, from 5.7% in 1997 to 25.18% in 2002 (mean value of 13.13% per year).⁷

Some risk factors for GERD have been evaluated in Asia-Pacific population, including elderly age, male, race, family history, high level of economic status, increased body mass index and smoking. The strongest evidence is provided for association of certain risk factors with the development of GERD in Asia-Pacific population, i.e. the increased body mass index and more than 25 clinical studies have supported the correlation.⁸

DIAGNOSIS

Careful history taking is the main method to establish GERD diagnosis. Specific symptom of GERD is heartburn and/or regurgitation that occur after meal. However, it should be emphasized that most of diagnostic studies of heartburn and regurgitation symptoms are performed in Caucasian population. In Asia, the symptoms of heartburn and regurgitation are not the typical features for GERD. However,

the experts have agreed that both symptoms are characteristics for GERD.¹

In a tertiary referral hospital, before performing endoscopic examination to establish the diagnosis of GERD, other further investigation (laboratory, ECG, USG, chest X-ray and other investigation in accordance with the indication) should be also carried out to exclude diseases with symptoms similar to the GERD. The Asia-Pacific experts have stated by acclamation that the regional strategy of diagnostic GERD must consider the possibility of GERD exists with other comorbidities such as gastric cancer and peptic ulcer. However, regarding the *H. pylori* test to exclude infection in patients with GERD symptoms in regions with high prevalence of gastric cancer and peptic ulcer, there is a controversial opinion of the experts. Nevertheless, the test is still recommended by considering risk factors including comorbidities, age, histological profile of the stomach, family history and patient's preference.¹

GERD-Q

GERD Questionnaire (GERD-Q) (**Table 1**) an instrument of questionnaire developed to assist establishing the diagnosis of GERD and measuring response to therapy. The questionnaire is developed based on clinical data and information obtained from high-quality clinical

Table 1. GERD-Q

Try to recall what you have experienced in the last 7 days.√

Put a check mark (√) only at one single space for each question and count your total GERD-Q score by doing summation of the point(s) for each question.

No.	Question	Frequency of score (point) for symptoms			
		0 day	1 day	2-3 days	4-7 days
1.	How often do you experience the sensation of burning behind your breastbone / sternum (heartburn)?	0	1	2	3
2.	How often do you experience the gastric content backing up into your throat / mouth (regurgitation)?	0	1	2	3
3.	How often do you feel epigastric pain?	3	2	1	0
4.	How often do you feel nauseated?	3	2	1	0
5.	How often do you have difficulty to have night sleep due to the burning sensation in the chest (heartburn) and/or the backing up of abdominal content?	0	1	2	3
6.	How often do you take additional medication for treating the burning sensation in the chest (heartburn) and/or the backing up of abdominal content (regurgitation), other than prescribed by your doctor? (such as the over the counter drugs for treatment of stomach complaints)	0	1	2	3
Result		If your GERDQ points <7, you probably do not have GERD. If your GERDQ points is 8-18, you probably have GERD			

studies as well as from qualitative interviews with patients in order to evaluate the simplicity of filling up the questionnaire. GERD questionnaire is a combination of validated questionnaires used in the DIAMOND study. Improved accuracy of diagnosis by combining several validated questionnaire will increase the sensitivity and specificity of diagnosis.^{9,10}

An analysis on more than 300 patients at a primary health care service demonstrates that GERD-Q may provide sensitivity and specificity of 65% and 71%, which is similar to results obtained by gastroenterologists. Moreover, GERD-Q also shows the capacity to evaluate relative impacts of GERD on patients' life and to provide assistance in selecting therapy.⁹

Table 1 is the GERD-Q that can be filled up by the patients themselves. For each question, respondent should fill up according to the frequency of symptoms that they have experienced in a week. Score 8 or more is the recommended cut-off point to detect individuals with high tendency to have GERD.¹⁰ GERD-Q has been validated in Indonesia.

Upper Gastrointestinal (UGI) Endoscopy

Upper gastrointestinal endoscopy (UGIE) is considered the gold standard for establishing the diagnosis GERD with erosive esophagitis. Using the UGIE, we can find the mucosal break of esophagus. Endoscopy in GERD patients is mainly used for individuals with alarm symptoms (progressive dysphagia, odynophagia, weight loss with unexplained etiology, new onset of anemia, hematemesis and/or melena, family history of gastric and/or esophageal malignancy, chronic use of NSAID medication, individuals with age over 40 years in a region with high prevalence of gastric cancer) and for those who do not respond to empirical treatment using PPI twice daily.^{1,11,12}

While until now, there is no gold standard for diagnosis of NERD. The following criteria is used as the guideline for establishing the diagnosis of NERD:¹

- No mucosal break found in the upper gastrointestinal endoscopy,
- Positive results on esophageal pH test,
- Twice-daily empirical therapy with PPI gives positive response.

Endoscopy for GERD is not always performed on the first visit since the diagnosis of GERD can be made based on symptoms and/or empirical therapy. The roles of upper gastrointestinal endoscopy in establishing the diagnosis of GERD are:

- Confirming the presence and absence of esophageal damages including erosion, ulceration, stricture, Barret's esophagus or malignancy, in addition to excluding other upper gastrointestinal abnormalities.
- Evaluating the severity of mucosal break using modified Los Angeles classification or Savarry-Miller classification.
- Biopsy specimens are taken when there is a suspicion of Barret's esophagus or malignancy.

Histopathological Examination

Histopathological examination as the diagnostic tool of GERD is essential to determine the presence of metaplasia, dysplasia or malignancy. No supporting evidence has been provided about whether biopsy specimen is needed in NERD cases. In the future, further studies on the role of high-resolution (magnifying scope) endoscopy in NERD cases are necessary.

24-hour pH-metry Test

The roles of conventional 24-hour pH-metry test or 48-hour capsule (if available) in the diagnosis of NERD are:^{13,14}

- Evaluating GERD patients who do not respond to PPI therapy.
- Evaluating whether the patients are those with extra-esophageal symptoms before the PPI therapy or after failed PPI therapy.
- Confirming the diagnosis of GERD prior to anti-reflux surgery or evaluating symptoms of NERD repeatedly following the surgery.

PPI Test

PPI test can be performed to establish the diagnosis in patients with typical symptoms and without alarm signs or risk for Barret's esophagus. The test is carried out by administering double-dose PPI for 1-2 weeks without the preceding endoscopy examination. If the symptoms subside with PPI administration and recur when the PPI treatment is stopped, then the diagnosis of GERD can be made. The test is considered as positive

result, if there is clinical improvement of more than 50% in 1 week.^{1,11,15}

A meta-analysis study demonstrates that PPI test has a sensitivity of 80% and specificity of 74% for establishing diagnosis of GERD patients with non-cardiac chest pain. It indicates that PPI test can be considered as a useful strategy and probably has economic value in management of patients with non-cardiac chest pain without alarm signs of suspected esophageal abnormalities.¹⁶

Other Diagnostic Tests

Alternative tests that can be performed other than endoscopy and pH-metry are:

- Barium esophagography. Although this test is not sensitive for GERD diagnosis, but in certain condition the test provides more advantages than endoscopy, i.e. in the case of esophageal stenosis and hiatal hernia.
- Esophageal manometry. The test has advantages, particularly for evaluating treatment of NERD patients and for the purpose of research.
- Impedance test. This new method can detect the presence of gastroesophageal reflux through altered resistance against electrical current between two electrodes when fluid and/or gas move between them. The test is mainly useful for evaluating NERD patient who does not response to PPI therapy; in which the documentation of non-acid reflux will change the management approach.¹⁴
- Bilitest test. The test can detect the presence of gastroesophageal reflux by using the characteristics of optical bilirubin. The test is essential, particularly for evaluating patients with persistent symptoms of reflux despite the normal result of pH-metry when they have acid exposure on distal esophagus.¹⁴
- Bernstein test. The test measures the sensitivity of esophageal mucosa by installing trans-nasal catheter and perfusion on distal esophagus with HCl 0.1 N in less than an hour. The test is a complementary to 24-hour esophageal monitoring pH in patients who had atypical symptoms and for research purpose.

Surveillance Barrett's Esophagus

The role of endoscopy surveillance in patients with Barrett's esophagus is still controversial even in the countries with high prevalence. In Asia, the prevalence of Barrett's esophagus is still low, which is reported about 0.08%. Meanwhile in the United States, it is reported that the incidence of esophageal cancer in patients with Barrett's esophagus is about 0.4%; while other studies reported that it ranges between 1-2%.^{1,17}

Up until now, the screening test for Barrett's esophagus is still controversial due to less impact of the screening test on mortality of esophageal adenocarcinoma. Surveillance endoscopy is suggested for individuals with high risks and it should be performed according to the grade of dysplasia found. For further discussion, please refer to the associated references.¹⁷

MANAGEMENT

Management means the action performed by doctors who treat GERD cases, including non-pharmacological therapy, pharmacological treatment, endoscopy and surgery. Basically, there are 5 targets that should be achieved and must always be a concern when we plan, change and stop the therapy for GERD patients. The five targets are eradicating symptoms/complaints, recovering esophageal lesion, preventing recurrent illness, improving quality of life and preventing the development of complications. This guideline of management is expected to be applied in the primary, secondary and tertiary health care services.¹⁸⁻²⁰

The clinical approach on the management of GERD includes treatment of GERD (NERD and ERD), refractory GERD and non-acid GERD. In the first line, the diagnosis of GERD is made more based on clinical symptoms and symptom-based GERD questionnaire. The management is provided based on clinical diagnosis (**Figure 1**).

Non-pharmacological Treatment

The main concern is targeted on modifying overweight and elevating head around 15-20 cm during sleep as well as other additional factors such as smoking cessation, stop drinking, reducing food intake and medications that

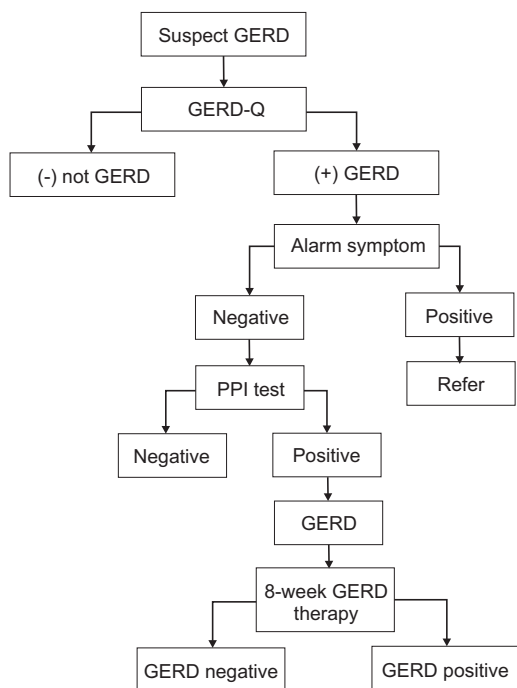


Figure 1. Algorithm of treatment based on diagnostic process in primary health care services

stimulate gastric acid and causing reflux, less satiating feeding and last evening meal at least 3 hours before bedtime.²¹

Pharmacological Treatment

There are drugs that have been known to have capacity to overcome GERD symptoms, which include antacids, prokinetics, H2-receptor antagonists, Proton Pump Inhibitor (PPI) and Baclofen.²² The effectiveness of each drug class is shown in **Table 2**.

Of all the abovementioned drugs, PPI is the most effective drug in eradicating symptoms and recovering esophagitis lesion in GERD.⁹ PPI

has been proven providing more rapid recovery on esophagitis lesion as well as eradicating GERD symptoms compared to the H2 receptor antagonists and prokinetics. If PPI is not available, H2RA can be administered.²⁴⁻²⁶

In individuals with heartburn symptom or episodic regurgitation, the use of H2RA (H2-Receptor Antagonist) and/or antacids can be helpful to provide rapid symptom eradication. Moreover, in Asia, the use of prokinetics (dopamine antagonists and serotonin receptor antagonist) may be beneficial as adjunctive therapy (**Figure 2**).¹

GERD treatment can be started with PPI after the diagnosis of GERD has been established (see diagnosis section). The initial dose of PPI is single dose each morning before meal for 2 – 4 weeks. If there GERD symptom is still found (PPI failure), PPI should be administered continuously in double dose until the symptoms has been eradicated. In general, double-dose therapy can be given up to 4-8 weeks (**Table 3**).

If there is no clinical improvement, endoscopy must be done to confirm the presence of any abnormality in upper gastrointestinal mucosa. Further treatment can be given according to the severity of mucosal damage.²⁹

For mild esophagitis, the treatment may be followed with ‘therapy on demand’ strategy. While for severe esophagitis, it can be followed with continuous maintenance therapy, which may be given up to 6 months.^{1,11,12}

Grade A and B are included in clinical category of mild esophagitis. Grade C and D are the clinical category for severe esophagitis.

Table 2. Effectiveness of drug treatment for GERD²³

Drug Class	Improving symptoms	Recovering esophageal lesion	Preventing complication	Preventing recurrent illness
Antacids	+1	0	0	0
Prokinetics	+2	+1	0	+1
H2-receptor antagonists	+2	+2	+1	+1
H2-receptor antagonists and prokinetics	+3	+3	+1	+1
High-dose H2-receptor antagonists	+3	+3	+2	+2
PPI	+4	+4	+3	+4
Surgery	+4	+4	+3	+4

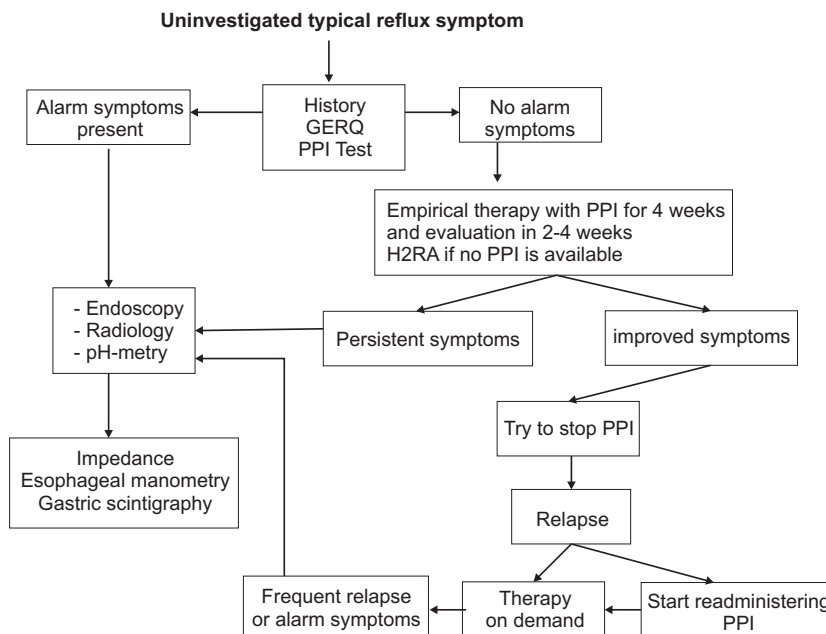


Figure 2. Algorithm of treatment based on diagnostic process in secondary and tertiary health care services.¹

For NERD, initial treatment can be provided by giving single dose PPI for 4-8 weeks. After the clinical symptoms diminish, therapy can be followed with PPI on demand. The ‘on demand’ treatment is suggested in order to maximize gastric acid suppression, which is administered in 30-60 minutes before breakfast.^{1,11}

Table 3. PPI dose for GERD treatment^{27,28}

PPI types	Single Dose	Double dose
Omeprazole	20 mg	20 mg twice daily
Pantoprazole	40 mg	40 mg twice daily
Lansoprazole	30 mg	30 mg twice daily
Esomeprazole	40 mg	40 mg twice daily
Rabeprazole	20 mg	20 mg twice daily

Table 4. GERD classification based on endoscopic results²⁹

NERD	ERD			
	Grade A	Grade B	Grade C	Grade D
Mucosal break (-)	Diameter <5 mm, single	Diameter <5 mm, several	Diameter >5 mm, single, several	Lesion encircling the lumen
No mucosal damage		lesions, colonized	lesions	

GERD, which is refractory to PPI therapy (no response to PPI therapy of twice daily for 8 weeks) must be confirmed by reevaluating the GERD diagnosis using endoscopy to confirm the presence of any esophagitis. If no esophagitis is found, the investigation is followed with pH-metry test.

Based on the results of pH-metry, we can determine the dominant factor for reflux of gastric content, either by hyperacidity or pathological anatomy factors such as (SEB disorder, hiatal hernia, etc). If the pH-metry demonstrates the domination of pathological anatomy factors and the clinical symptoms are still there, the diagnostic test using esophageal impedance and pH can be considered (**Figure 3**) to confirm the next therapeutical measure (tertiary treatment measure).^{1,11}

Now, the treatment for non-acid reflux (NAR) is still developing. Studies on Baclofen (a GABA-B agonist) has provided promising results; however, further data is needed to recommend the drug routinely.^{30,31} The recommended treatment includes avoiding large and late meal, maintain head up position until 3 hours after the meal, reduced body weight and head-up tilt sleeping. However, no study has confirmed that such treatments are clinically significant.

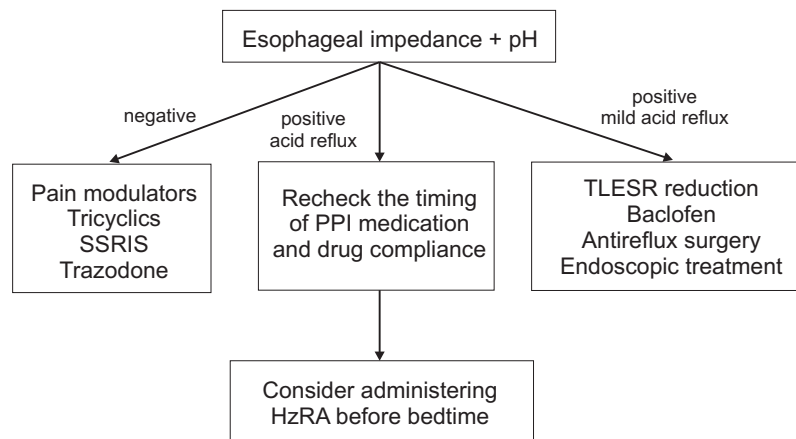


Figure 3. Algorithm on the Management of Refractory GERD following the pH-metry

Other lifestyle interventions such as smoking cessation and stop drinking alcohol as well as changing the pattern of food intake can significantly reduce the symptoms of GERD.²¹ Modified life style is used as the first line therapy, such as reducing body weight, reducing smoking, stomach emptying of more than 3 hours before bedtime.¹ A recent systematic study shows that of all lifestyle intervention, only weight reduction and head-up tilt sleeping that affect the GERD symptoms significantly.

Now, the consensus on the management of GERD, both the Asia-Pacific and American Consensus, do not suggest excessive lifestyle changes in the management of such condition.^{1,19} It is suggested since altered lifestyle does not significantly reduce GERD symptoms and causes excessive stress to the patients. However, based on a meta-analysis conducted on those lifestyle factors, the Asia-Pacific consensus suggest to do modifications on overweight and head-up tilt sleeping.¹

Endoscopic Treatment

GERD complications such as Barrett's esophagus, esophageal stricture, stenosis or bleeding can be treated with endoscopy using Argon plasma coagulation, ligasi, Endoscopic Mucosal Resection, bougination, hemostasis or dilatation.

Endoscopic treatment for GERD is still developing and until now it is still in the context of research. Endoscopic treatments that have been developed are:

- Radiofrequency energy delivery

- Endoscopic suturing

However, there is still no report available on endoscopic treatment for GERD until now in Indonesia.

Surgical Treatment

Surgical treatment includes antireflux surgery (Nissen fundoplication, corrective surgery for hiatal hernia, etc) and surgery to fix complications. Antireflux surgery (Nissen fundoplication) can be suggested for patients who are intolerant to maintenance therapy or those who with persistent disturbing symptoms (refractory GERD). Available studies show that if it is performed well, the effectiveness of the antireflux surgery is equal with medical treatment; however, it brings side effects such as dysphagia, bloating, difficulty in burping and intestinal disorder following the surgery.^{1,12,32}

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