다양한 식도증상에 따른 접근법

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삼성서울병원 Webinar (2016년 8월 2일)

Symptoms related to esophagus

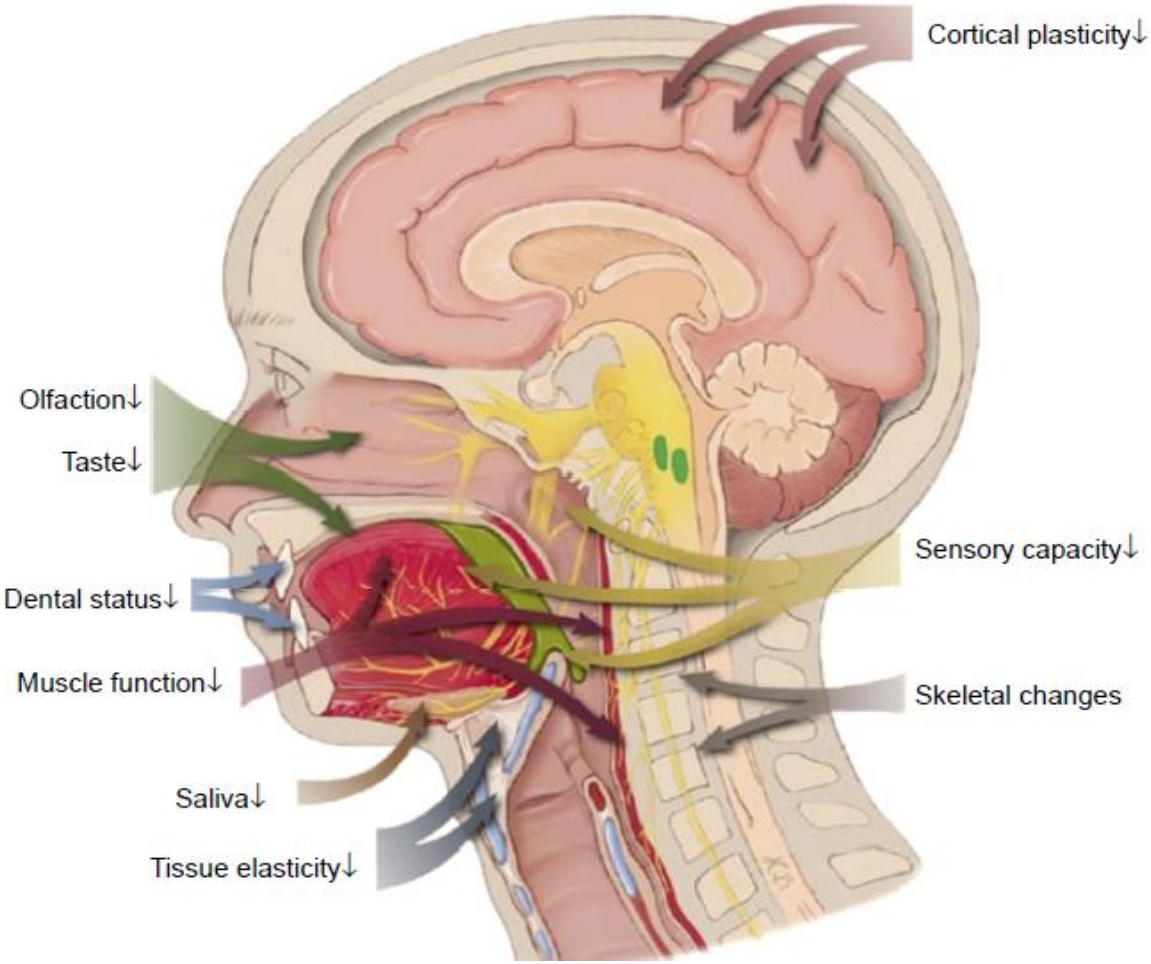
- Dysphagia
  - Esophageal (transport)
  - Oropharyngeal (transfer)
- Heartburn
- Regurgitation
- Odynophagia
- Chest pain
- Globus
- Supraesophageal symptoms
  - Cough and hoarseness

Dysphagia

- Problems with the transit of food or liquid from the mouth to the stomach

- Common clinical problem in the elderly
  - Due to aging per se?

Factors associated with dysphagia in the elderly



Wirth R et al, Clin Interv Aging 2016;11:189-208

Dysphagia in the elderly

- Aging alone causes mild esophageal motility abnormalities, which are rarely symptomatic.
- Should not be attributed to the normal aging
- Many diseases with the potential to provoke dysphagia show increasing prevalence with increasing age

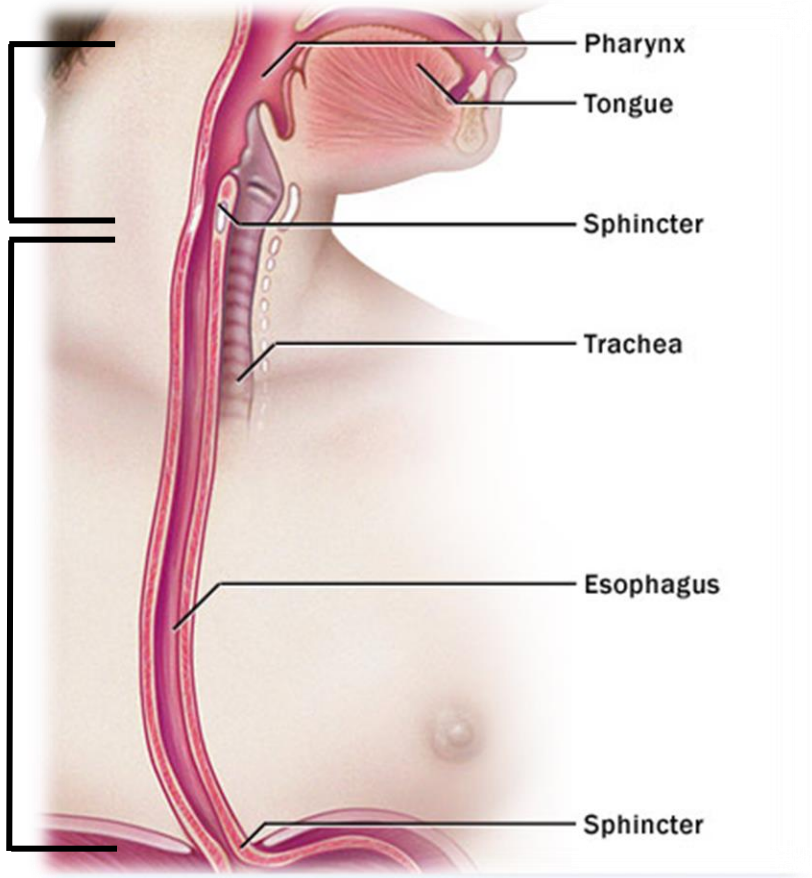
Need for an **immediate evaluation** to define the exact cause and initiate appropriate therapy

4개월 간 GERD 치료, M/67

Two types of dysphagia

- Oropharyngeal dysphagia
  (=transfer dysphagia)

- Esophageal dysphagia
  (=transport dysphagia)



Oropharyngeal dysphagia

- Typical symptoms
  - Drooling, coughing, and gurgling upon eating
  - Nasal regurgitation of food or liquid
  - Very soon after the onset of eating

- Cervical location of the dysphagia?
  - Occasionally in esophageal dysphagia

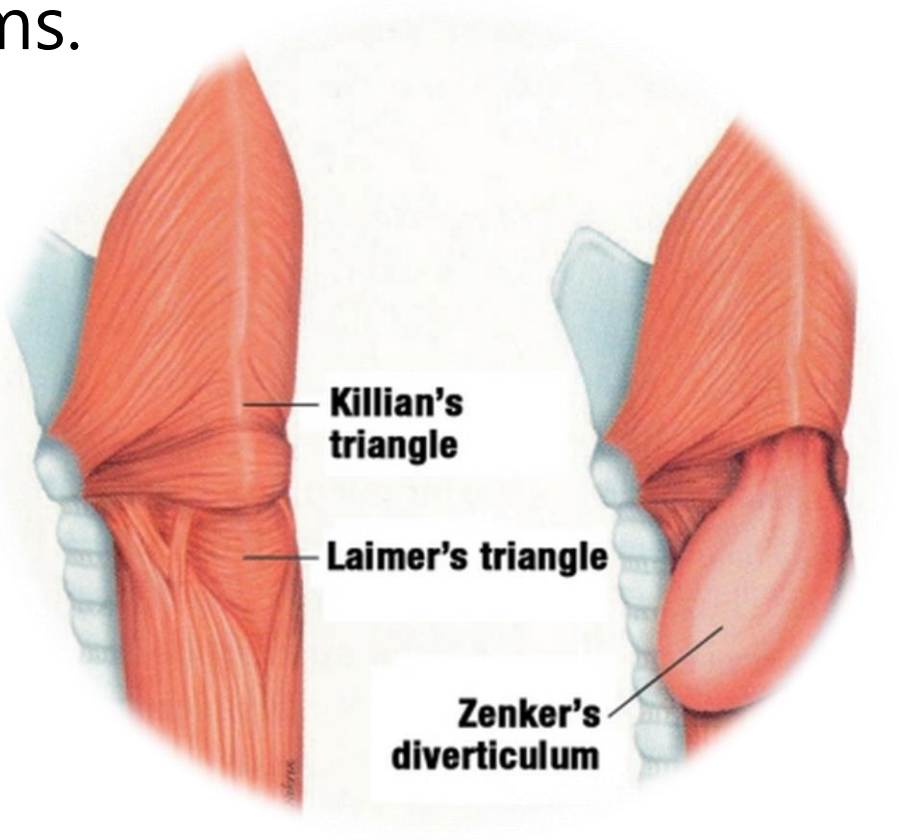
Causes of oropharyngeal dysphagia

Anatomic	Neurologic	Muscular
Zenker's Diverticulum	Cerebrovascular Accident	Polymyositis
Tumor	Post-Polio Syndrome	Myasthenia Gravis
Enlarged Thyroid	Radiation Injury	Muscular dystrophy
Osteophyte	Parkinsonism	Radiation Injury
Head/Neck Surgery	Head/Neck Surgery	Thyroid Disease
Web	Multiple Sclerosis	Head/Neck surgery
Abscess	CNS tumor	
	Botulism	
	Supranuclear Palsy	
	Myotonic Dystrophy	
	Amyotrophic Lateral Sclerosis	

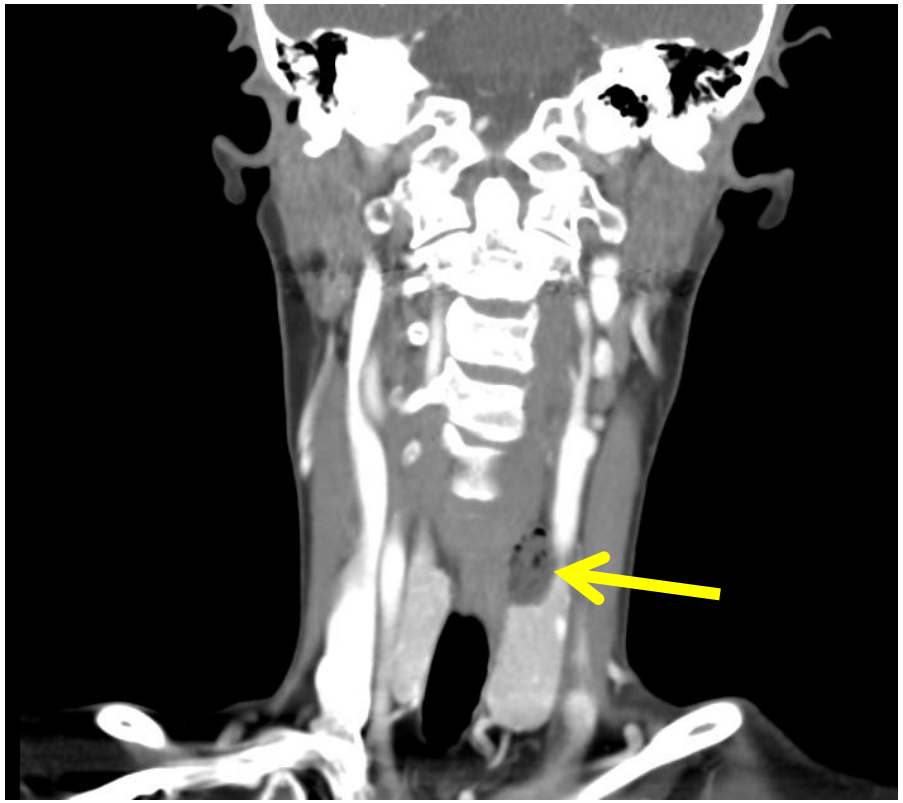
Abdel Jalil AA et al. Am J Med 2015;128:1138.e17-23

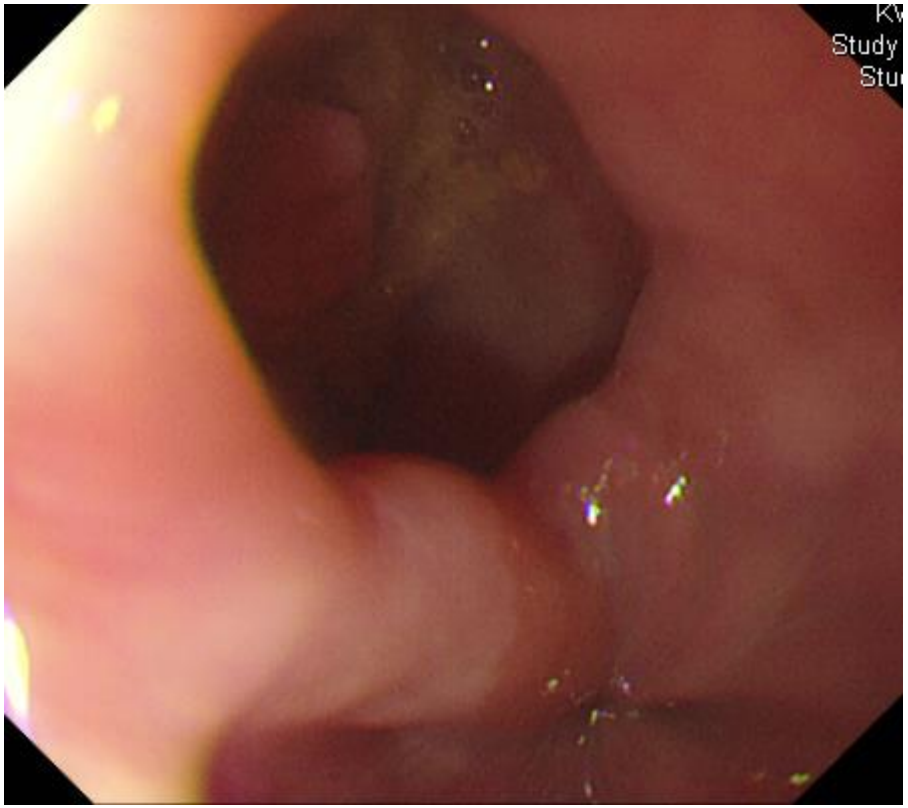
Zenker's diverticulum (=hypopharyngeal diverticulum)

- Usually asymptomatic
- Decision to treat is based on the severity of symptoms.



CT에서 우연히 발견된 게실, F/54





Esophageal dysphagia

- Structural dysphagia
  - oversized bolus or a narrow lumen

- Motor dysphagia
  - abnormalities of peristalsis or impaired sphincter relaxation after swallowing

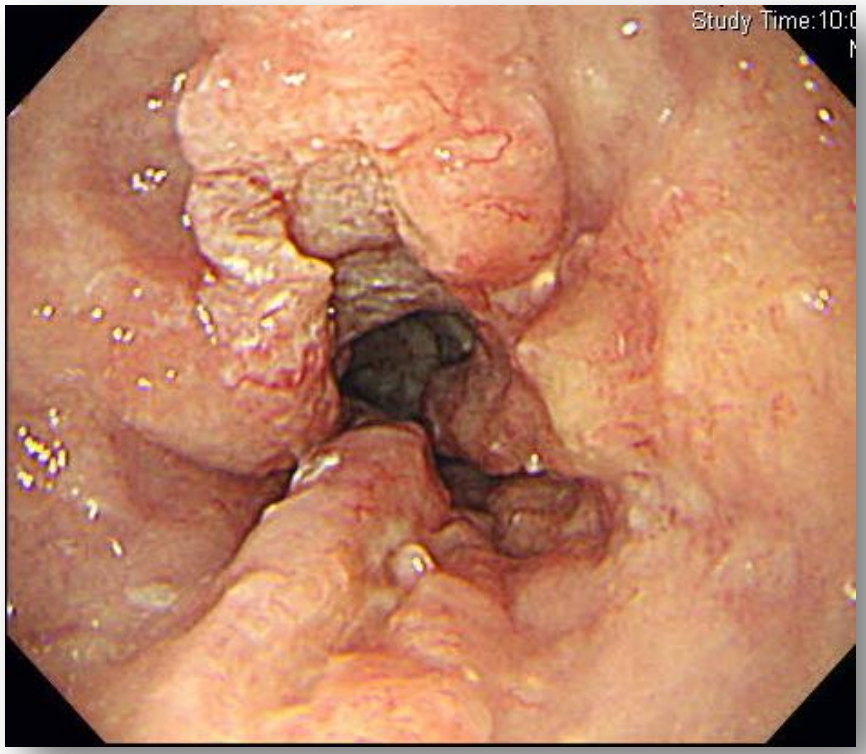
Structural esophageal dysphagia

- Solid food dysphagia when narrowed to <13 mm
  - Also with larger diameters in the setting of poorly masticated food or motor dysfunction
  - Circumferential lesions: more likely to cause

- Common causes: masses (both intrinsic and extrinsic), stricture (peptic, RT, op, EoE), rings, webs

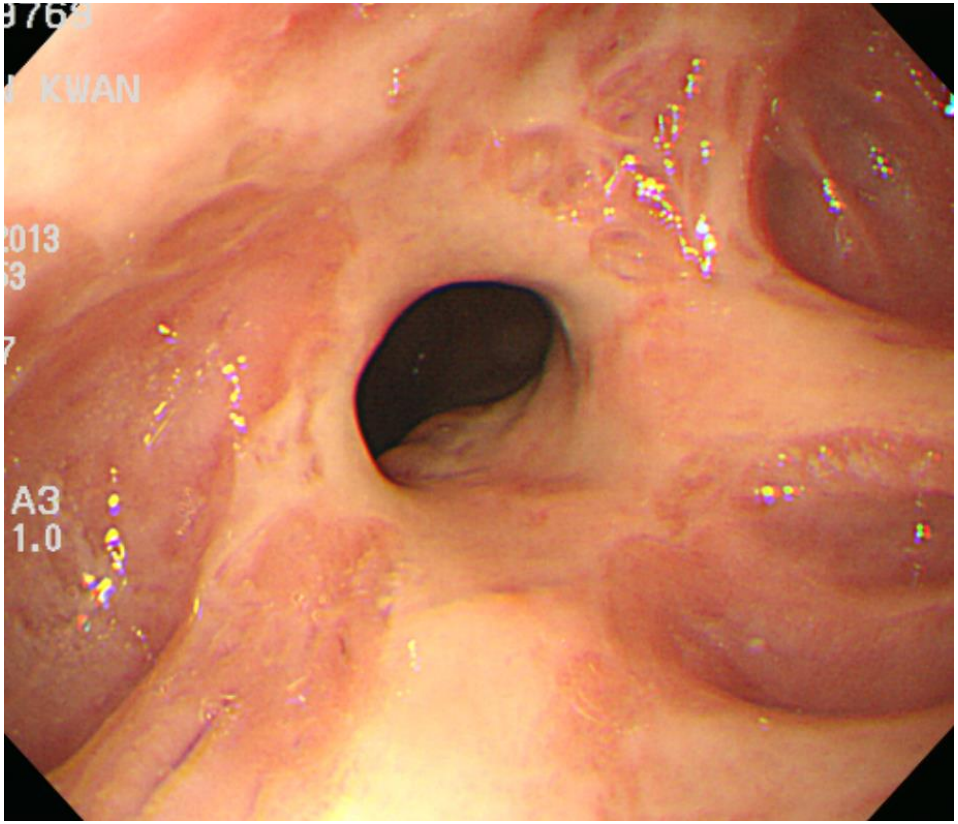
Esophageal cancer

- Progressive over weeks to months
- From solid to liquid
- Weight loss
- Risk factors

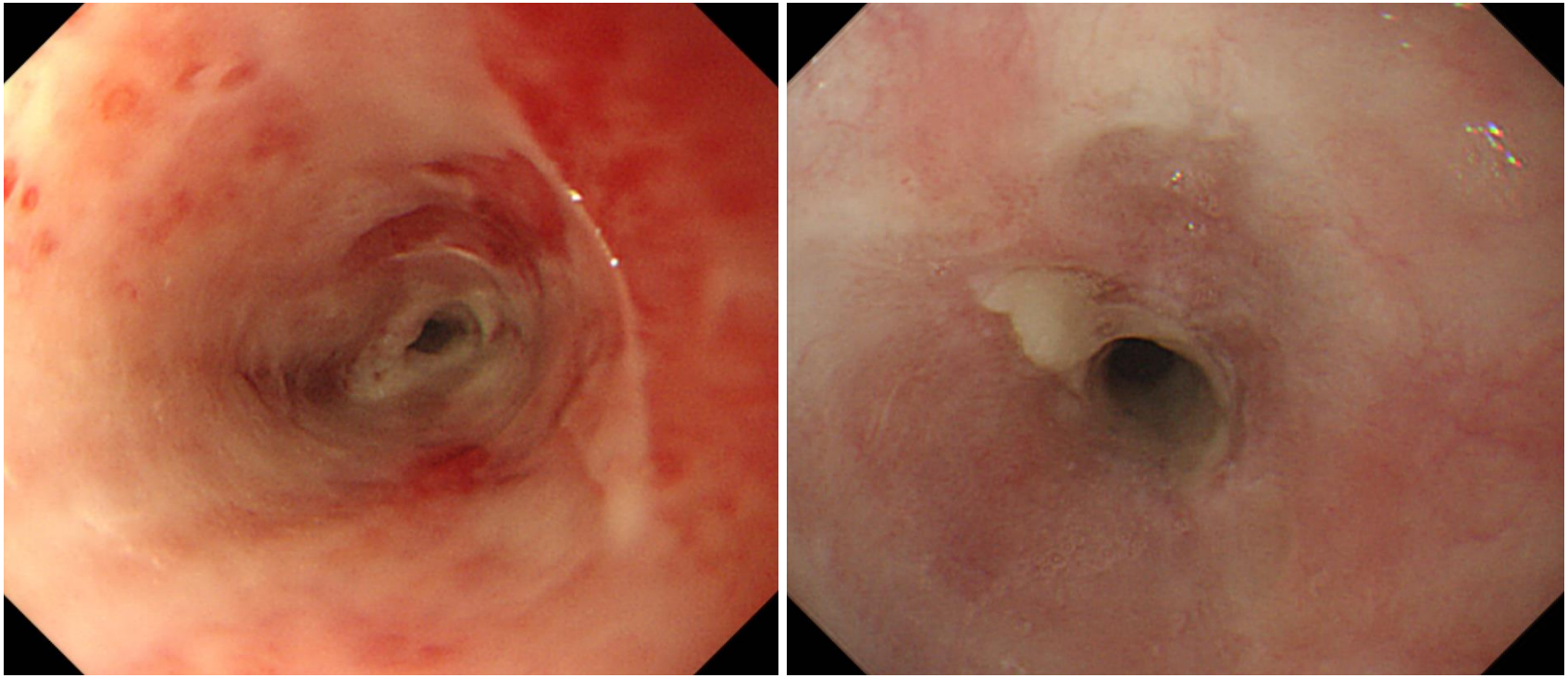


Peptic stricture

- A prolonged history of heartburn/regurgitation



RT-induced esophageal stricture



Motor dysphagia

- Diseases affecting smooth muscle involve the esophageal body and/or and the LES.
- Constant (or intermittent) dysphagia with both liquids and solids

- Common causes: achalasia, esophageal spasm, systemic sclerosis, EoE

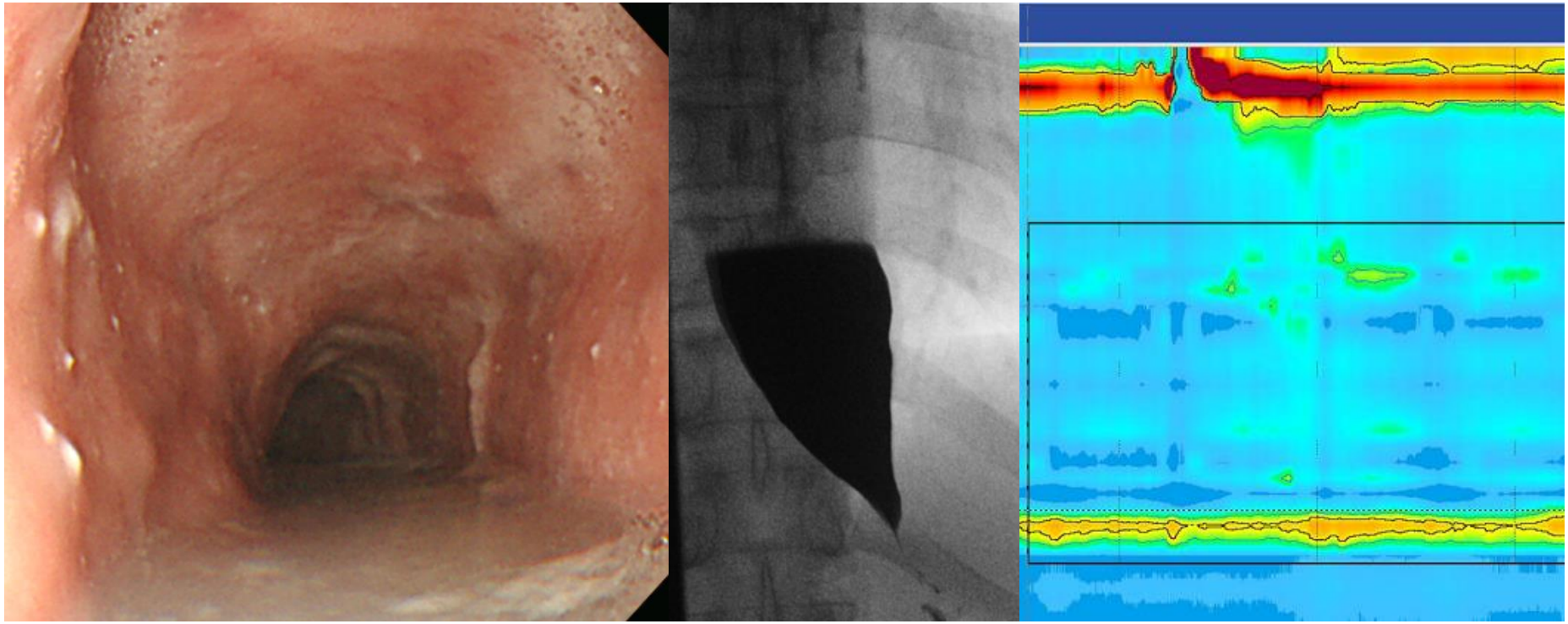
Symptoms of achalasia

1. Dysphagia for **solids and liquids** (>90%)
2. Regurgitation of undigested food (76-91%)
3. Weight loss (35-91%)
4. Chest pain (25-64%)
5. Heartburn (18-52%)
6. Nocturnal cough (30%)

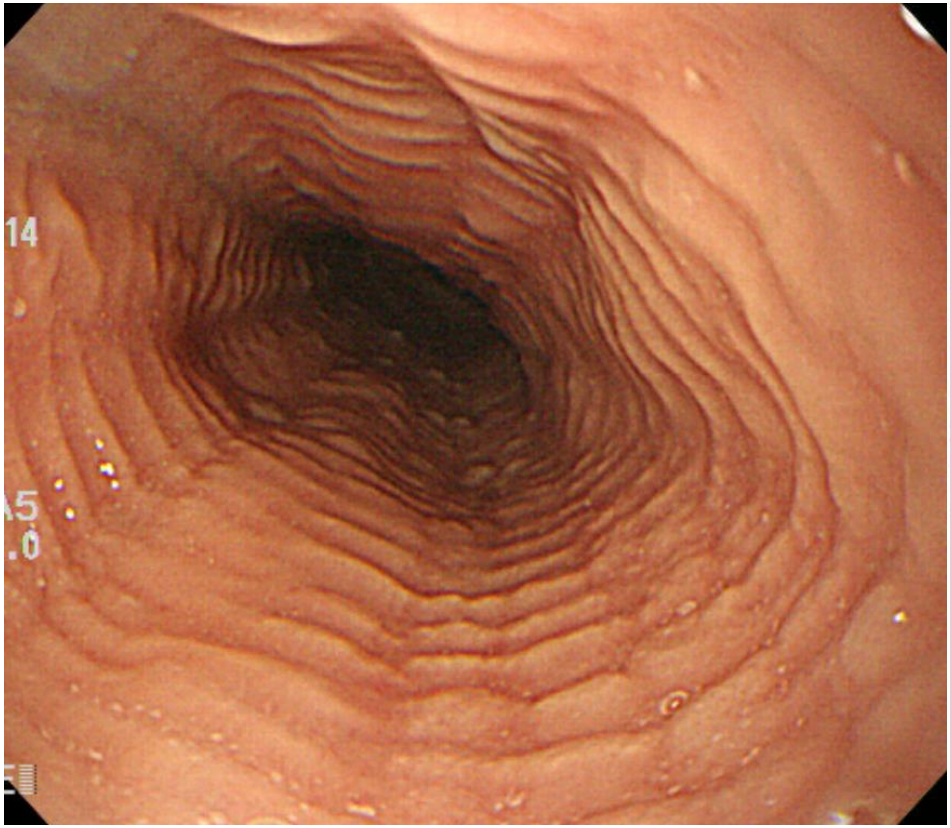
→ Often diagnosed as refractory GERD

Boeckxstaens GE et al, Lancet 2014;383:83-93

Diagnosis of achalasia



Eosinophilic esophagitis (EoE)



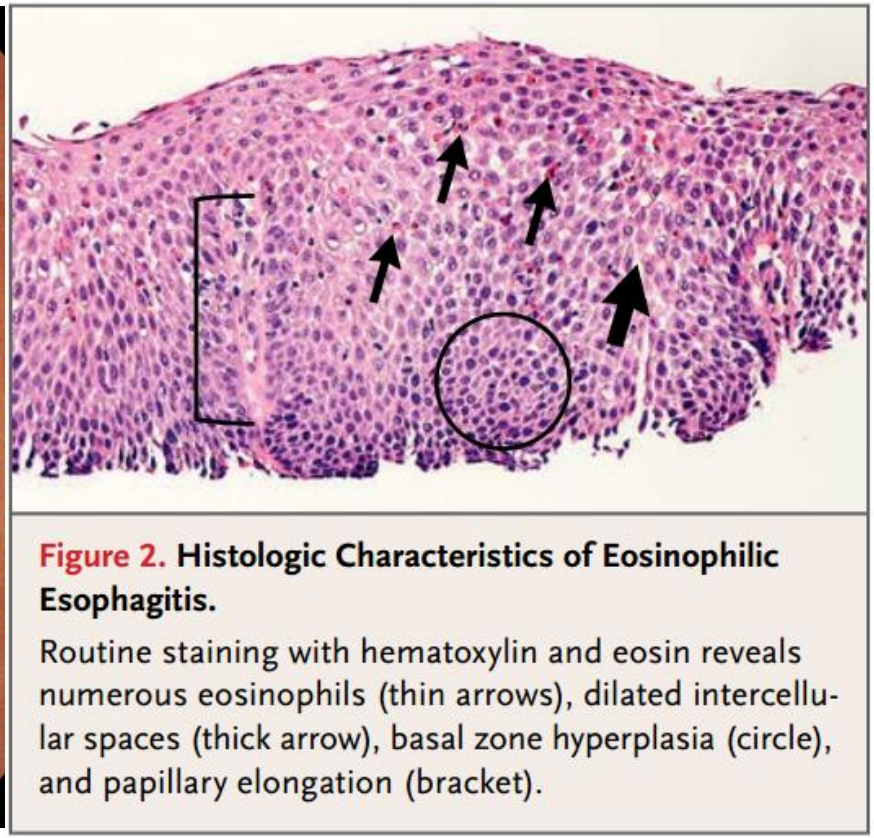
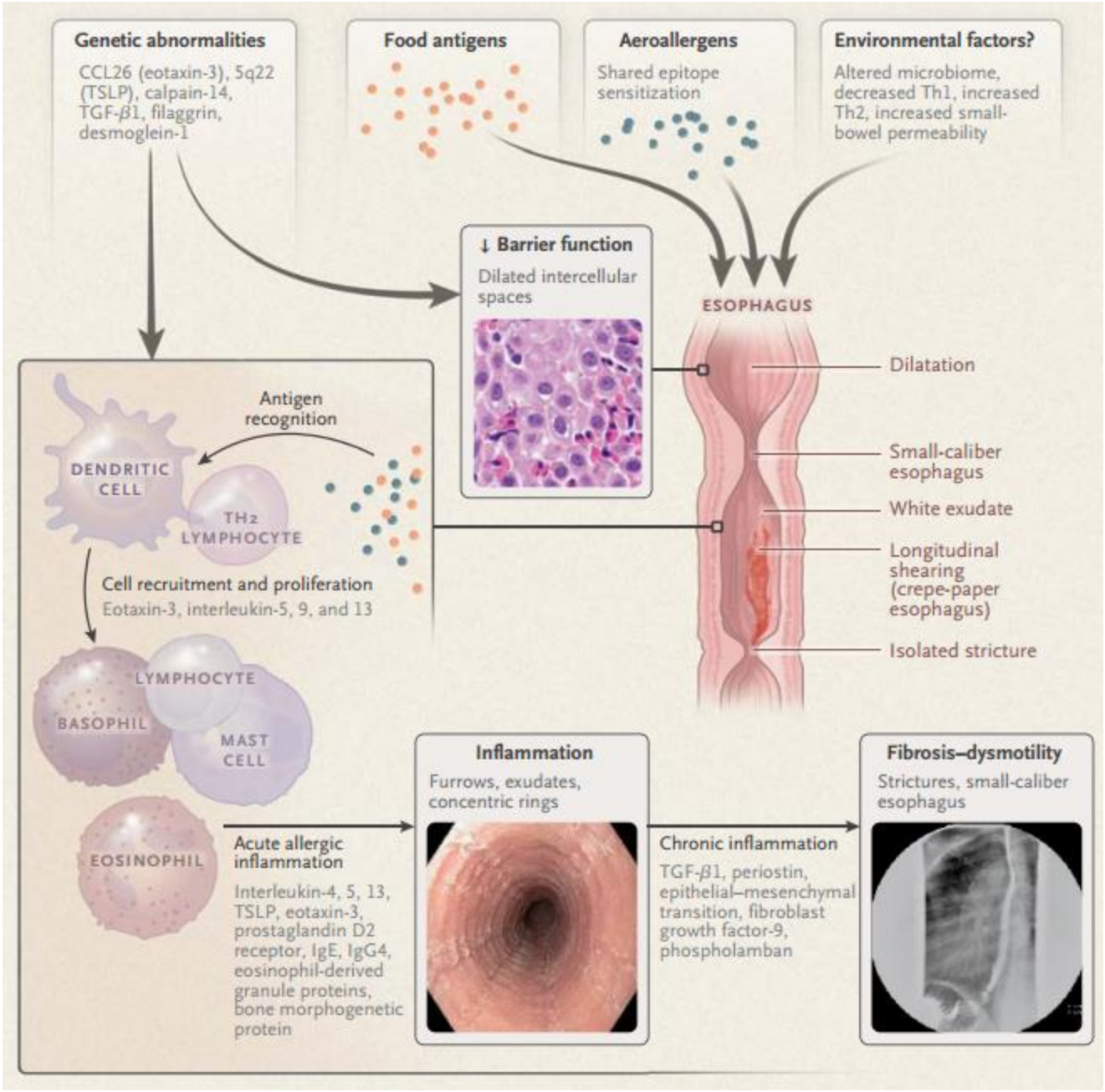


Figure 2. Histologic Characteristics of Eosinophilic Esophagitis.

Routine staining with hematoxylin and eosin reveals numerous eosinophils (thin arrows), dilated intercellular spaces (thick arrow), basal zone hyperplasia (circle), and papillary elongation (bracket).

Furuta GT and Katzka DA, N Engl J Med 2015;373:1640-1648



Furuta GT and Katzka DA, N Engl J Med 2015;373:1640-1648

Table 1. Medical Treatment of Active Eosinophilic Esophagitis.

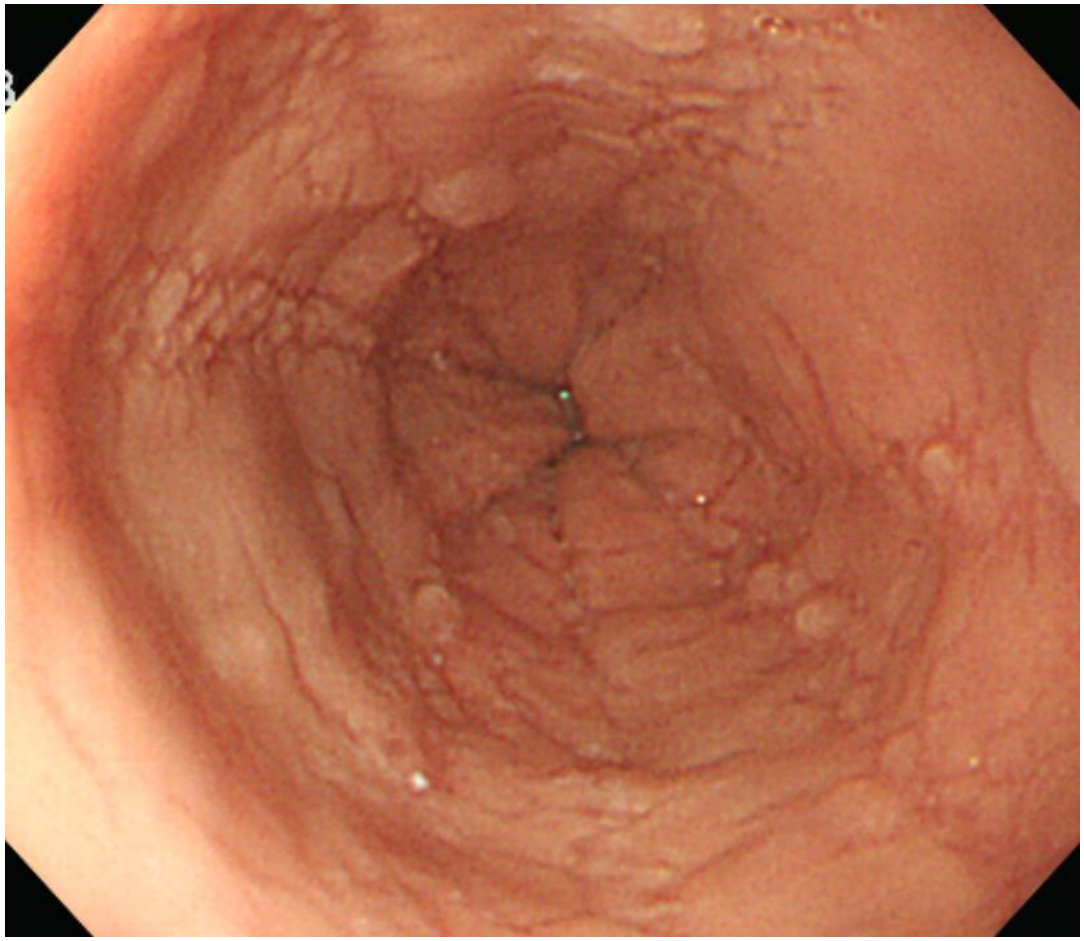
Method	Specific Recommendation or Dosage
Elemental diet therapy	—
Elimination diet therapy	
Six-food elimination	Elimination of milk, wheat, eggs, soy, seafood, and nuts
Four-food elimination	Elimination of milk, wheat, eggs, and soy
Allergy testing–based	Elimination of foods on the basis of results of radioallergosorbent testing, skin-prick testing, or atopy-patch testing*
Omeprazole (proton-pump inhibitor)†	Children with body weight 10 to 20 kg: 10 mg twice a day Children with body weight >20 kg: 20 mg twice a day Adults: 40 mg once or twice a day
Glucocorticoids	
Fluticasone	Children: 220 to 440 μg twice a day Adults: 440 to 880 μg twice a day
Budesonide	Children: 0.25 to 0.5 mg twice a day Adults: 1 to 2 mg twice a day

* Approximately 45% of patients have a sustained response to this type of diet therapy.[68]

† An equivalent proton-pump inhibitor can be administered.

Furuta GT and Katzka DA, N Engl J Med 2015;373:1640-1648

Asymptomatic EoE, M/70



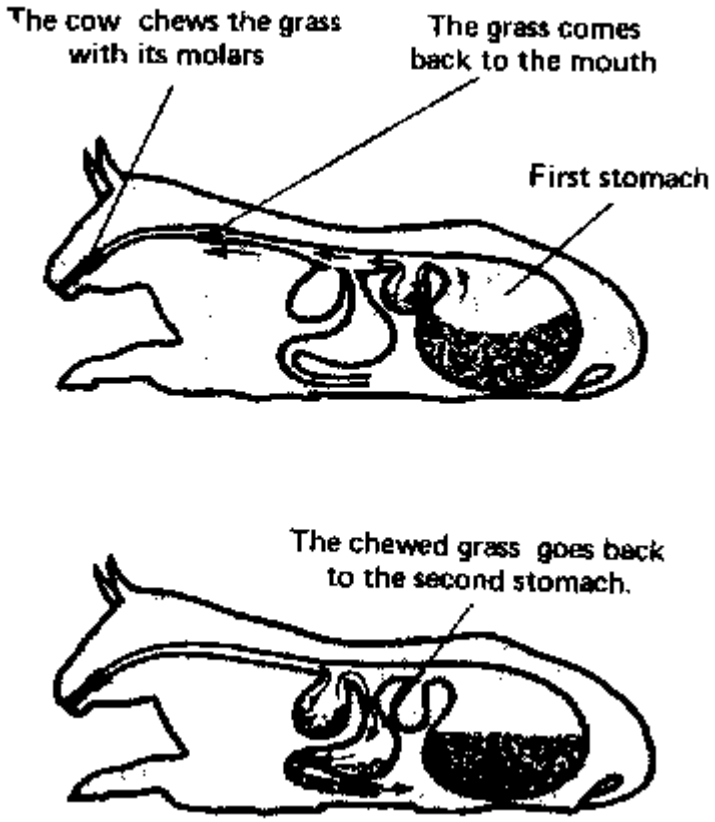
Asia-Pacific consensus on the management of gastroesophageal reflux disease: Update

Kwong Ming Fock,* Nicholas J Talley,† Ronnie Fass,‡ Khean Lee Goh,§ Peter Katelaris,¶ Richard Hunt,** Michio Hongo,†† Tiing Leong Ang,* Gerald Holtmann,‡‡ Sanjay Nandurkar,§§ San Ren Lin,¶¶ Benjamin CY Wong,*** Francis KL Chan,††† Abdul Aziz Rani,‡‡‡ Young-Tae Bak,§§§ Jose Sollano,¶¶¶ Lawrence KY Ho**** and Sathoporn Manatsathit††††

- **Statement 1:** GERD is defined as a disorder in which gastric contents reflux recurrently into the esophagus, causing troublesome symptoms and/or complications.
- **Statement 2:** Typical symptoms of reflux are **heartburn** (retrosternal burning sensation) and **acid regurgitation**, which are commonly experienced by Asian patients.

Fock KM et al, J Gastroenterol Hepatol 2008;23:8-22

Rumination syndrome



- Effortless, often repetitive, regurgitation of recently ingested food into the mouth (in humans)
- Not preceded by nausea or retching
- May be ***erroneously*** considered to have **gastroparesis or GERD**

Tack J, et al, Aliment Pharmacol Ther 2011;33:782-788

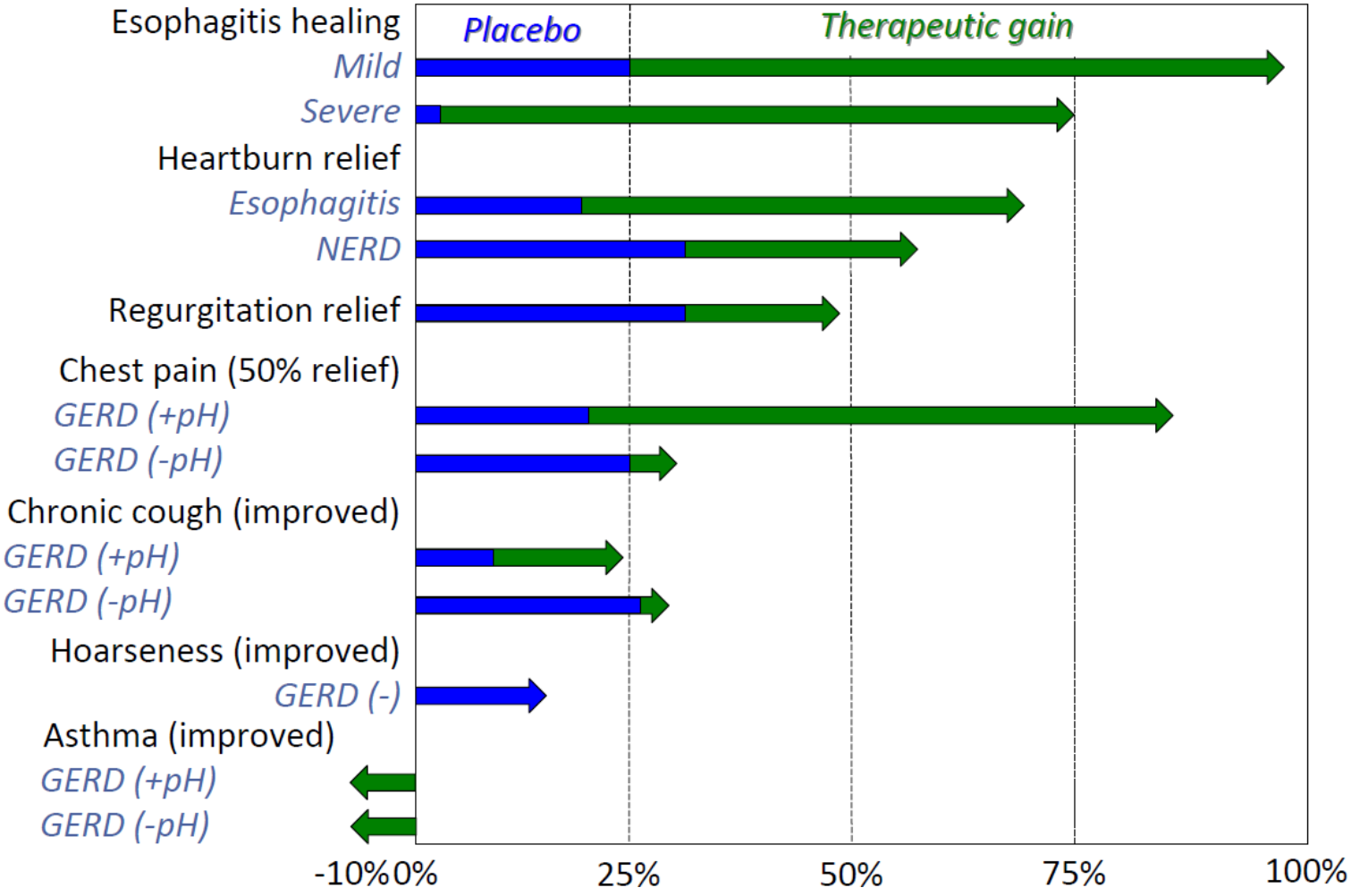
Treatment for rumination syndrome

- The mainstay of treatment
  - explanation of the condition and mechanism
  - behavioural modifications
- Diaphragmatic breathing during the postprandial period
  - disappearance of rumination in 30–66% and improvement in another 20–55%
- Chewing gum
  - reduces the number of rumination events in young children and adolescents

Tack J, et al, Aliment Pharmacol Ther 2011;33:782-788

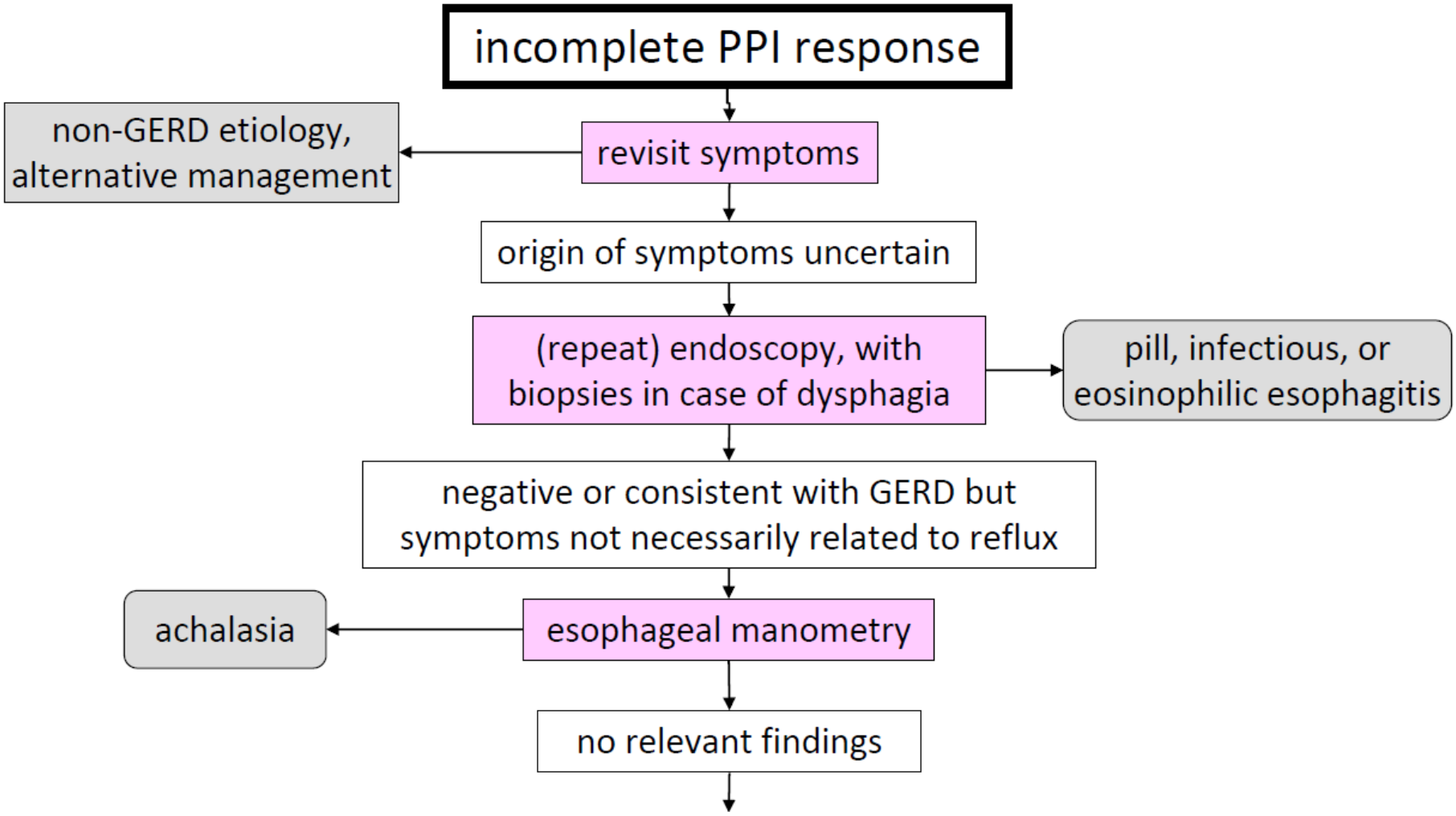
PPI efficacy for potential manifestations of GERD

Estimates based on available RCT data

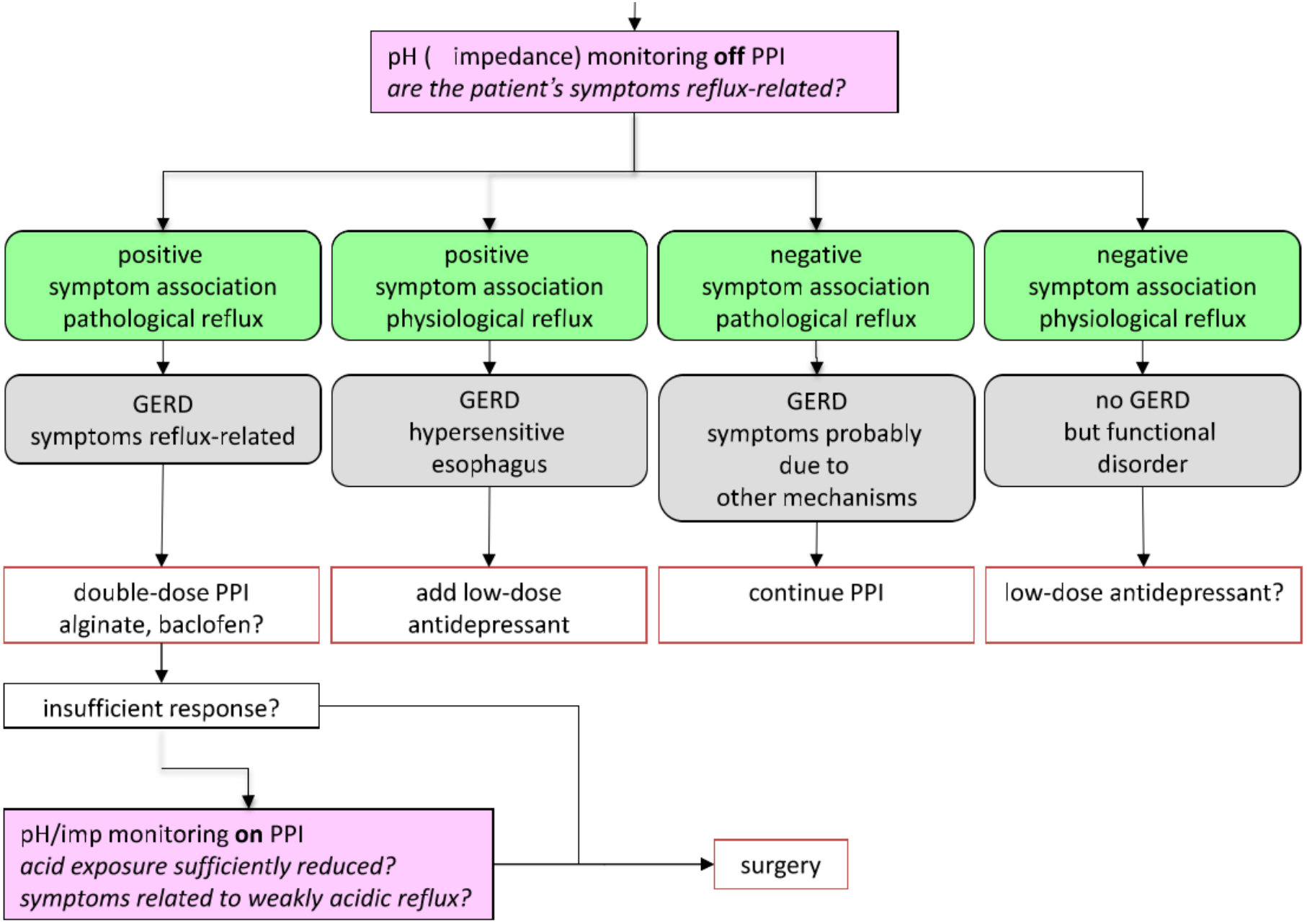


Kahrilas PJ and Boeckxstaens G. Gut 2012;61:1501-1509

Refractory GERD management



Kahrilas PJ, et al. Best Pract Res Clin Gastroenterol 2013;27:401-414



Kahrilas PJ, et al. Best Pract Res Clin Gastroenterol 2013;27:401-414

Odynophagia

- Pain upon swallowing
- Strongly suggests the mucosal injury
- Causes: pill-induced esophagitis or infectious esophagitis, peptic esophagitis, RT-induced esophagitis

Esophageal candidiasis

- Presentation: Odynophagia with dysphagia
  - May be an incidental finding

- Treatment for symptomatic and/or immunocompromised patients
  - Fluconazole 100 mg/day for 7-14 days

Antifungal treatment is not associated with remission for asymptomatic esophageal candidiasis: observational study (N=142)

TABLE 4. Univariate and Multivariate Analyses of Predisposing Factors for Nonremission of Esophageal Candidiasis

Variables	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age (years)	1.052 (1.009–1.098)	0.019	1.031 (0.978–1.087)	0.258
Sex				
Female	1		1	
Male	0.905 (0.375–2.186)	0.825	0.752 (0.250–2.259)	0.612
Diabetes	0.172 (0.022–1.345)	0.093	0.247 (0.029–2.117)	0.202
Cardiovascular disease	8.074 (1.405–46.412)	0.019	5.661 (0.785–40.831)	0.085
Steroid use	3.857 (0.738–20.152)	0.110	2.649 (0.313–22.443)	0.372
History of pulmonary tuberculosis	6.183 (1.807–21.159)	0.004	4.495 (1.023–19.762)	0.047
Triglyceride (mg/dL)	0.995 (0.988–1.002)	0.157	0.994 (0.985–1.003)	0.165
Rheumatoid factor (IU/mL)	1.071 (0.981–1.169)	0.127	1.031 (0.945–1.124)	0.490
Esophageal Candidiasis Grade				
I	1		1	
II	1.539 (0.671–3.533)	0.309	1.164 (0.423–3.200)	0.768
III	9.000 (0.768–105.430)	0.080	6.932 (0.469–102.427)	0.159
Antifungal treatment	0.743 (0.313–1.762)	0.500	0.682 (0.238–1.950)	0.475

Min YW, Kim E, et al, Medicine 2015;94:e1969

Details of antifungal treatment in the real practice

TABLE 3. Comparison of Antifungal Treatment Between Remission and Nonremission Group

Variables	Remission (n = 111)	Nonremission (n = 31)	*P* Value
Antifungal treatment	82 (73.9)	21 (67.7)	0.499
Antifungal agent			0.467
Fluconazole	69 (84.1)	20 (95.2)	
Itraconazole	3 (3.7)	0 (0)	
Nystatin	3 (3.7)	1 (4.8)	
Unknown	7 (8.5)	0 (0)	
Treatment duration (days)*	9.0 ± 2.8	10.2 ± 3.1	0.099
Treatment duration categories*			0.090
≤7 days	32 (46.4)	8 (40.0)	
>7 and <14 days	28 (40.6)	5 (25.0)	
≥14 days	9 (13.0)	7 (35.0)	
Daily dose (mg)*	106.5 ± 35.3	107.5 ± 33.5	0.912
Total dose (mg)*	973.9 ± 443.1	1075.0 ± 408.3	0.363
Total dose categories*			0.438
≤700 mg	28 (40.6)	5 (25.0)	
>700 and <1400 mg	18 (26.1)	7 (35.0)	
≥1400 mg	23 (33.3)	8 (40.0)	

Data are shown as the mean ± SD or number (%) of patients.
* Subgroup analysis was performed in a group of patients who received fluconazole.

Min YW, Kim E, et al, Medicine 2015;94:e1969

Chest pain

Noncardiac chest pain (NCCP)

- Retrosternal pain by esophageal pathology
- Sensory innervation of intrathoracic organ is intertwined.
- Pain upon exertion vs during and/or after meals

  → lack of accuracy in making a diagnosis

Prevalence of RE in NCCP

- A retrospective study (N=217)

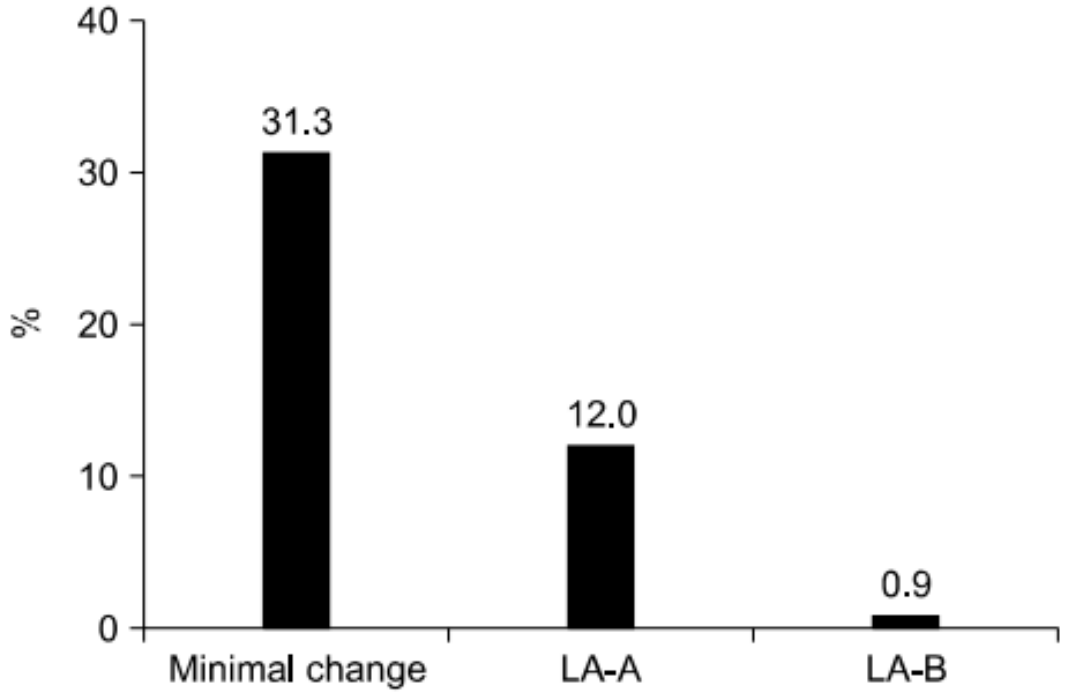
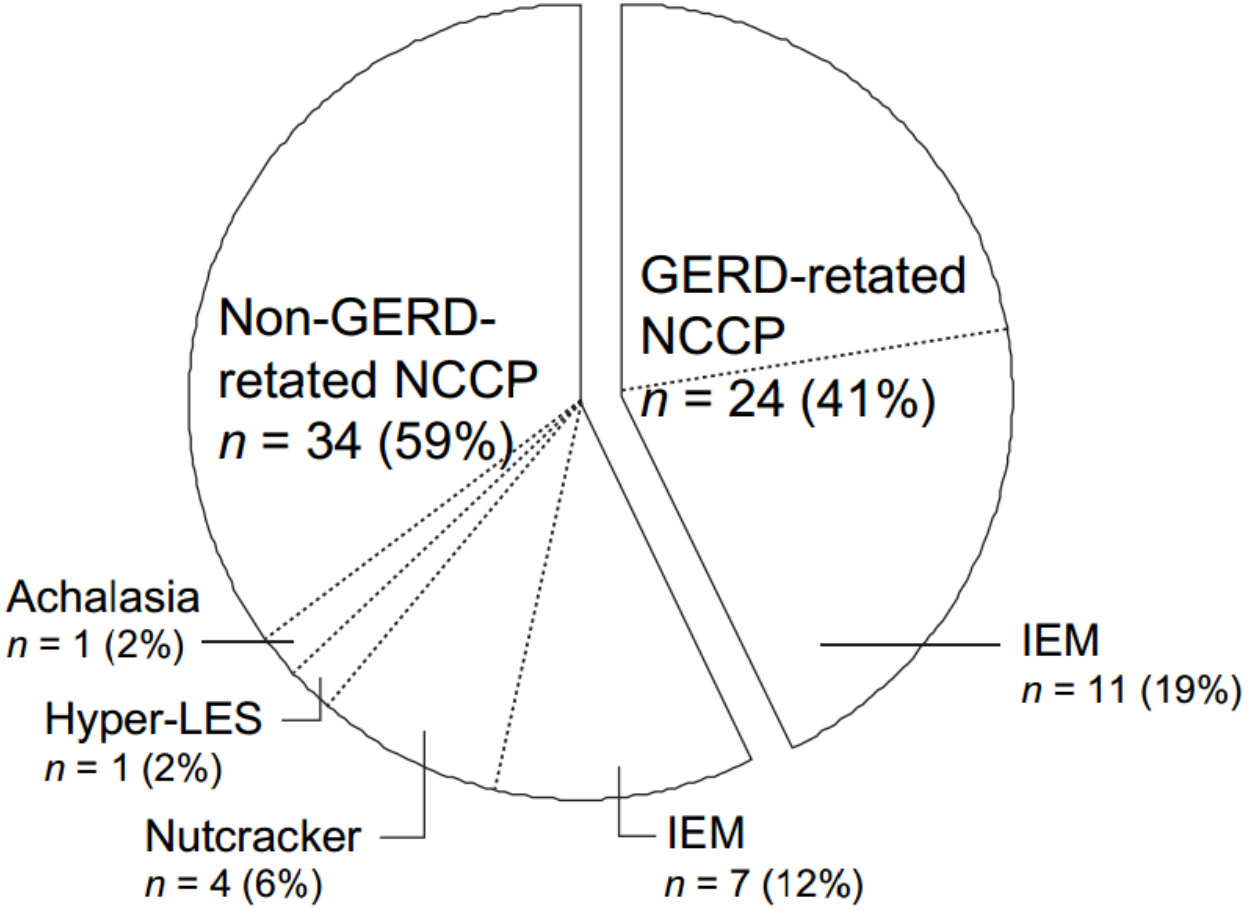


Fig. 2. Prevalence of reflux esophagitis in patients with noncardiac chest pain. Among them, 68 patients (31.3%) in minimal change esophagitis; 26 patients (12.0%) in Los Angeles (LA) grade A; 2 patients (0.9%) in LA grade B. There were no patients with severe erosive esophagitis.

Mok JY, et al, Korean J Helicobacter Up Gastrointest Res 2016;16:88-91

Upper GI evaluation in NCCP

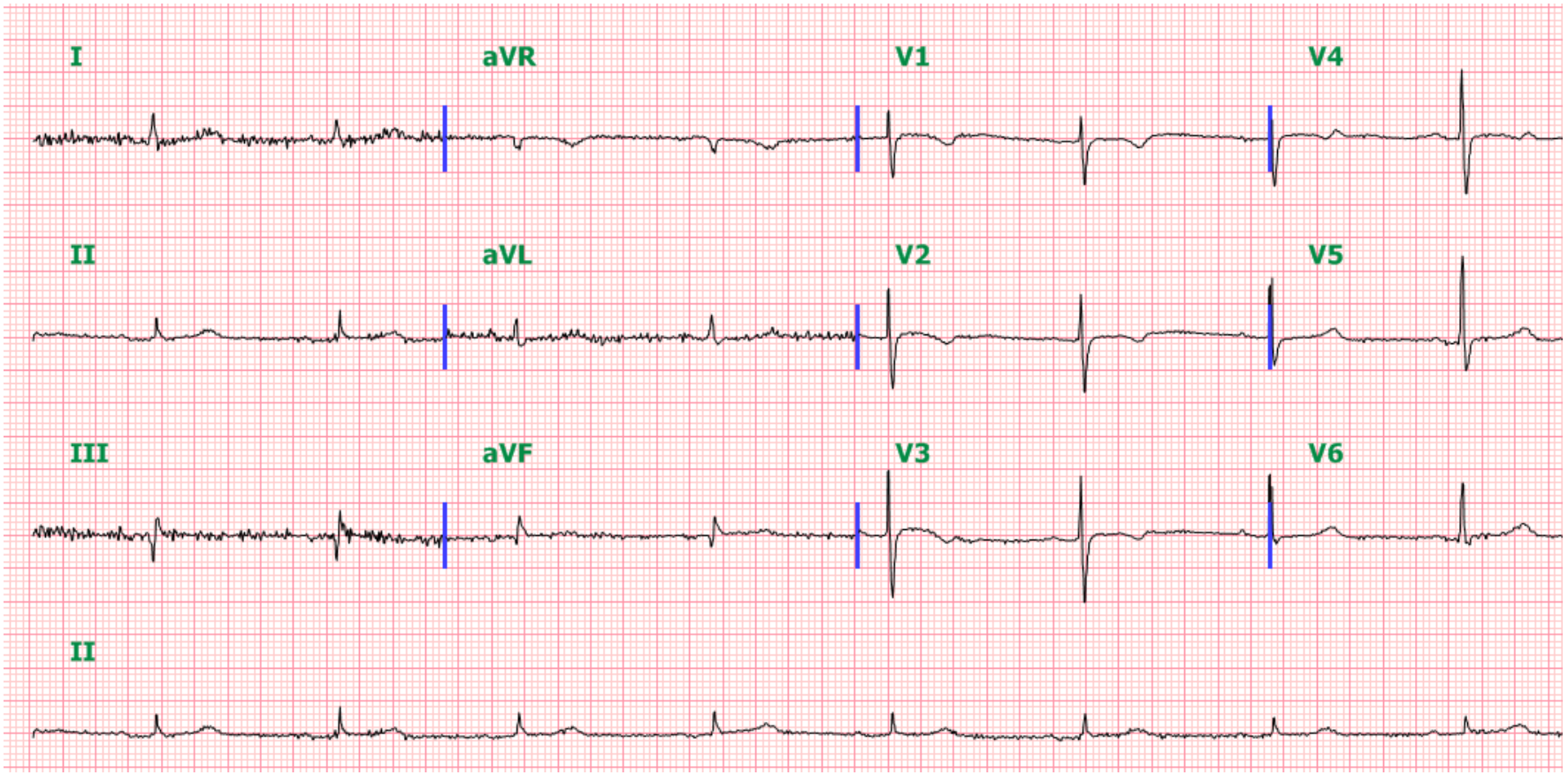
- A prospective analysis in 58 NCCP patients



Kim JH, Rhee PL, et al, J Gastroenterol Hepatol 2007;22:320-325

‘식도염이 심하다‘, 76/F

NSTEMI → PCI



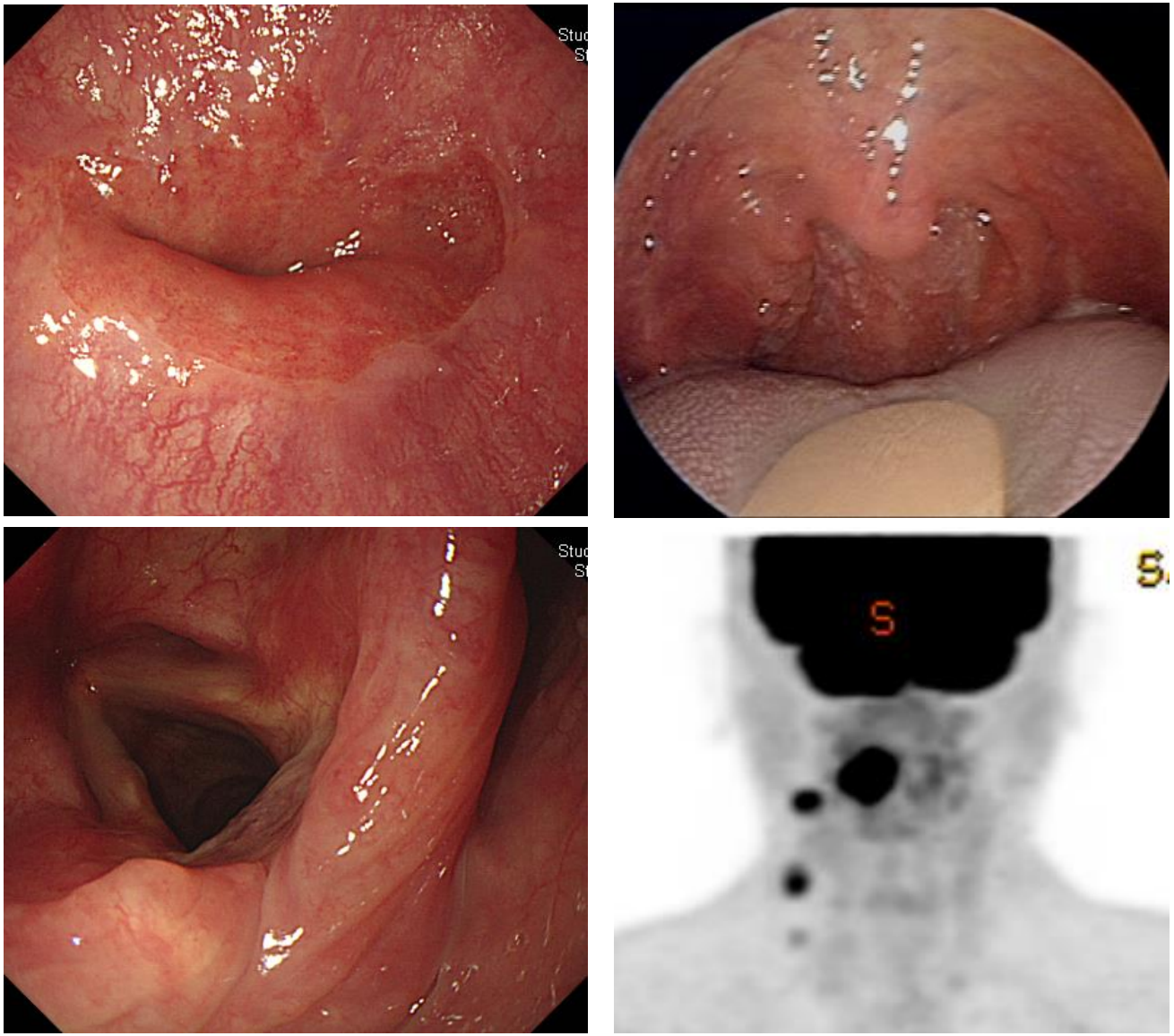
Globus

- Non-painful sensation of ‘lump’ in the throat
- Usually in the region of the sternal notch

- Experienced without swallowing
- May actually get better with swallowing

Kahrilas PJ and Smout AJ, Am J Gastroenterol 2010;105:747-756

Rt tonsillar cancer with neck meta

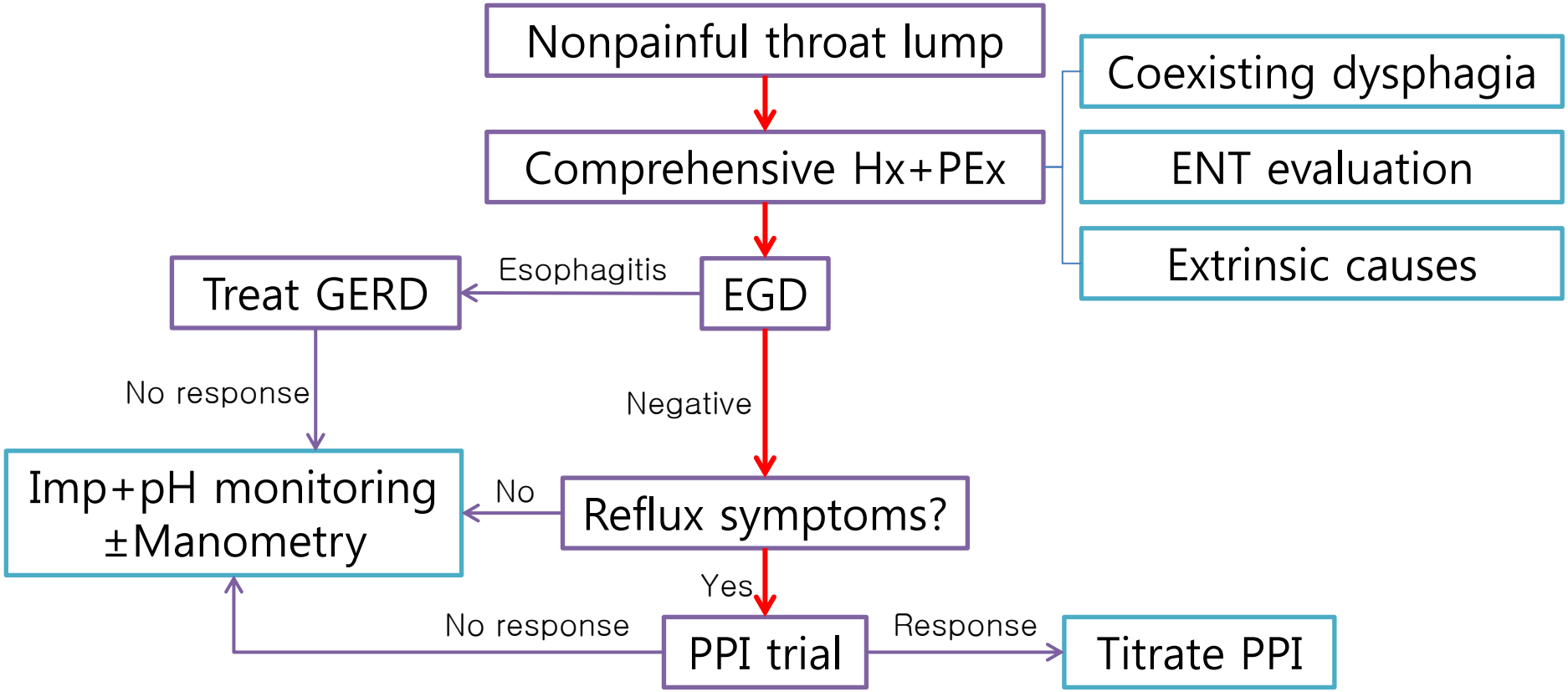


Potential causes of globus

- **Gastroesophageal reflux disease**
- Abnormal upper esophageal sphincter function
- Esophageal motor disorders
- Pharyngeal inflammatory causes
- Upper aerodigestive malignancy
- Hypertrophy of the base of the tongue
- Retroverted epiglottis
- Thyroid diseases
- Cervical heterotopic gastric mucosa
- Rare laryngopharyngeal tumors
- **Psychological factors and stress**

Lee BE and Kim KH, World J Gastroenterol 2012;18:2462-2471

Approach for patients with globus



Supraesophageal symptoms (=extraesophageal symptoms)

- Recognition of the relationship of GERD with several pulmonary and otolaryngologic problems like cough, hoarseness, and asthma
- Weaker association than previously noticed

Kahrilas PJ and Smout AJ, Am J Gastroenterol 2010;105:747-756

No effect of PPI on poorly controlled asthma

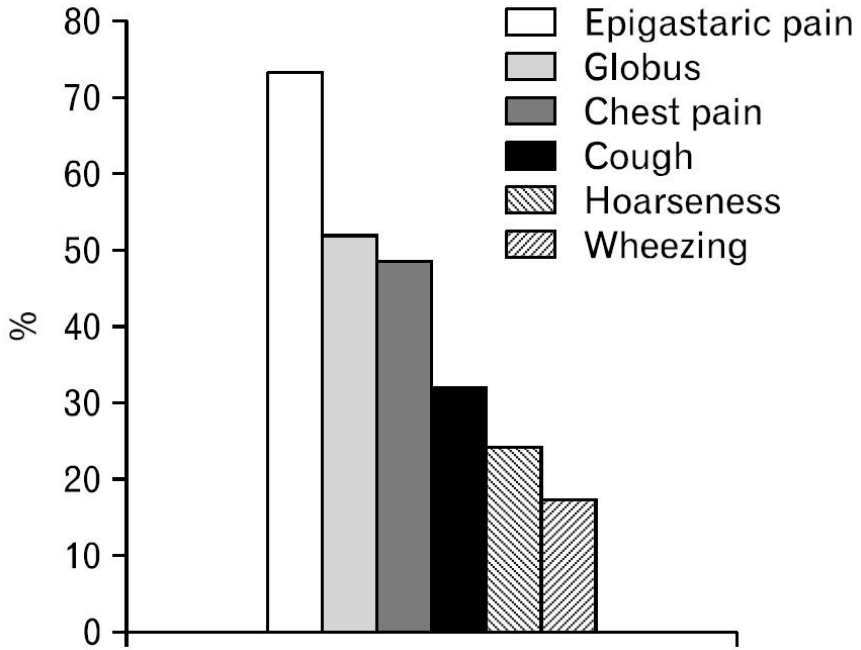
- A parallel-group, double-blind trial (N=412)

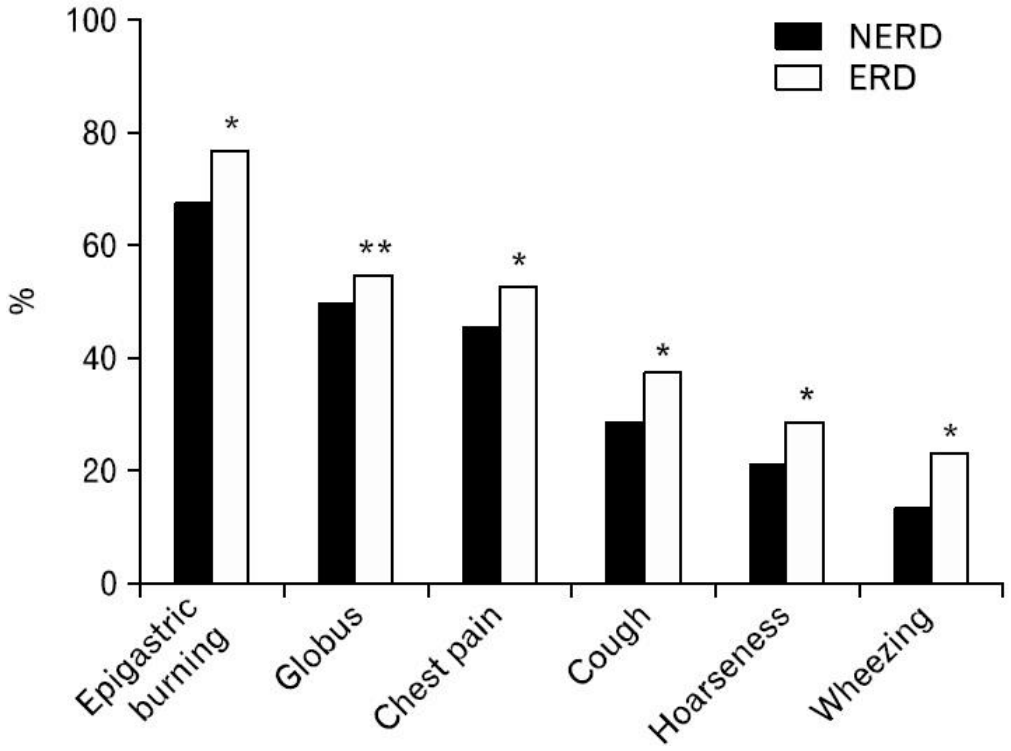
Variable	Placebo (N=193)	Esomeprazole (N=200)	Incidence-Rate Ratio, Esomeprazole vs. Placebo (95% CI)	P Value	
				Esomeprazole vs. Placebo†	Gastroesophageal-Reflux Interaction‡
Asthma episodes, according to definition that did not include use of beta-agonists as a criterion					
No. of events	201	224			
No. of events/person-yr	2.3	2.5	1.1 (0.8–1.5)	0.66	0.93
Patients with ≥1 event (%)	42	42			

† P values are for the treatment effect of esomeprazole as compared with placebo.
‡ P values are for the modification of the treatment effect by pH-monitoring results, as estimated by linear regression.

N Engl J Med 2009;360(15):1487-1499

Extra-esophageal symptoms
- in Korean GERD patients (N=1,712)





Min YW, Rhee PL, et al, J Neurogastroenterol Motil 2014;20:87-93

Overdiagnosis of GERD as the sole cause of a patient's complaints