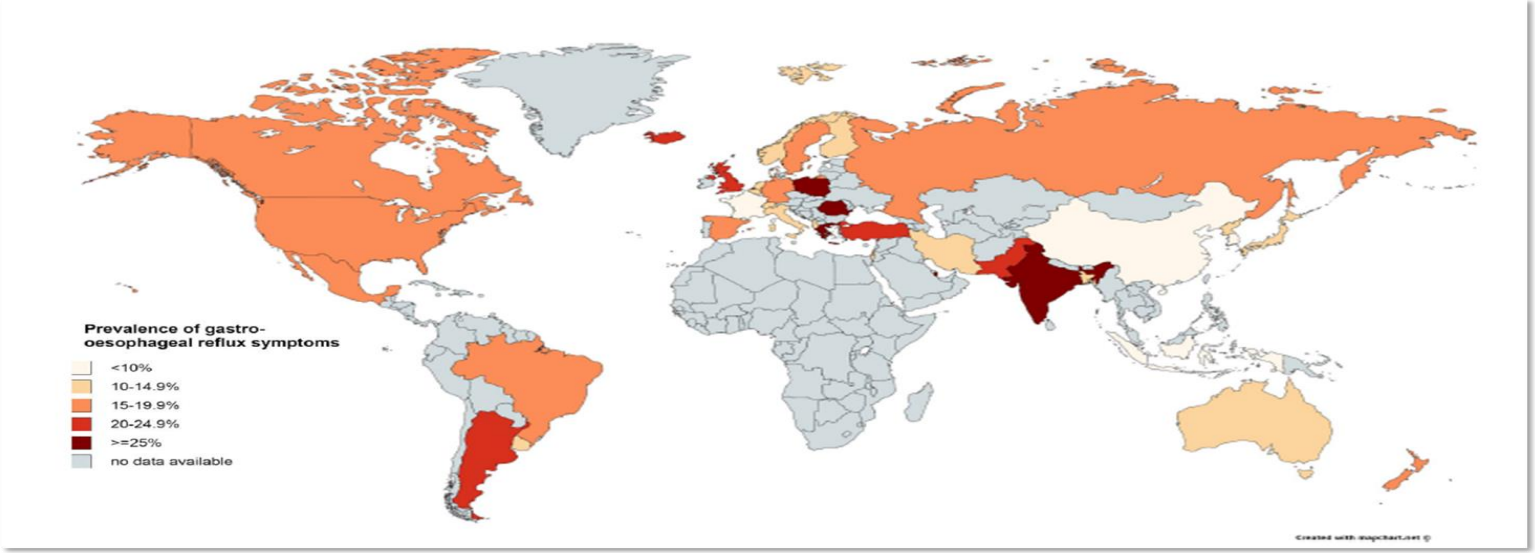
Malattia da reflusso gastro-esofageo

Paolo Usai Satta

SC Gastroenterologia, ARNAS G. Brotzu, Cagliari

Global Prevalence of GERD

- N=108 studies included in the meta-analysis
- Prevalence varied according to country (from 2.5% in China to 51.2% in Greece)
- In case of weekly heartburn/regurgitation was considered, pooled prevalence was 13.3%
- Risk factors: ≥50 years, smoking, NSAID/aspirin use and obesity



Eusebi LH, et al. Gut 2018; 67:430–440

GERD: Pathophysiology

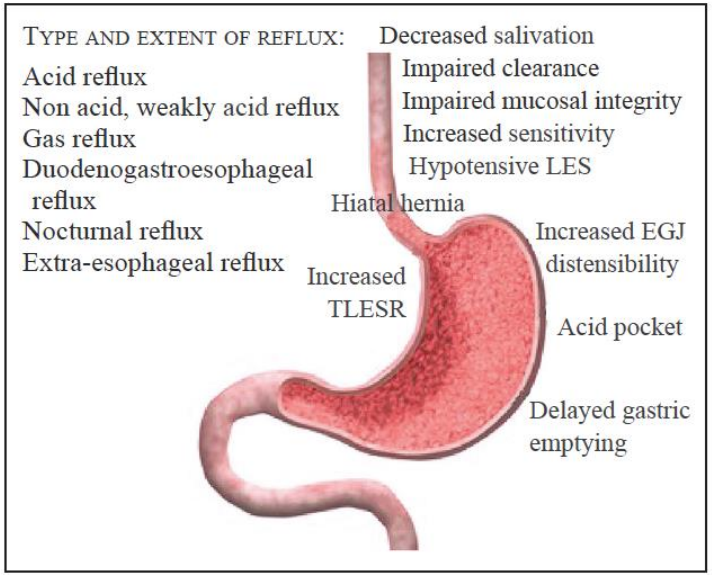


Figure 1.—Overview of pathophysiological factors leading to GERD.

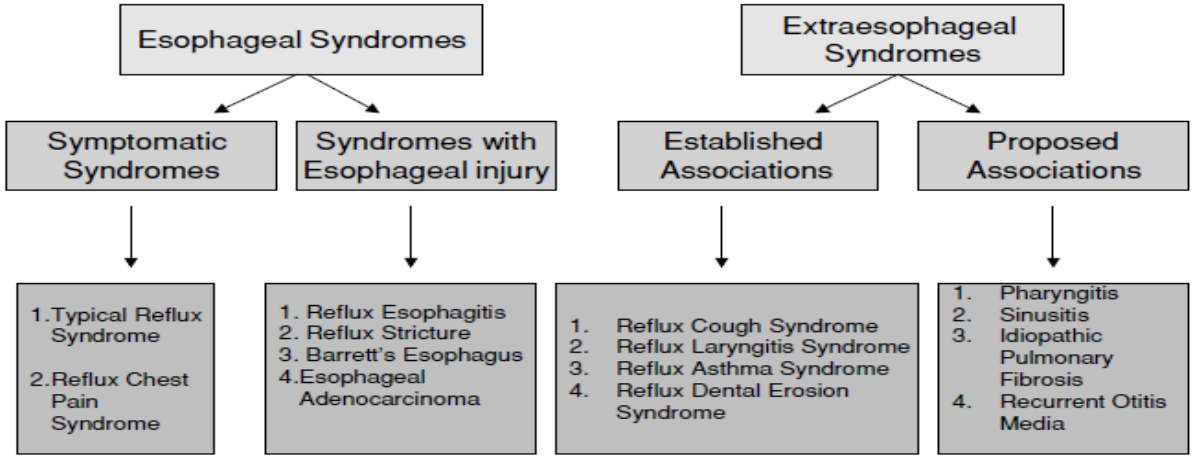
Usai Satta P et al., Minerva Gastroent Dietol 2017

Fattori di rischio della MRGE

- Età (> 50 aa)
- Ernia iatale
- Sovrappeso e obesità
- Fumo
- Farmaci (FANS, etc)

GERD: Montreal Consensus

GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms or complications



Vakil N et al., Am J Gastroenterol 2006; 101:1900-1920

CME

New

ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease

Philip O. Katz, MD, MACG[1], Kerry B. Dunbar, MD, PhD[2,3], Felice H. Schnoll-Sussman, MD, FACG[1], Katarina B. Greer, MD, MS, FACG[4], Rena Yadlapati, MD, MSHS[5] and Stuart Jon Spechler, MD, FACG[6,7]

Am J Gastroenterol 2022;117:27–56.

AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review

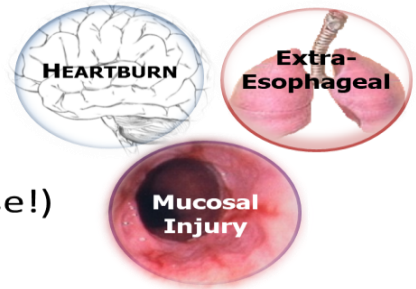
Rena Yadlapati,* C. Prakash Gyawali,‡ and John E. Pandolfino,§ on behalf of the CGIT GERD Consensus Conference Participants

Clinical Gastroenterology and Hepatology 2022;20:984–994

GERD: Clinical Spectrum

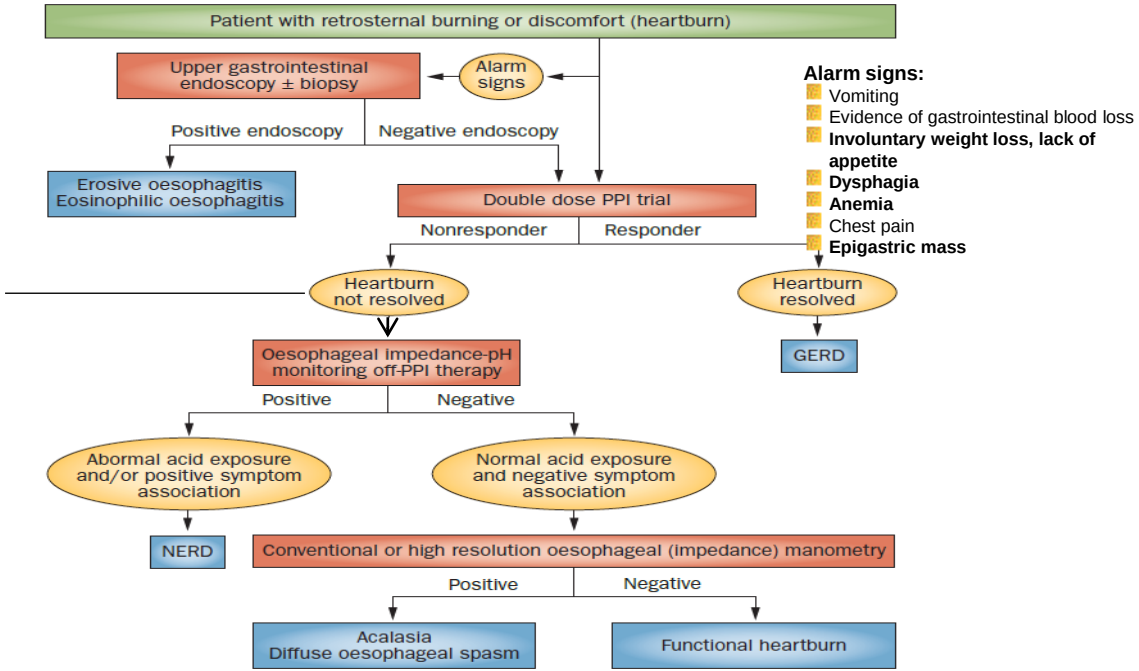
Likely Due to Reflux

- Heartburn/Burning discomfort
- Regurgitation
- Chest Pain (rule out heart disease!)
- Dysphagia
- Dental erosions
- ENT/Cough/Asthma
- Sleep disturbances
- Dyspeptic symptoms:
  - EPS (epigastric pain and/or burning),
  - PDS (Bloating, Belching, Nausea, Vomiting, Early satiety, post-prandial fullness)



Locke GR 3rd et al. Gastroenterology 1997; 112(5):1448-56
Talley N. Aliment Pharmacol Ther 2004; 20 Suppl 5:27-37
Bardhan KD et al. Digestion 2004; 69(4):229-37

GERD: Diagnostic Algorithm

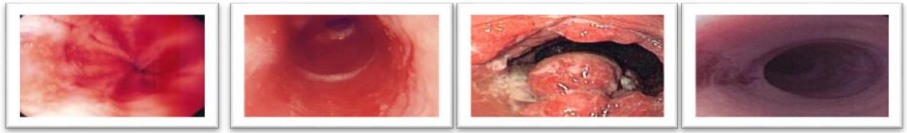


Modified from Savarino E, et al. Nat Rev Gastroenterol Hepatol. 2013;10(6):371-80

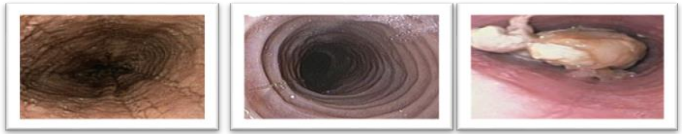
Why Upper GI Endoscopy?

To investigate and assess:

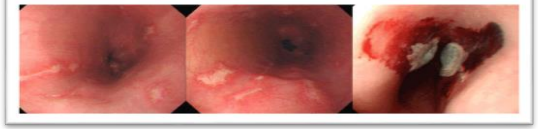
- Esophagitis, Barrett's metaplasia, stricture, neoplasia



- Eosinophilic oesophagitis



- Pill-induced oesophagitis



- Gastric or duodenal ulcer

E' utile un PPI test?

CME

ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease

1. For patients with classic GERD symptoms of heartburn and regurgitation who have no alarm symptoms, we recommend an 8-week trial of empiric PPIs once daily before a meal (strong recommendation, moderate level of evidence).
2. We recommend attempting to discontinue the PPIs in patients whose classic GERD symptoms respond to an 8-week empiric trial of PPIs (conditional recommendation, low level of evidence).

Am J Gastroenterol 2022;117:27–56.

Digestive and Liver Disease 52 (2020) 966–980

Contents lists available at ScienceDirect

Digestive and Liver Disease

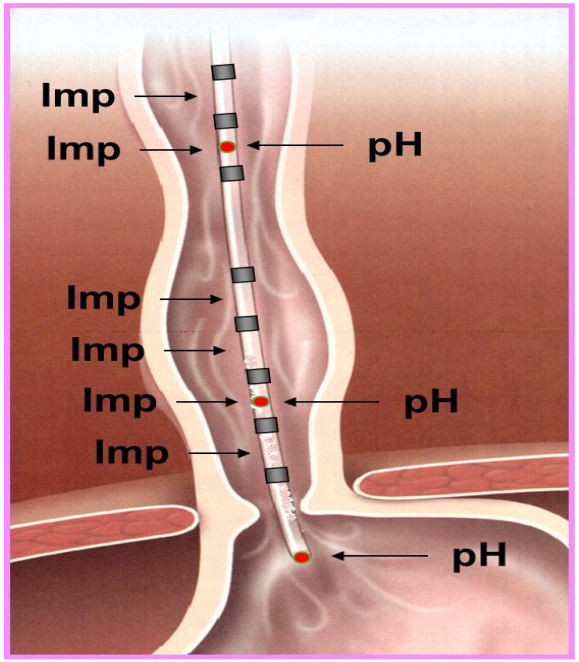
journal homepage: www.elsevier.com/locate/dld

Review Article

A SIGE-SINGEM-AIGO technical review on the clinical use of esophageal reflux monitoring☆

Edoardo Savarino[a,*], Marzio Frazzoni[b], Elisa Marabotto[c], Patrizia Zentilin[c], Paola Iovino[d], Mario Costantini[e], Salvatore Tolone[f], Edda Battaglia[g], Michele Cicala[h], Paolo Usai-Satta[i], Nicola de Bortoli[j], Roberto Penagini[k,l], Vincenzo Savarino[c]

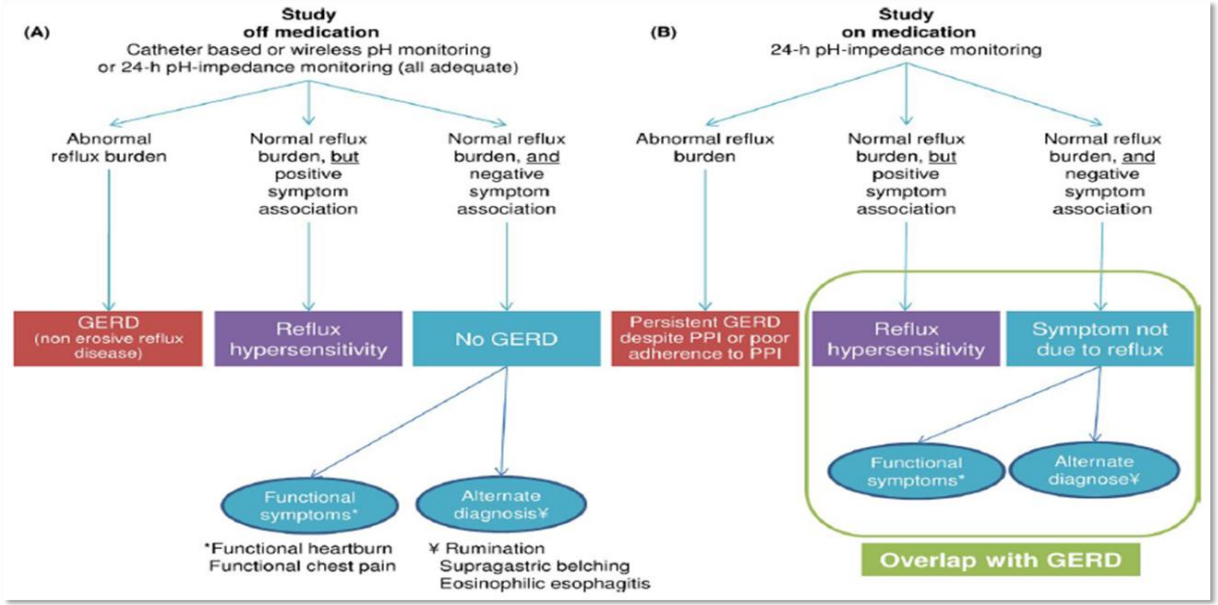
E' utile una pH-impedenziometria?



1. Esophageal acid exposure
2. Esophageal non-acid exposure
3. Gastric pH
4. Proximal migration
5. Chemical and bolus clearance
6. Air detection
7. Impedance-Baseline
8. Post-prandial reflux
9. GERD diagnosis ON-PPI therapy
10. Symptom association analysis (Acid and Non-Acid)
    - Symptom Index
    - Symptom association Analysis

Zentilin P et al., *Did Liv Dis* 2004; 36:565-9

E' utile una pH-impedenzometria?

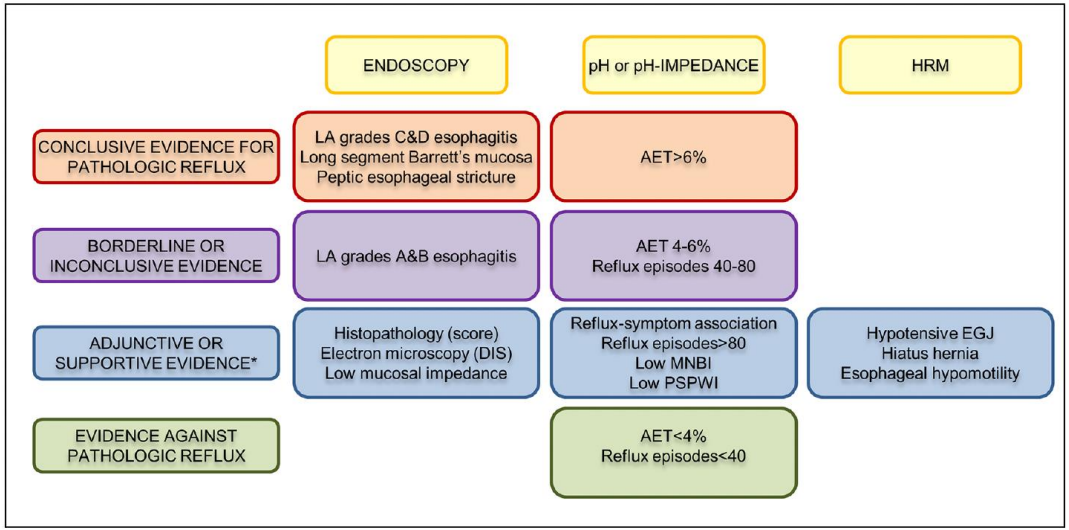


Roman S et al. Neurogastroenterol Motil. 2017;29(10):1-15
Savarino E et al. Nat Rev Gastroenterol Hepatol. 2017;14(11):665-676

OPEN ACCESS

Modern diagnosis of GERD: the Lyon Consensus

C Prakash Gyawali,[1] Peter J Kahrilas,[2] Edoardo Savarino,[3] Frank Zerbib,[4] Francois Mion,[5,6,7] André J P M Smout,[8] Michael Vaezi,[9] Daniel Sifrim,[10] Mark R Fox,[11,12] Marcelo F Vela,[13] Radu Tutuian,[14] Jan Tack,[15] Albert J Bredenoord,[8] John Pandolfino,[2] Sabine Roman[5,6,7]



How many cases of laryngopharyngeal reflux suspected by laryngoscopy are gastroesophageal reflux disease-related?

Nicola de Bortoli, Andrea Nacci, Edoardo Savarino, Irene Martinucci, Massimo Bellini, Bruno Fattori, Linda Ceccarelli, Francesco Costa, Maria Gloria Mumolo, Angelo Ricchiuti, Vincenzo Savarino, Stefano Berrettini, Santino Marchi

Table 4 Correlation between multichannel intraluminal impedance and pH analysis and the reflux finding score/ reflux symptom index analysis

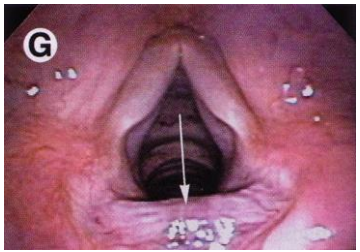
	ERD/NERD	HE	No GERD[1]	*P* value
AET (%)	7.4 ± 3.2	3.5 ± 1.7	1.9 ± 0.8	< 0.05
Reflux number (*n*)	103.2 ± 12.1	44.7 ± 6.2	35.1 ± 7.4	< 0.05
Proximal refluxes (mean %)	31	29	18	< 0.05
Acid refluxes (*n*)	62.5 ± 15.4	32.9 ± 5.1	19.7 ± 6.2	< 0.05
Non-acid refluxes (*n*)	40.1 ± 7.6	13.1 ± 4.4	15.8 ± 4.9	< 0.05
Gas refluxes (*n*)	11.6 ± 9.7	13.1 ± 8.1	21.7 ± 15.3	< 0.05
SAP/SI	Positive	Positive	Negative	-
RFS	10.9 ± 3.3	9.1 ± 2.7	7.6 ± 3.1	NS
RSI	14.3 ± 5.2	16.3 ± 4.7	15.8 ± 4.9	NS

AIM: To investigate the prevalence of gastroesophageal reflux disease (GERD) in patients with a laryngoscopic diagnosis of laryngopharyngeal reflux (LPR).

Table 2 Results of the visual analytic scale

Symptoms	Pre-PPI	Post-PPI	*P* value
Chest pain	7.1 ± 2.4	3.3 ± 0.9	0.0001[1]
Heartburn	8.5 ± 3.2	2.3 ± 1.1	0.0001[1]
Regurgitation	6.8 ± 1.5	4.1 ± 1.9	0.0001[1]
Epigastric pain	5.9 ± 3.6	3.7 ± 2.4	0.0021
Hoarseness	7.4 ± 2.2	6.8 ± 2.7	0.273
Globus	9.3 ± 3.8	7.9 ± 3.5	0.087
Cough	7.9 ± 2.6	6.8 ± 2.8	0.069
Throat discomfort	8.1 ± 3.4	6.9 ± 2.1	0.058
Dysphonia	6.5 ± 2.1	5.5 ± 3.5	0.121

CONCLUSION: MII-pH analysis confirmed GERD diagnosis in less than 40% of patients with previous diagnosis of LPR, most likely because of the low specificity of the laryngoscopic findings.



World J Gastroenterol 2012 August 28; 18(32): 4363-4370

Terapia MRGE *non eziologica* : PPI

GUARIGIONE ESOFAGITE SEVERA DOPO IPP

12 Placebo Controlled RCTs

Intention to Treat analysis

Trial	Dose	*n*	4 weeks Healed	4 weeks % Healed	8 weeks Healed	8 weeks % Healed
Castell *et al.* 1996	LAN30	164	111	67.7	128	78.0
	OME20	144	97	67.4	118	81.9
Castell *et al.* 2002	LAN30	646	351	54.3	461	71.4
	ESO40	640	411	64.2	534	83.4
Fennerty *et al.* 2005	LAN30	502	238	47.4	367	73.1
	ESO40	499	278	55.7	386	77.4
Hetzel *et al.* 1988	OME20	51	30	58.8	38	74.5
	OME40	52	38	73.1	41	78.8
Howden *et al.* 2002	ESO40	57	n/a	n/a	47	82.5
	LAN30	52	n/a	n/a	48	92.3
Kahrilas *et al.* 2000	ESO40	166	98	59.0	137	82.5
	OME20	182	85	46.7	135	74.2
Labenz *et al.* 2005	ESO40	374	259	69.3	327	87.4
	PAN40	395	219	55.4	324	82.0
Mee *et al.* 1996	LAN30	46	18	39.1	29	63.0
	OME20	48	24	50.0	30	62.5
Mulder *et al.* 1996	LAN30	29	21	72.4	24	82.8
	OME40	37	26	70.3	32	86.5
Richter *et al.* 2001	ESO40	317	216	68.1	272	85.8
	OME20	320	153	47.8	220	68.8
Sontag *et al.* 1992	OME20	52	n/a	n/a	35	67.3
	OME40	50	n/a	n/a	36	72.0
Schmitt *et al.* 2006	ESO40	189	115	60.8	167	88.4
	OME20	169	81	47.9	131	77.5

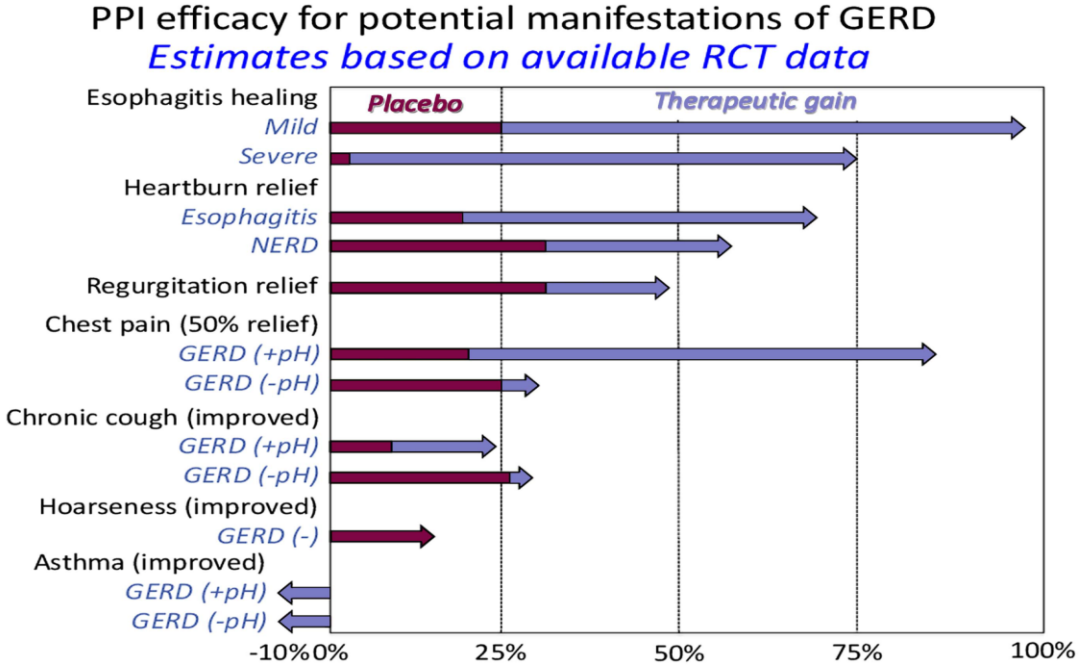
ESO40, esomeprazole 40 mg; LAN30, lansoprazole 30 mg; OME20, omeprazole 20 mg; OME40, omeprazole 40 mg; PAN40, pantoprazole 40 mg; n/a, data not available.

60%

>80%

Edwards SJ et al. Aliment Pharmacol Ther 30, 547–556

Efficacy of PPI in Atypical GERD



Terapia di Mantenimento

10. For patients with GERD who require maintenance therapy with PPIs, the PPIs should be administered in the lowest dose that effectively controls GERD symptoms and maintains healing of reflux esophagitis (conditional recommendation, low level of evidence).
11. We recommend against routine addition of medical therapies in PPI nonresponders (conditional recommendation, moderate level of evidence).
12. We recommend maintenance PPI therapy indefinitely or antireflux surgery for patients with LA grade C or D esophagitis (strong recommendation, moderate level of evidence).

Am J Gastroenterol 2022;117:27–56.

Con il patrocinio di
GASTRO ENTEROLOGIA
PROGRESSI E NUOVE FRONTIERE IN
GASTROENTEROLOGIA ED ENDOSCOPIA DIGESTIVA
BELLUNO
15-16 GIUGNO 2023

MRGE refrattaria?

Table 4. Possible Causes of Refractory Gastroesophageal Reflux Symptoms

Non-GERD
Functional heartburn
Functional dyspepsia
Esophageal motility disorder (eg, achalasia)
Eosinophilic esophagitis
Insufficient acid suppression
Lack of compliance
Improper dosing time
Reduced bioavailability of PPIs
Hypersecretory state (eg, Zollinger-Ellison syndrome)
Weakly acidic or non-acidic reflux
Concomitant functional disorder or psychological comorbidity
Delayed gastric emptying
Reflux hypersensitivity

Con il patrocinio di
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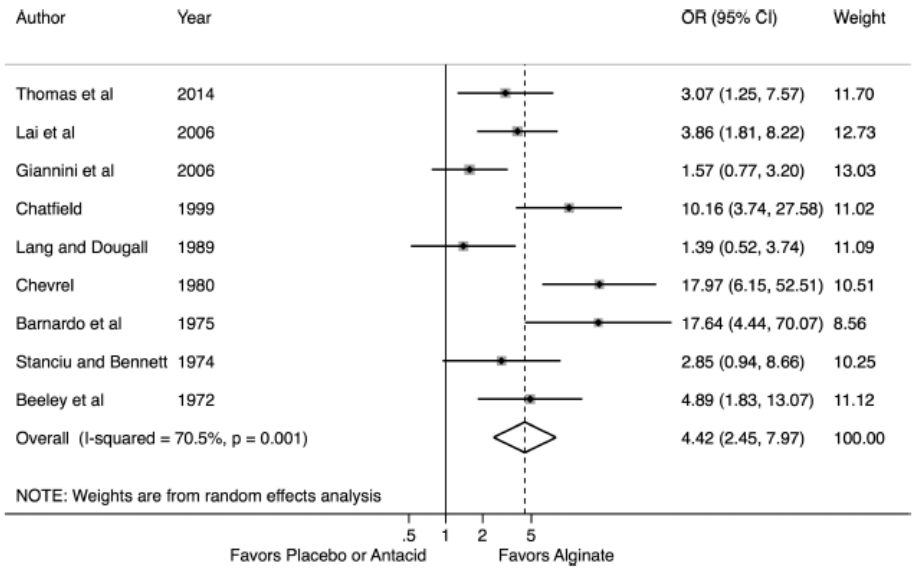
GERD: alternative approaches

- Anti H2 (nocturnal breakthrough or PPI allergy)
- Alginate
- Hyaluronic acid
- Vonoprazan (potassium-competitive acid blockers, P-CABs)
- Baclofen (GABA agonist)
- Prokinetics (mosapride?)
- Antidepressant (amitriptiline)
- Surgery

GERD: alginate



Dis Es 2017

GERD: hyaluronic acid

AP&T Alimentary Pharmacology and Therapeutics

Randomised clinical trial: mucosal protection combined with acid suppression in the treatment of non-erosive reflux disease – efficacy of Esoxx, a hyaluronic acid–chondroitin sulphate based bioadhesive formulation

V. Savarino*, F. Pace† & C. Scarpignato‡ for the Esoxx Study Group†

Conclusion
The synergistic effect of Essox with PPI treatment suggests that mucosal protection added to acid suppression could improve symptoms and HRQL in NERD patients.

Aliment Pharmacol Ther 2017; **45**: 631-642

GERD: surgery

Pauwels A, et al Gut 2019

ORIGINAL ARTICLE

How to select patients for antireflux surgery? The ICARUS guidelines (international consensus regarding preoperative examinations and clinical characteristics assessment to select adult patients for antireflux surgery)

Recommendations	Based on statement(s)
Antireflux surgery can be considered for patients with typical symptoms of heartburn, with a good response to proton pump inhibitors (PPIs).	1
Patients with functional heartburn and patients with eosinophilic oesophagitis are poor candidates for antireflux surgery.	4, 6
Patients with morbid obesity and patients with substance abuse are not excluded from antireflux surgery.	9, 11
Endoscopy (during the last year) is mandatory prior to referral for antireflux surgery. There is no need to wean the patient off PPI for endoscopy.	13, 14
Patients with GORD symptoms and a hiatal hernia, Barrett's oesophagus or erosive oesophagitis grade B or higher at endoscopy are good candidates for antireflux surgery.	15, 16b, 18
Patients without erosive oesophagitis are not excluded from antireflux surgery.	17
There is no need to obtain routine biopsies of the distal oesophagus in patients considered for antireflux surgery.	19
A barium X-ray should be obtained in patients with suspicion of a hiatal hernia or short oesophagus when considered for antireflux surgery.	20
Patients with GORD symptoms and a hiatal hernia on X-ray are good candidates for antireflux surgery.	21, 22
Patients with GORD symptoms and a para-oesophageal hernia on X-ray are good candidates for antireflux surgery in addition to para-oesophageal hernia repair.	23
A short oesophagus on barium X-ray does not exclude the patient from antireflux surgery.	24
Oesophageal manometry and oesophageal pH monitoring (±impedance) are mandatory prior to referral for antireflux surgery. The latter is preferentially done off PPI and in patients with NERD.	25, 30, 31
Patients with normal pH-monitoring off PPI are poor candidates for antireflux surgery.	32
Response to baclofen does not enhance patient eligibility for antireflux surgery.	35
There is no need to assess gastric emptying rate in patients considered for antireflux surgery.	36, 37

TAKE HOME MESSAGE

- Fisiopatologia complessa e multifattoriale della MRGE

- PPI test debole nei sintomi «atipici»

- Ph-impedenzometria 24 h attuale gold standard

- La laringite posteriore non è sinonimo di reflusso sovra-esofageo (o laringo-faringeo)

- PPI cardine di una terapia comunque sintomatica

- Intervento chirurgico in casi selezionati e ben studiati

- Necessari futuri farmaci che possano modificare la storia naturale della malattia