IL MANAGEMENT DEL PAZIENTE REFRATTARIO ALLA TERAPIA MEDICA

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GASTRO-OESOPHAGEAL REFLUX DISEASE
WHY DO PPIs FAIL?

- **Symptoms still due to acid reflux**
- **Regurgitation as the dominant symptom**
- **Symptoms associated with non acid (weakly acidic) reflux**
- **Symptoms not due to gastro-oesophageal reflux**
  (*atypical heartburn, many symptoms, depression, anxiety!!!*)

SYMPTOMS STILL DUE TO ACID REFLUX

- **Check compliance and adequacy of prescription!!**
- **Increase the dose**

  hypersensitivity to acid
  PPI resistance

- **Switch to another PPI (lanso 30 → esome 40,** *Fass 2006* **)**
- **Address night-time symptoms (the NAB issue)**

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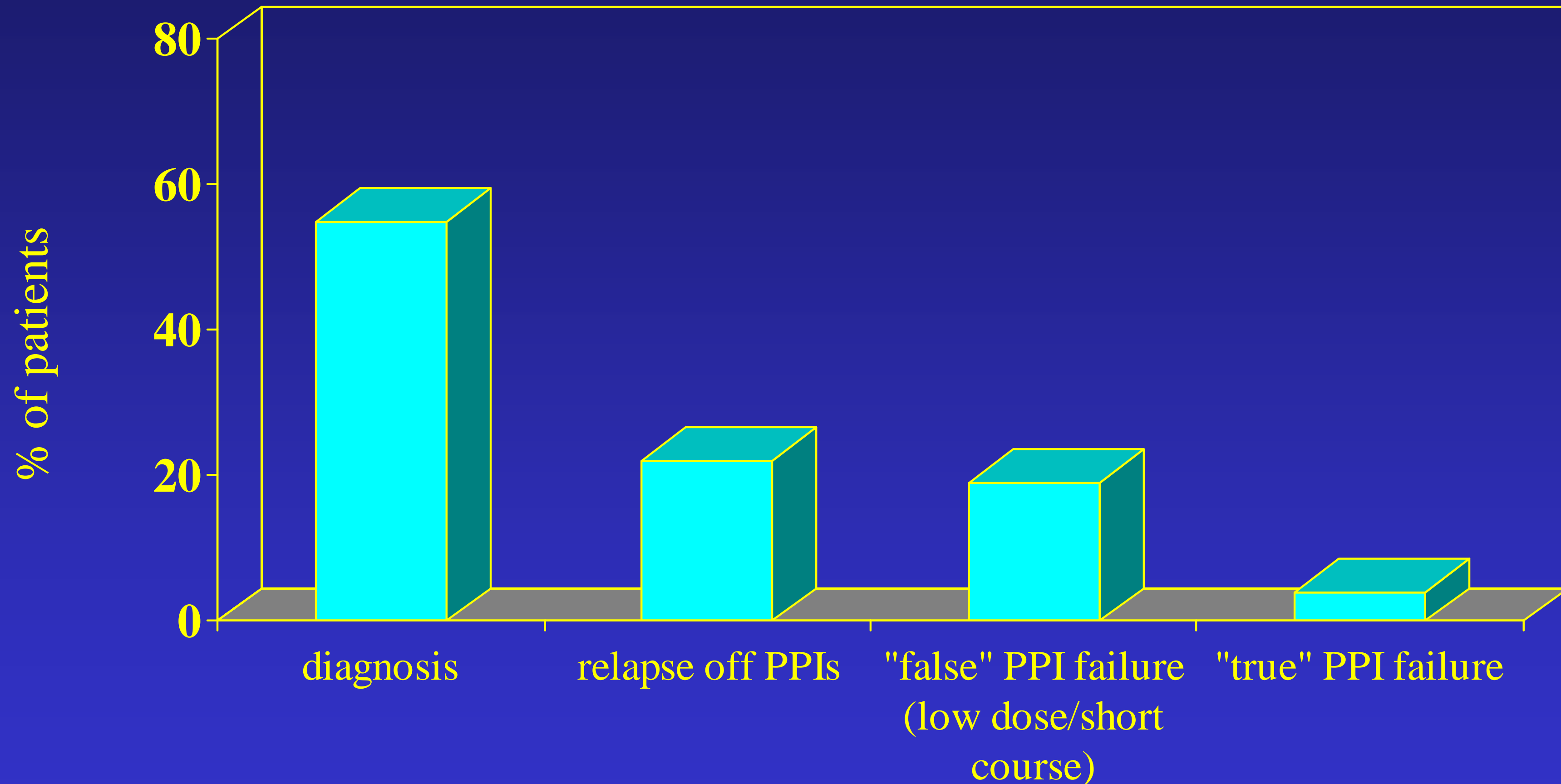
REASONS FOR REFERRAL OF PTS WITH GOR SYMPTOMS IN THE OUTPATIENTS CLINIC

Cantù et al, 2004



GP: inadequate prescription!
Patient: low compliance/ poor understanding of GORD!

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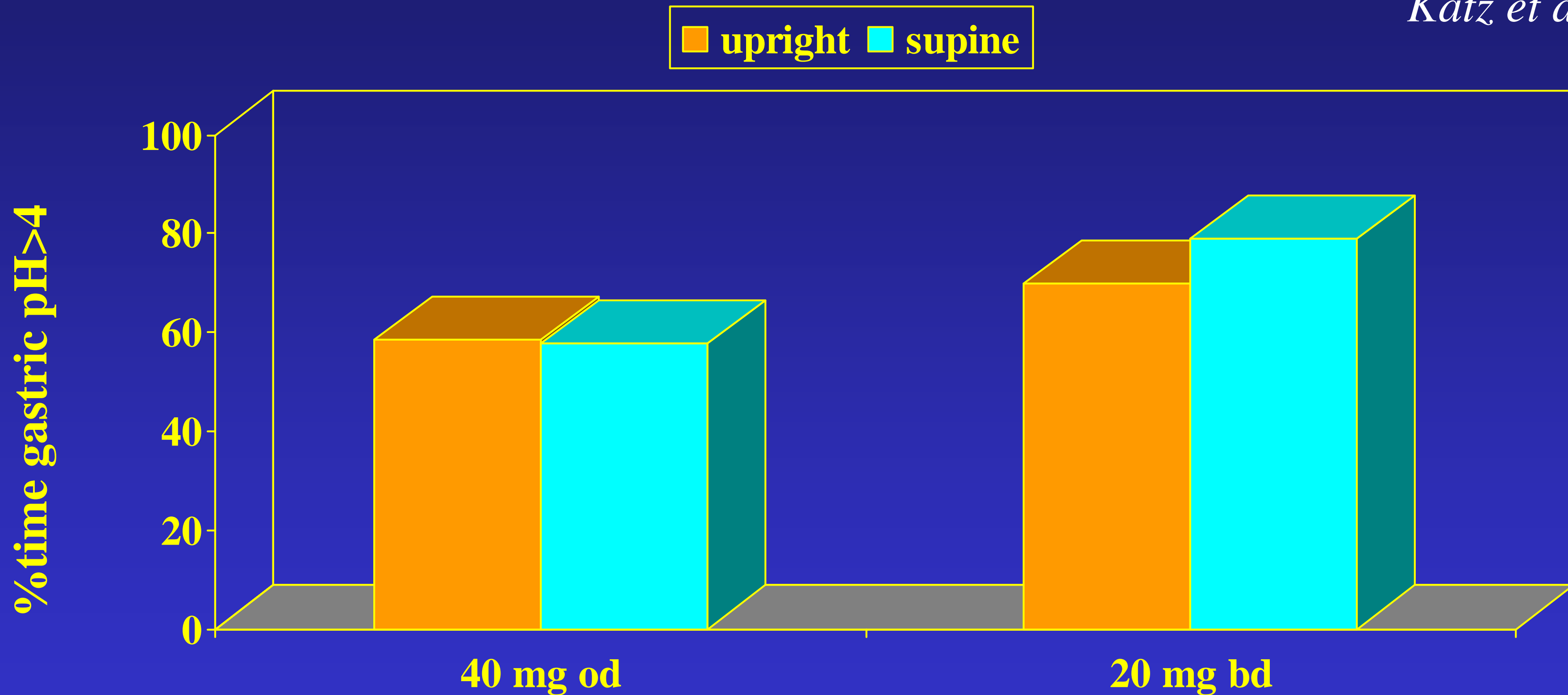
Life style changes!

SPLITTING ESOMEPRAZOLE DOSE IMPROVES NOCTURNAL ACID SUPPRESSION

Katz et al, 2004

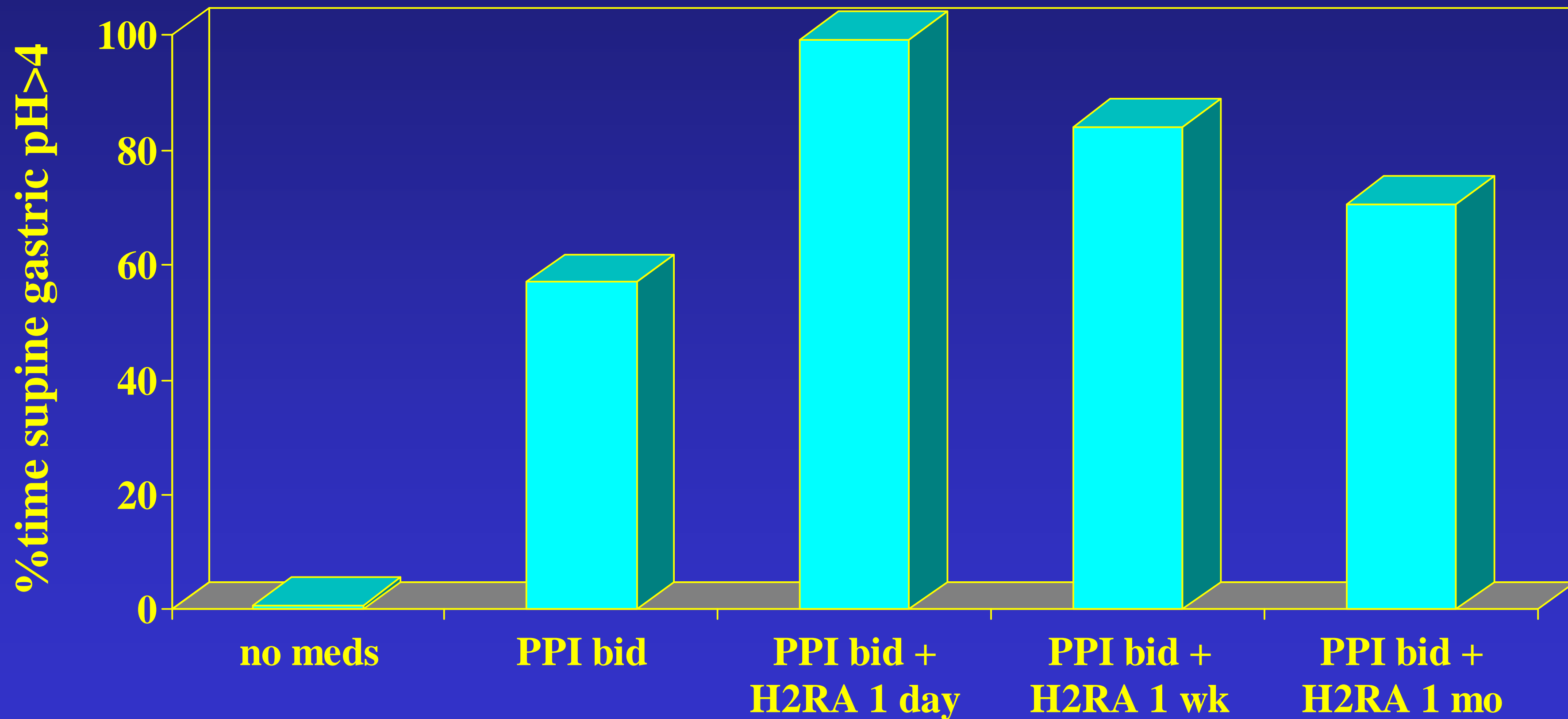


Better control of nocturnal reflux with evening vs morning rabeprazole 20 mg in pts with nocturnal symptoms *Pehlivanov et al, 2003*

RANITIDINE 300 mg AT BEDTIME ON NOCTURNAL INTRAGASTRIC ACIDITY IN GORD PTS

* $p<0.001$ vs all other regimens

Fackler et al, 2002



Occasional use of H_2 RA at bedtime!

NIGHT-TIME SYMTOMS
other options

- **Fundoplication**
- **Anti TLOSR therapy (evening baclofen 10 mg)**

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REGURGITATION AS THE DOMINANT SYMPTOM

Fundoplication

? Future: endoscopic therapy (+PPI)

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Is pH + impedance monitoring useful to identify pts sensitive to weakly acidic reflux who will benefit from fundoplication?

PAIN MODULATORS

- **Controlled trials in NCCP patients:**

Trazodone *(Clouse et al, 1987)* **100-150 mg/die**

Imipramina *(Cannon et al, 1994)* **50 mg a sera**
(inizio con 10 mg)

Sertralina *(Varia et al, 2000)* **50-200 mg/die**

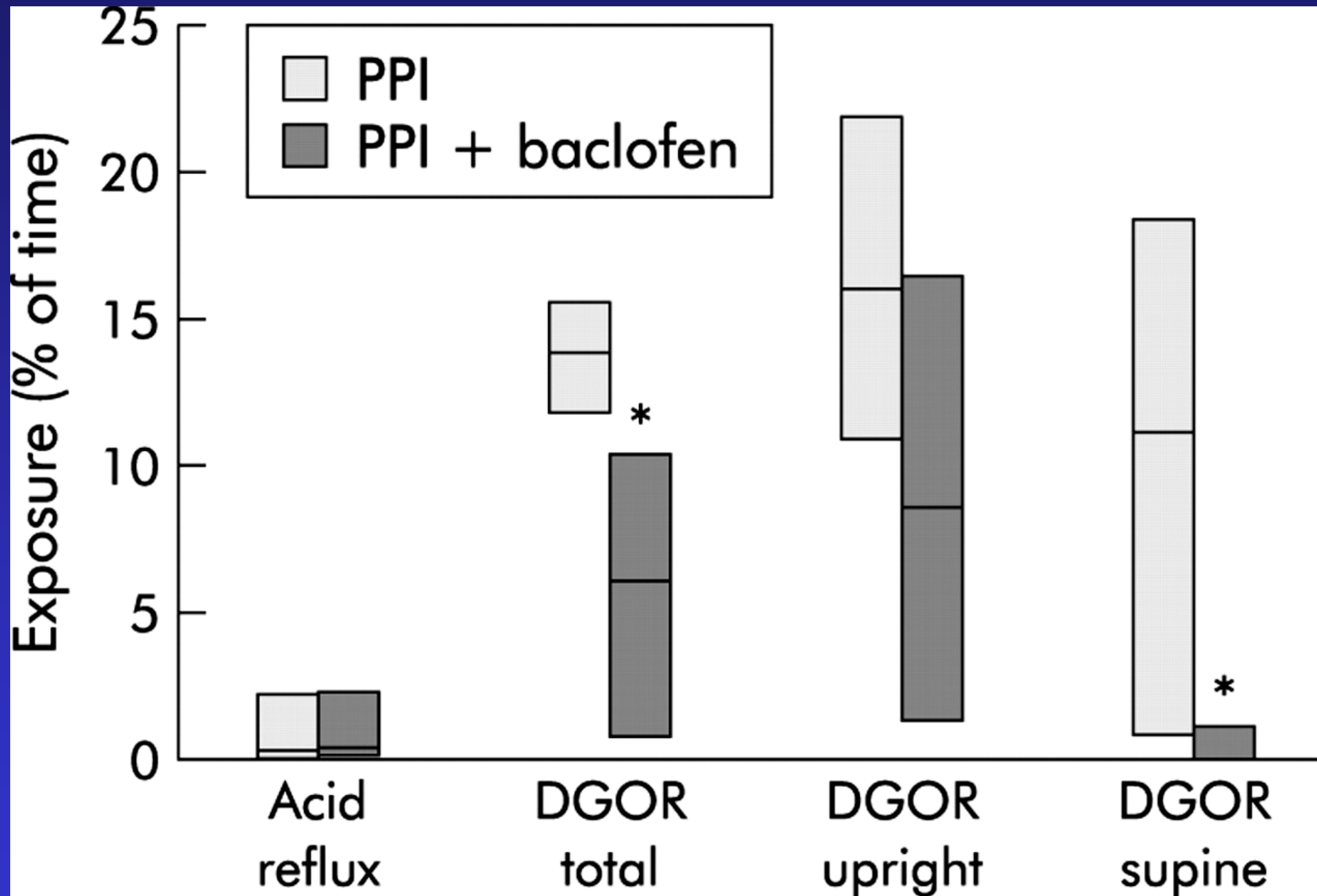
(promising data with citalopram ***Broekaert et al, 2006*****)**

Response to imipramine in 2-3 weeks

SSRIs if important mood disorder; >1 month to achieve a response

ANTI-TLOSR THERAPY

Koek et al., 2003



Heartburn severity score (1-3) from 1.6 (PPI) to 0.8 (PPI+baclofen), $p<0.05$

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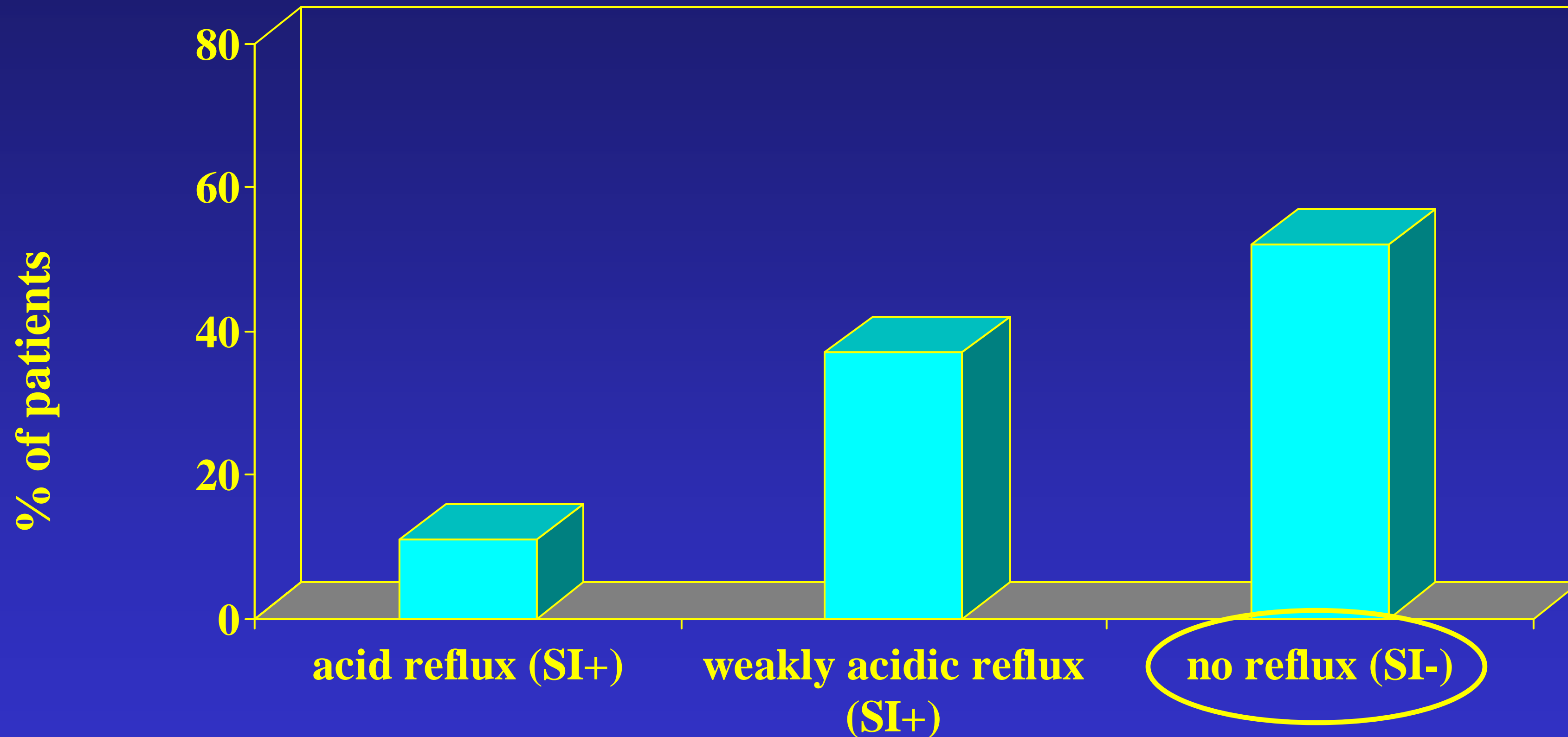
24h pH+IMPEDANCE IN 144 PTS REFRACTORY TO PPIs BD

Mainie et al, 2006



Symptomatic weakly ac. reflux in 17% and no reflux in 63% of 60 refractory pts on PPIs *by SAP analysis*

Zerbib et al, 2006

HOW TO APPROACH PATIENTS "REFRACTORY TO PPIs" IN CLINICAL PRACTICE?

Review the patient's history *(generally endoscopy done)*

a) if GER is likely to be the cause of symptoms:

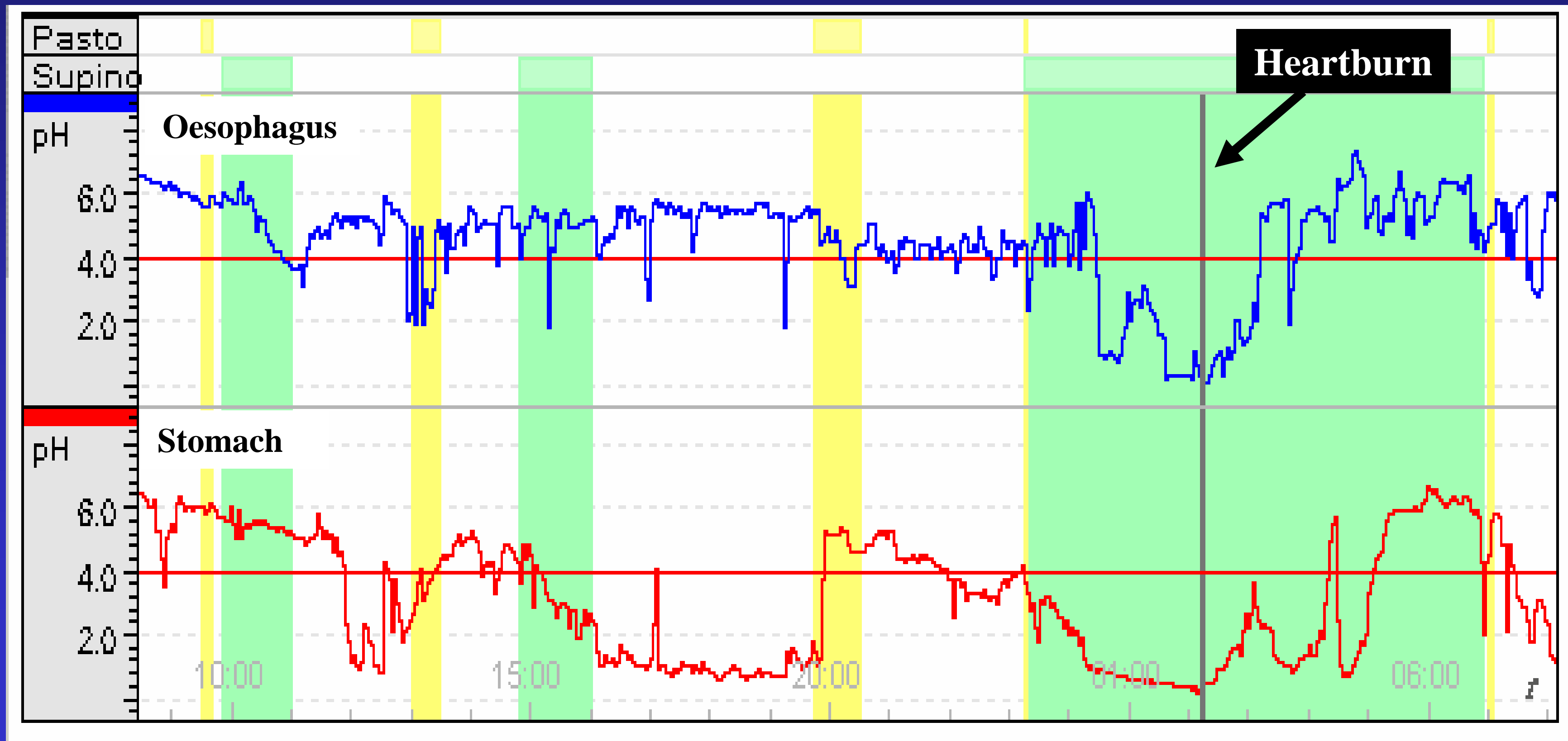
1) check compliance and /or modify PPI administration

2) if the pt is still unsatisfied: oesophageal and gastric pH monitoring (or oesophageal pH + impedance) generally on double dose PPIs with symptom-reflux association analysis

15-20% of patients will not have symptoms during the 24h test!!

Mainie et al, 2006; Zerbib et al, 2006

OESOPHAGEAL AND GASTRIC pH MONITORING ON PPIs (patient with unsatisfactory control of symptoms)



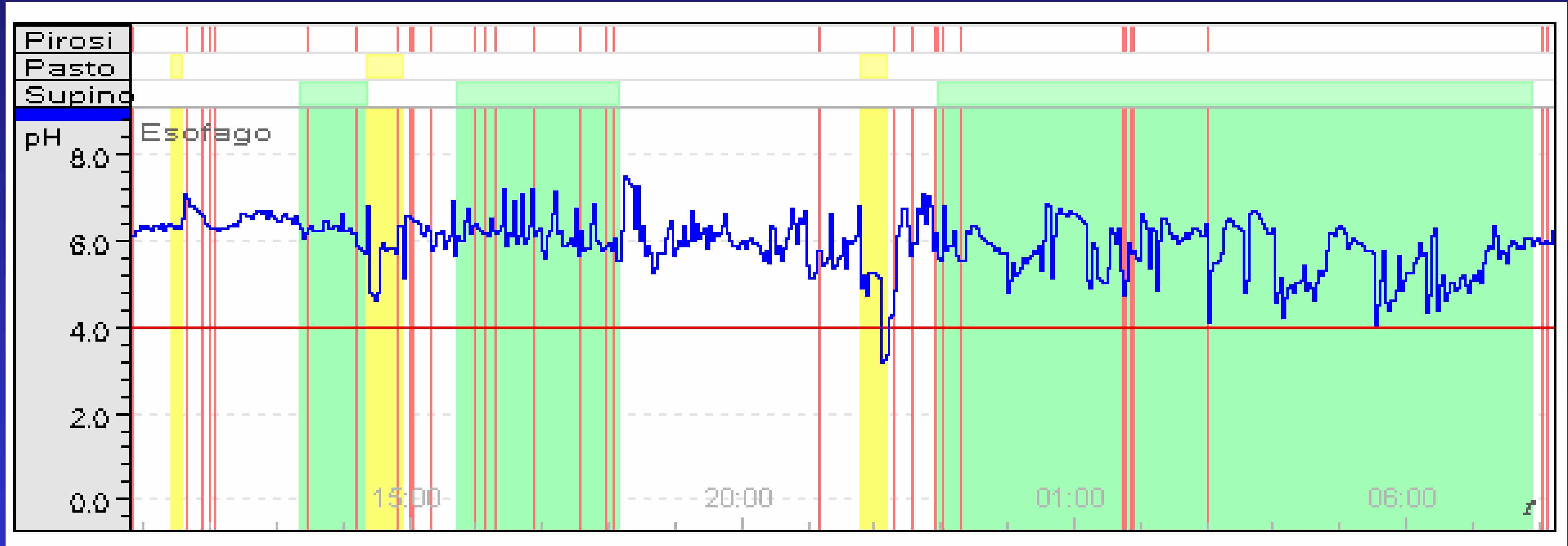
HOW TO APPROACH PATIENTS "REFRACTORY TO PPIs" IN CLINICAL PRACTICE?

b) If it is uncertain that GER is the cause of symptoms (and dose/duration of PPI treatment has been adequate)

c) If we want to refer a patient with regurgitation to the surgeon:

oesophageal pH (+ impedance ?) monitoring off PPIs in order to exclude/confirm GERD; 48-96h wireless pH monitoring if symptom is unfrequent

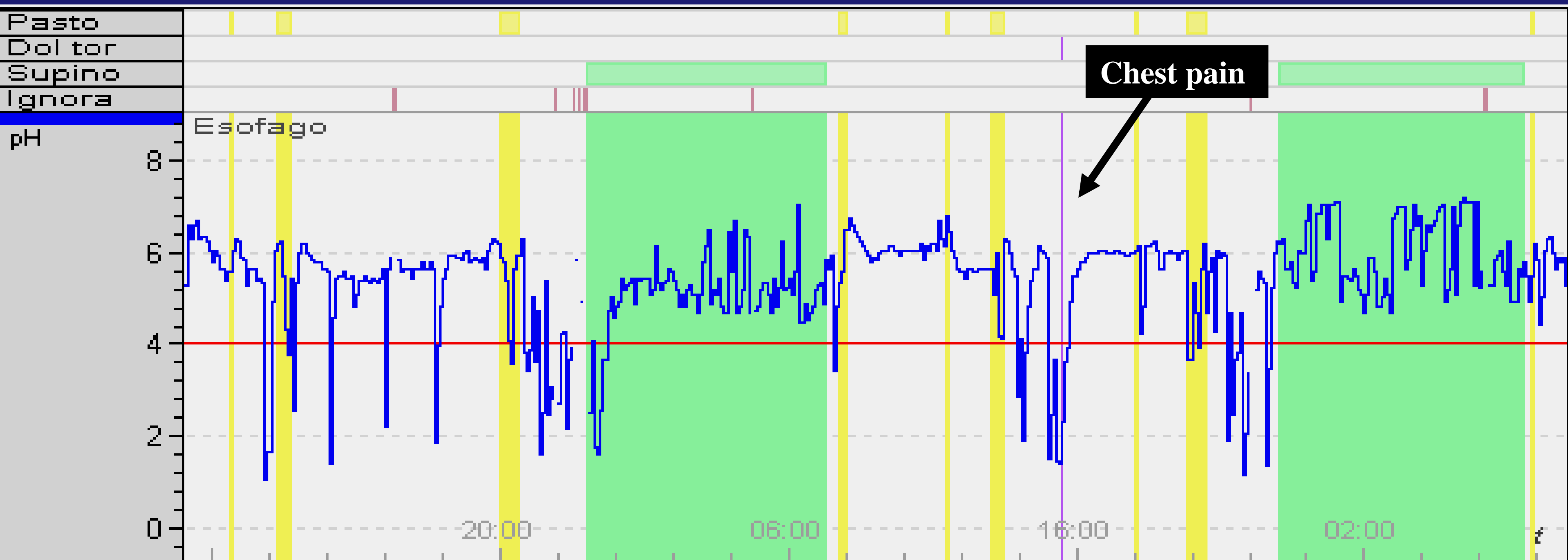
OESOPHAGEAL pH MONITORING OFF PPIs
(young patient with atypical heartburn not responsive to PPIs)



Normal oesophageal acid exposure

Heartburn *(red vertical lines)* not related to acid reflux

48 h WIRELESS OESOPHAGEAL pH MONITORING OFF PPIs (pt with IHD on cardio treatment with residual chest pain)



pH<4(%)	total	upright	supine
Day 1	5.1	6.1	3.4
Day 2	3.7	5.7	0.0

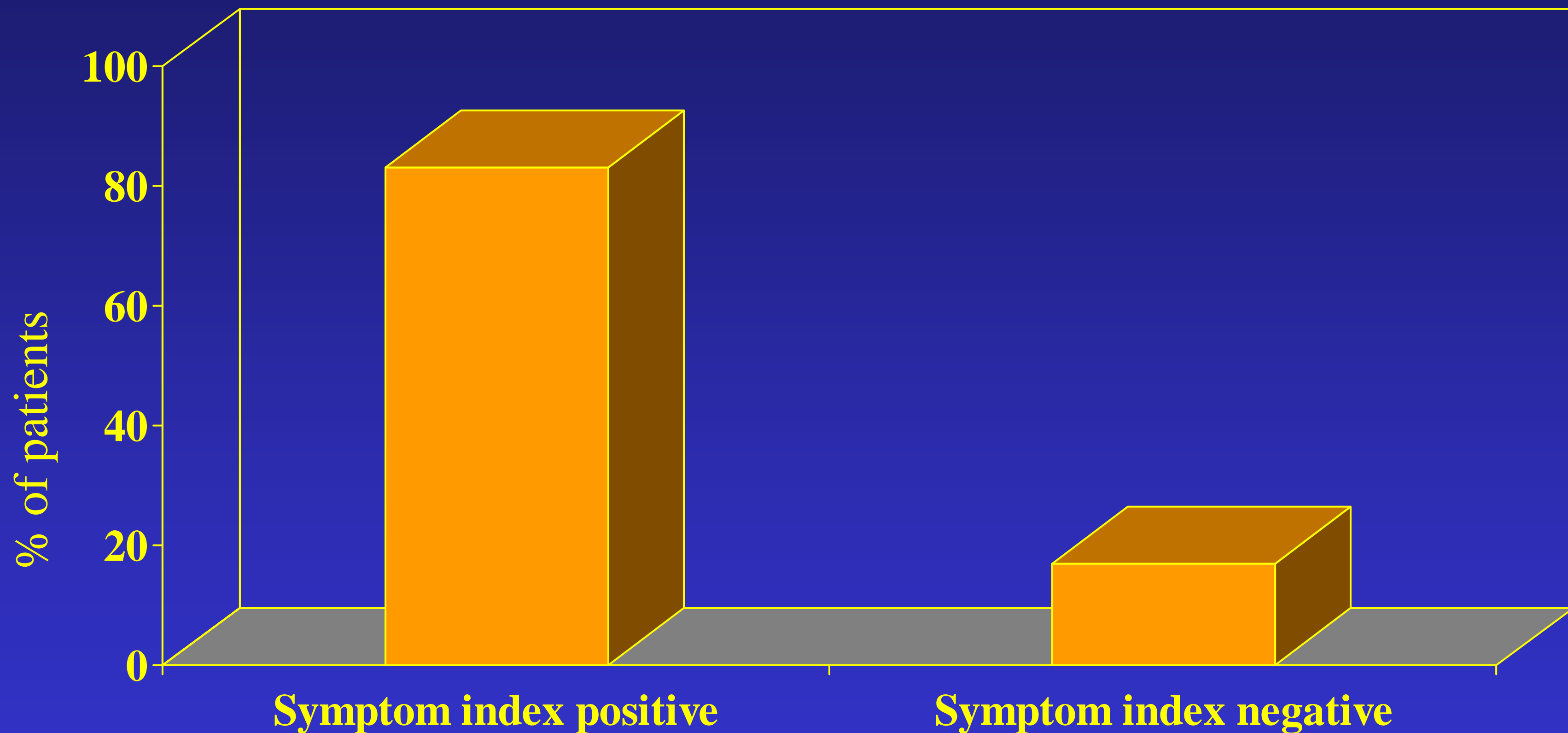
SIRO PENAGINI 1885-1952

HYPERSENSITIVE PATIENTS

Endoscopy negative patients with heartburn and/or chest pain + normal oesophageal acid exposure and positive Symptom Index

SYMPTOM IMPROVEMENT WITH OME 20X2 VS PLACEBO

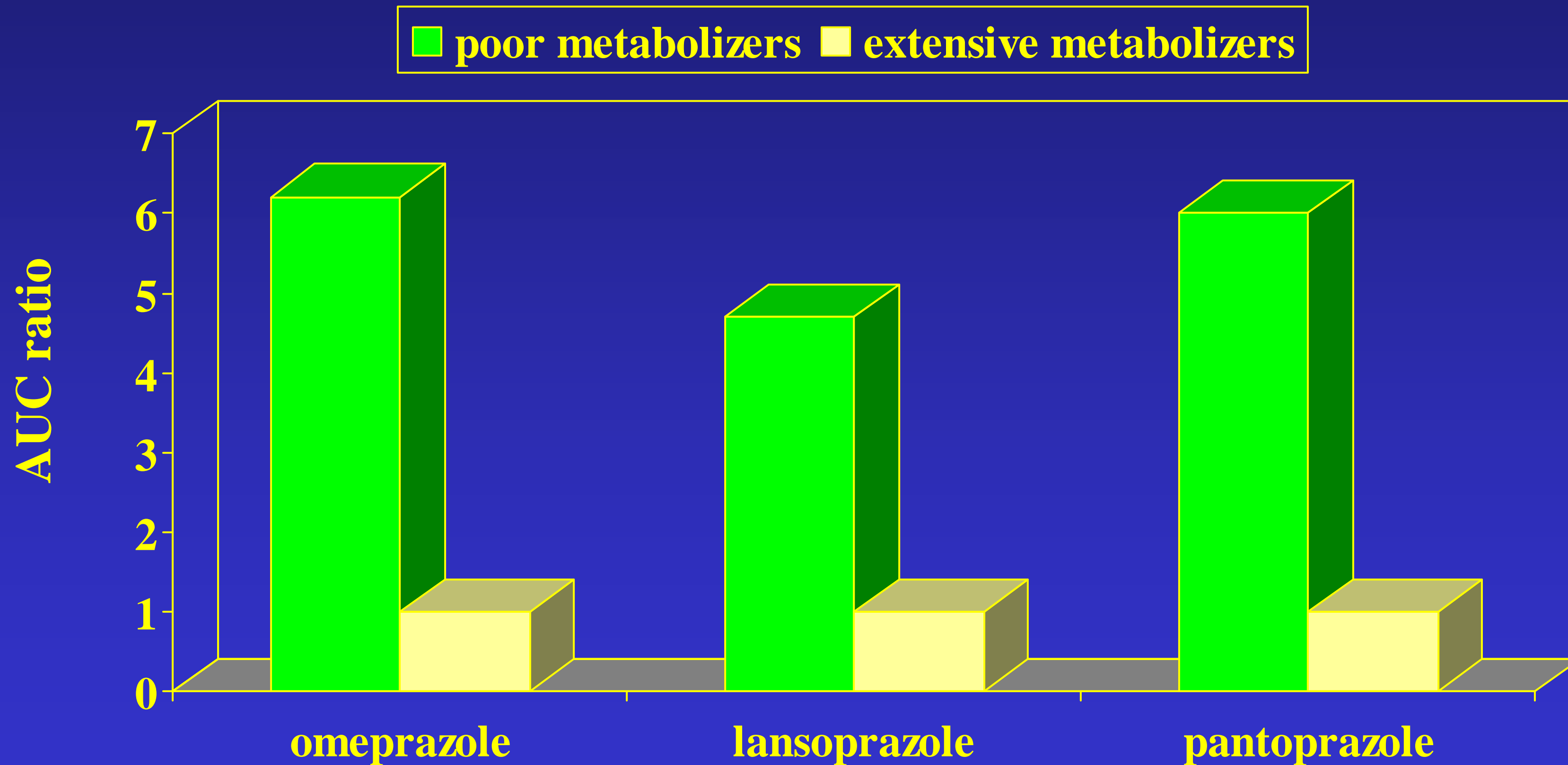
Watson et al., 1997



High dose PPIs are effective in pts. with good correlation between symptoms and acid reflux (positive Symptom Index)

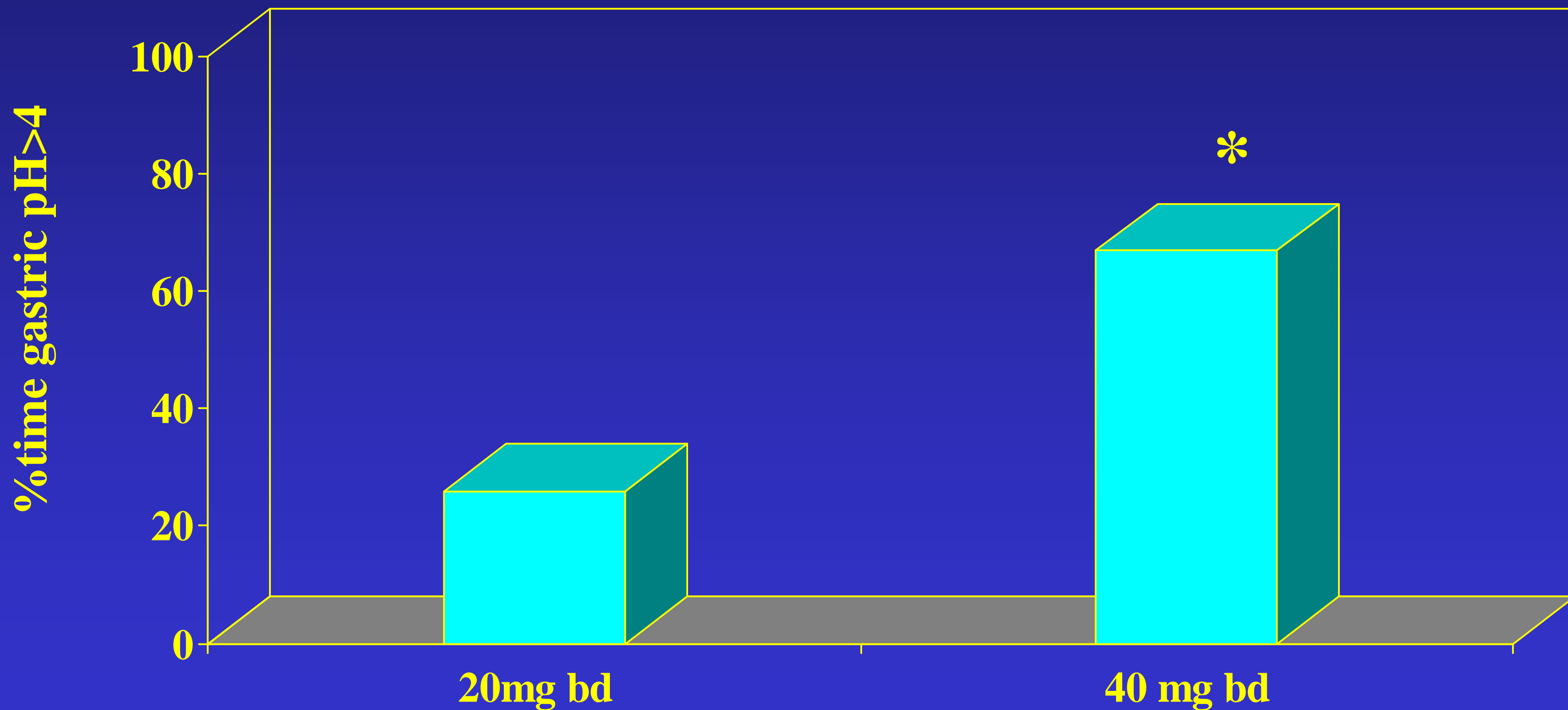
RATIO OF AUC BETWEEN POOR AND EXTENSIVE METABOLIZERS

McColl et al, 2002



INTRAGASTRIC pH>4 DURING OME 40 BD IN PTS WITH FAILURE OF OME 20 BD

* p<0.01



Leite et al, 1996