Ösophaguserkrankungen

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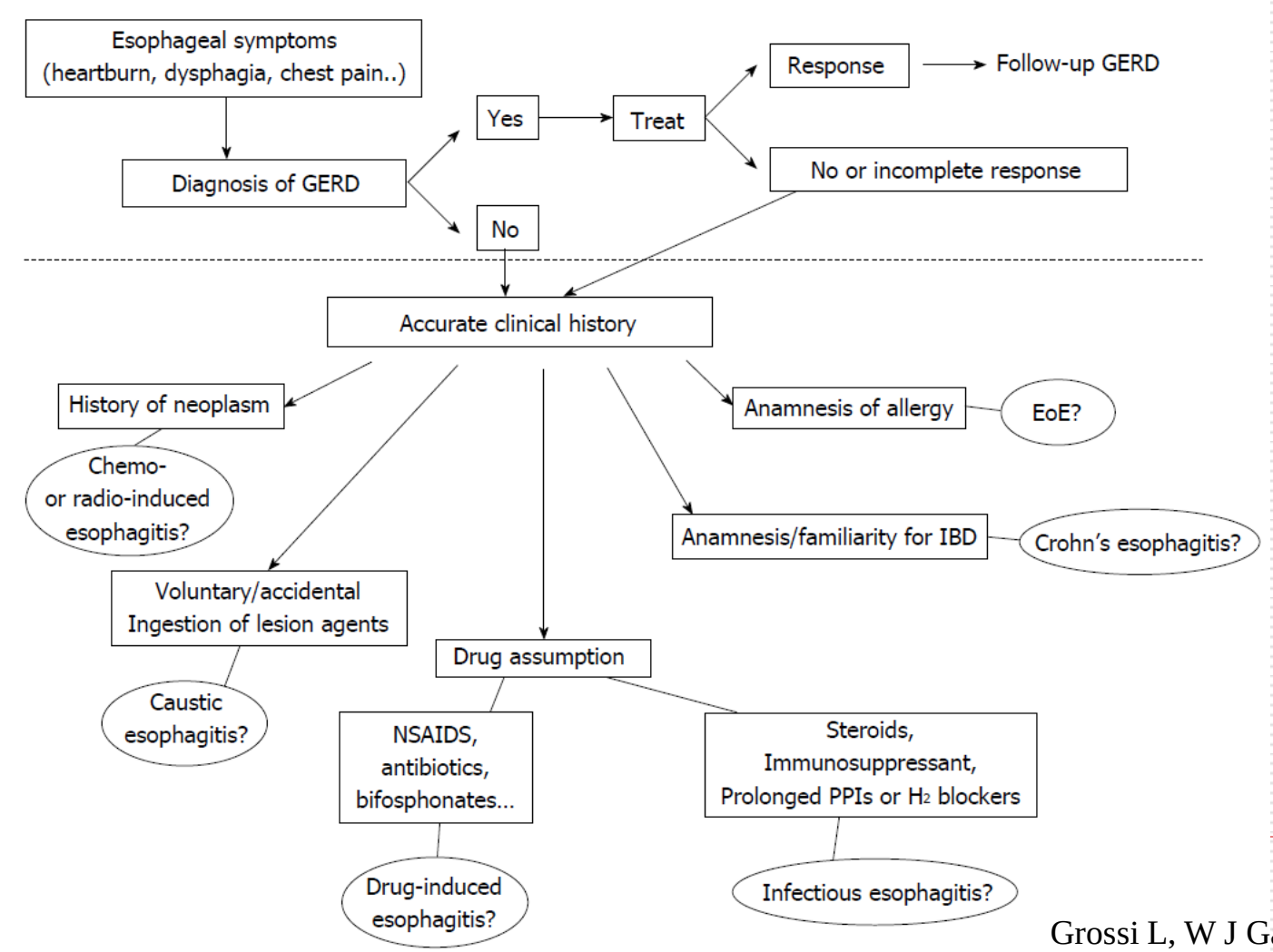
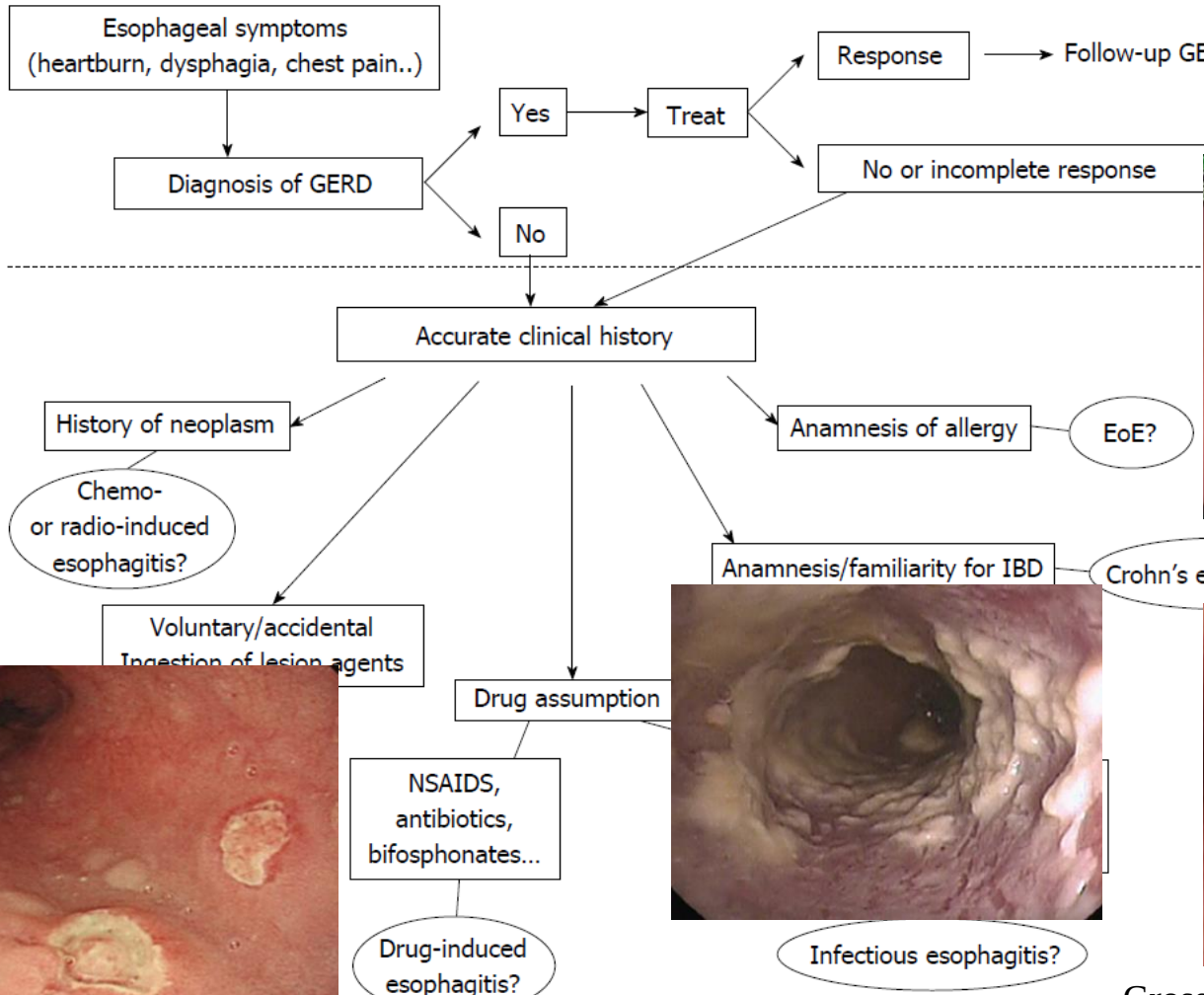
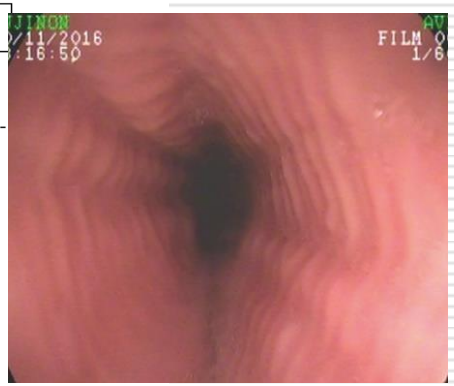
Esophagitis and its causes: Who is "guilty" when acid is found "not guilty"?

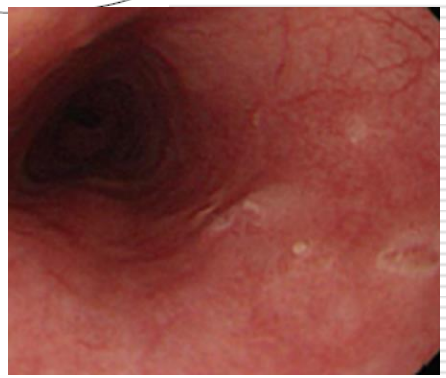


Grossi L, W J Gastroenterol 2017

Esophagitis and its causes: Who is "guilty" when acid is found "not guilty"?







Grossi L, W J Gastroenterol 2017

Eosinophilic Esophagitis Update: New Guidelines of the European Study Group EUREOS

- Chronische, fokale immun-mediierte eosinophile Inflammation
- Kinder und jüngere Erwachsene (Peak: 30 -50a), Männer 2–3fach höher
- Zweithäufigste entzündliche Erkrankung der Speiseröhre
- Häufigste Ursache für Dysphagie u. Bolusobstruktion (Kindern und Erwachsenen)
- Schwache genetische Faktoren + starke Bedeutung von Umweltfaktoren (IgE-vermittelte Lebensmittelallergien, Assoziation:Rhinitis, Asthma, Ekzem)

Miehlke S, Z Gastroenterol 2018; Lucendo AJ, United European Gastroenterol J 2017;

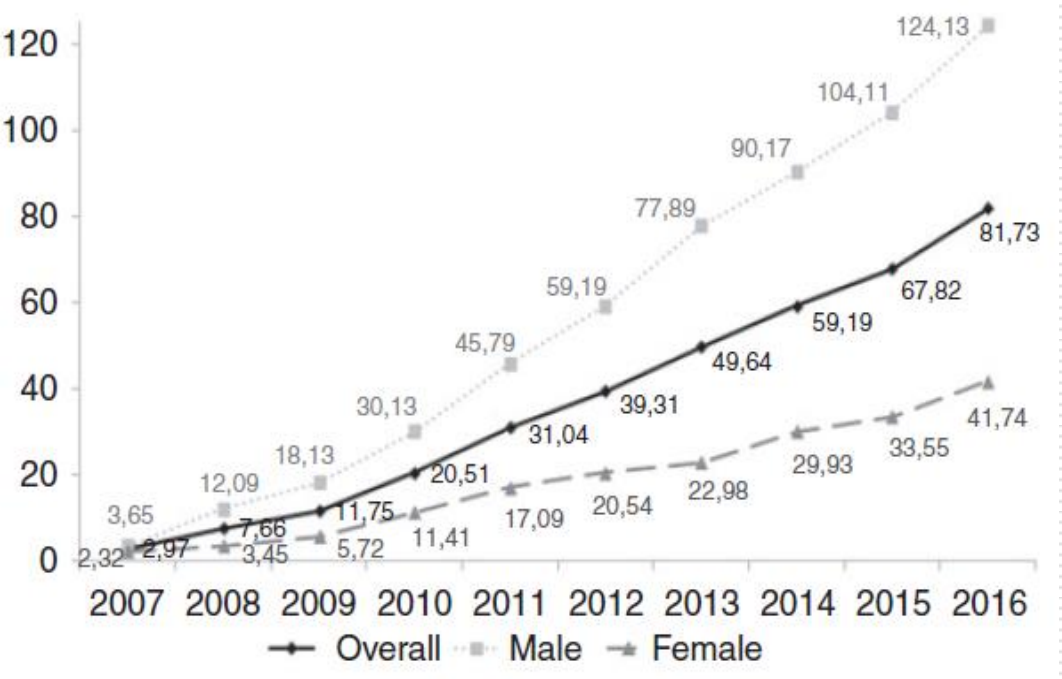
Eosinophilic Esophagitis Update: New Guidelines of the European Study Group EUREOS

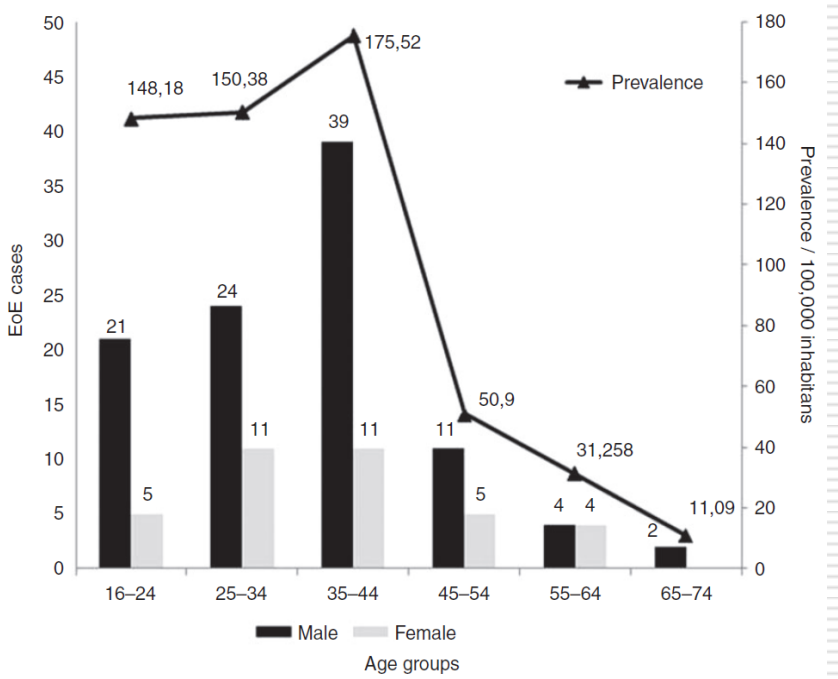
- Inzidenz in EU: 6-13/100.000EW, bei Dysphagie und Bolusobst. 23-50%
- eher progredienter Verlauf, Strikturen (fibrostenotisch), Motilitätsstörungen
- Diagnose: >15 eosinophile Granulozyten/hpf; „patchy disease“, 6 Biopsien
- Gastroskopie: 70-90% Veränderungen (ödematös, blass SH, weißliches Exsudat, Furchen, Ringe, Strikturen, EREFS-Score)
- Symptome: Erwachsene: Dysphagie + Bolusobstruktion
  Kinder: Reflux, Übelkeit/Erbrechen, Nahrungsverweigerung

Miehlke S, Z Gastroenterol 2018; Lucendo AJ, United European Gastroenterol J 2017;

Rising incidence and prevalence of adult eosinophilic esophagitis

Prevalence/100.000 inhabitans





Molina Infante J, UEG Journal 2018

Eosinophilic Esophagitis Update: New Guidelines of the European Study Group EUREOS

	EoE	PPI-responsive EoE (ehemals PPI-REE)	GERD
Alter	Kinder + Erwachsene	Kinder + Erwachsene	Erwachsene > Kinder
Geschlecht	männliche Prädominanz	männliche Prädominanz	Männer = Frauen
dominantes Symptom	Dysphagie, Bolusobstruktion	Dysphagie, Bolusobstruktion	Sodbrennen, Regurgitation
endoskopische Befunde	Normal < 10 %, Ödem, Exsudat, Furchen, Ringe, Strikturen	Normal < 10 %, Ödem, Exsudat, Furchen, Ringe, Strikturen	Normal 70 – 80 %, Erosionen, Ulzerationen, Strikturen, Barrett-ösophagus
Histologie	Eosinophile (> 15 eos/hpf), Mastzellen	Eosinophile (> 15 eos/hpf), Mastzellen	Neutrophile, Lymphozyten, wenig Eosinophile < 5 – 10 eos/hpf)
saurer Reflux pH-metrisch nachweisbar	selten	gelegentlich	meistens
Ätiologie	Nahrungsmittelallergene aerogene Allergene	unklar	saurer/nicht saurer Reflux
Immunantwort/Zytokine	Th2 Eotaxin-3, IL-5, IL-13	Th2 Eotaxin-3, IL-5, IL-13	Th1 IL-8, MCP-1, RANTES

Miehlke S, Z Gastroenterol 2018; Lucendo AJ, United European Gastroenterol J 2017;

Eosinophilic Esophagitis Update: New Guidelines of the European Study Group EUREOS

Metaanalyse zur Effektivität von Eliminationsdiäten bei EoE

Intervention	Studien (n)		histologische Remission (%)	
	Erwachsene	Kinder	Erwachsene	Kinder
Elementardiät	12	1	90	94
6-Food-Eliminationsdät	7	4	73	71
allergietestgesteuerte Eliminationsdiät	12	2	32	48

Miehlke S, Z Gastroenterol 2018

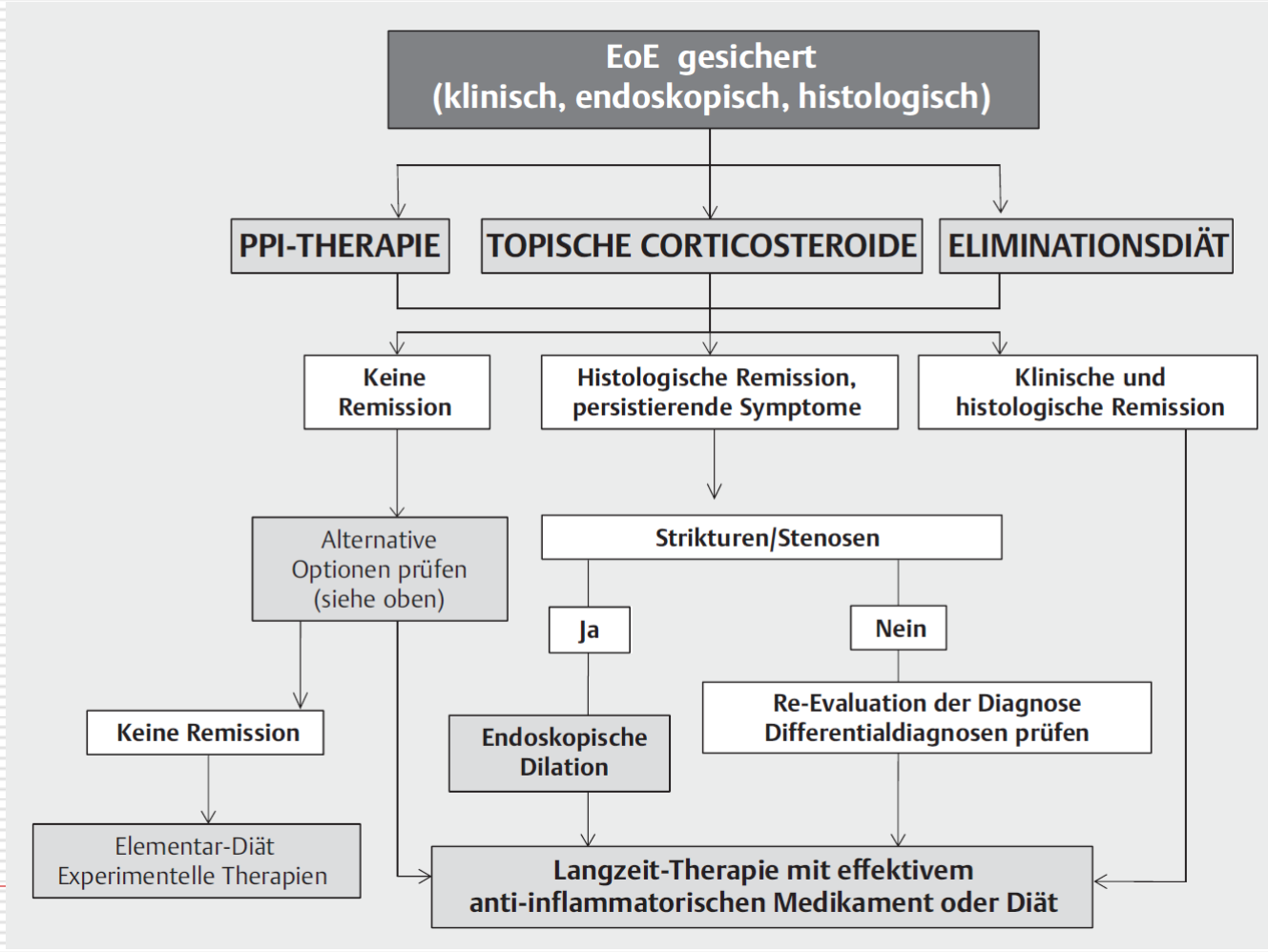
Eosinophilic Esophagitis Update: New Guidelines of the European Study Group EUREOS

Randomisierte, placebokontrollierte Studien zur Therapie der EoE mit topischen Steroiden

Autor, Jahr	Pat. (n)	mittl. Alter	topisches Steroid	Darreichung	Dosis/d	Dauer (Wochen)	histologische. Remission (%)[1]
Konikoff 2006 [83]	36	9,6	Fluticason	Spray	2 × 440 ug	12	50/9
Straumann 2010 [84]	36	36,0	Budesonid	Suspension	2 × 1 mg	2	72/11
Dohil 2010 [85]	32	7,8	Budesonid	Suspension	1 – 2 mg gewichts-adaptiert	12	87/0
Alexander 2012 [86]	42	37,5	Fluticason	Spray	2 × 880 ug	6	62/0
Butz 2014 [87]	24	12,6	Fluticason	Spray	2 × 880 ug	12	65/0
Gupta 2015 [88]	81	9,1	Budesonid	Suspension	0,35 bis 2,8 mg altersadaptiert	12	94/53/23/6
Miehlke 2016 [89]	76	39,7	Budesonid	Orodispersible Tabl. Suspension,	2 × 1 mg/2 × 2 mg	2	100/95/95/0
Dellon 2017 [90]	93	21,5	Budesonid	Suspension	2 × 2 mg	12	39/3
Lucendo 2017 [91]	88	37,0	Budesonid	Orodispersible Tabl.	2 × 1 mg	6	93/0

Miehlke S, Z Gastroenterol 2018

Eosinophilic Esophagitis Update: New Guidelines of the European Study Group EUREOS



3D`s
Drug
Diet
Dilation

Miehlke S, Z Gastroenterol 2018

Therapie der Eosinophilen Ösophagitis
Orodispersible Budesonid Tablette (2 x 1mg/d, Jorveza®)

- **Phase II Studie**: 2 Wochen, n=76; 2x1 vs 2x2 mg/d vs Placebo:
  100% vs 95% vs 0% histologische Remission

- **Phase III Studie:** 6 Wochen, n=88, 2 x 1 mg/d vs Placebo
  93% vs 0% klinisch-histologische Remission

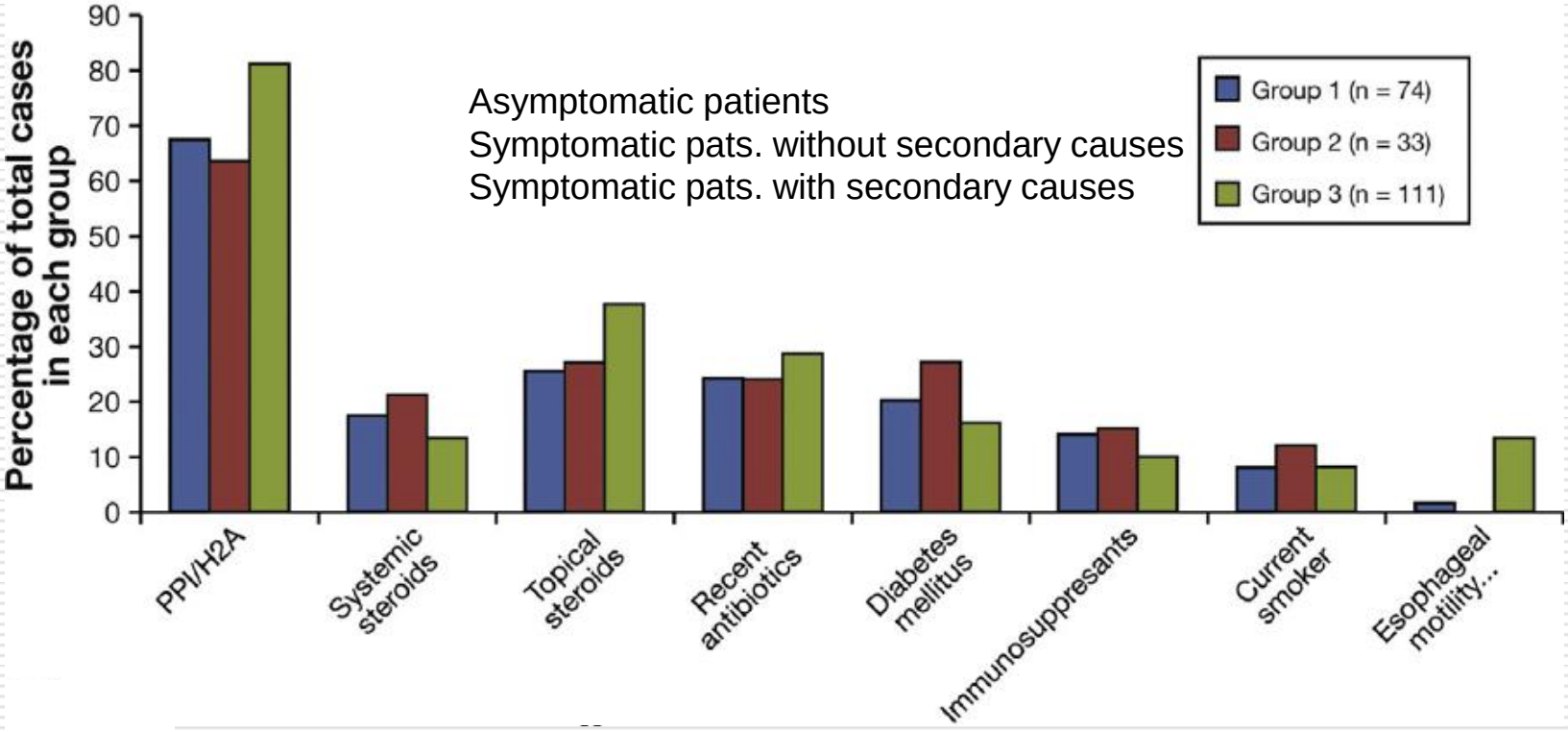
- Dzt. EU-weite RCT: einjährige Remissionserhaltende Therapie

- NW: Candida Ösophagitis 10%

Lucendo AJ, Gastroenterology 2017, 152:207, Miehlke S, Gut 2016

Course of Esophageal Candidiasis and Outcomes of Patients at a Single Center

Mayo Clinic, 2013–16, 218 immunocompetent pats. with Candida esophagitis



Hoversten P, Clin Gastroenterol Hepatol 2018

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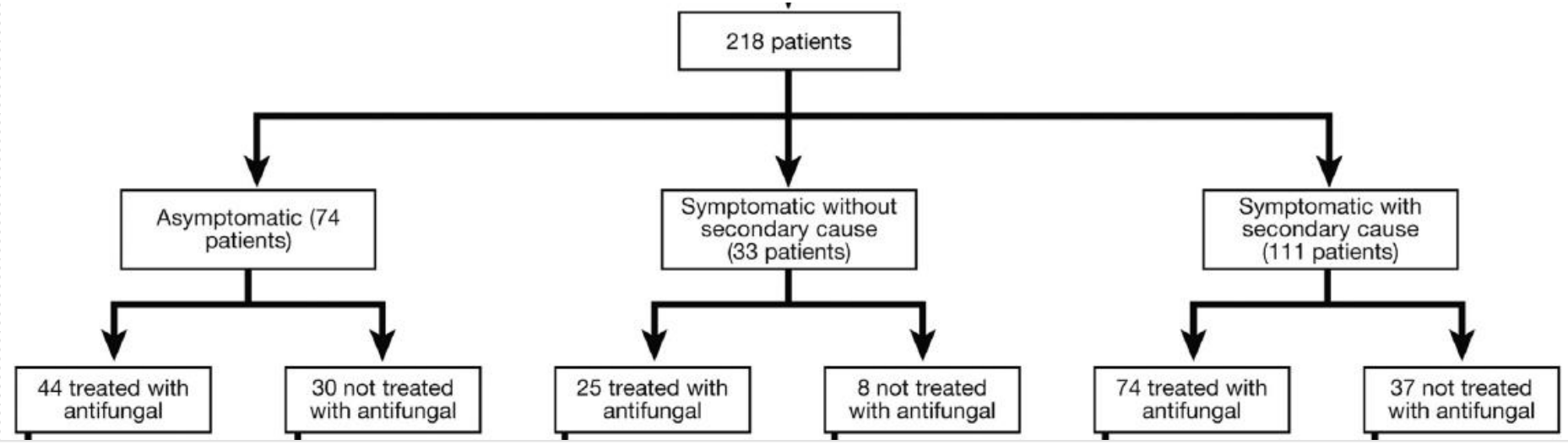


90% asymptomatic at follow-up

91% asymptomatic at follow-up

81% asymptomatic at follow-up

35% asymptomatic at follow-up

68% asymptomatic at follow-up

66% asymptomatic at follow-up

Hoversten P, Clin Gastroenterol Hepatol 2018

Barrett`s Esophagus (BE)

- Prevalence of BE in unselected general population 1-2% (EU), 5-6% (US)
- Factors associated with BE:
  - GERD symptoms
  - Older age
  - Male gender
  - Central obesity
  - Tobacco smoking
  - Caucasian race
  - Positive family history

- Premalignant condition predisposing to esophageal adencarcinoma
- Risk of cancer progression is low (about 0,3% per year)
- Incidence of adencarcinoma has increased over last 40y (5y-survival <10%)
- Endoscopic surveillance at regular intervals

Amadi C, W J Gastroenterol 2017; Jankowski J, Lancet 2018

Cancer incidence and mortality risks in a large US Barrett`s esophagus cohort

- Kaiser Permanente Northern California Cancer Registry 1995 -2012
- 8929 pats. with Barrett esophagus

- Pats. with BE: increased risks of 40% of any cancer (SIR =1,4, CI 1.31-1.49)

- Esophageal adenocarcinoma risk was increased 24 times

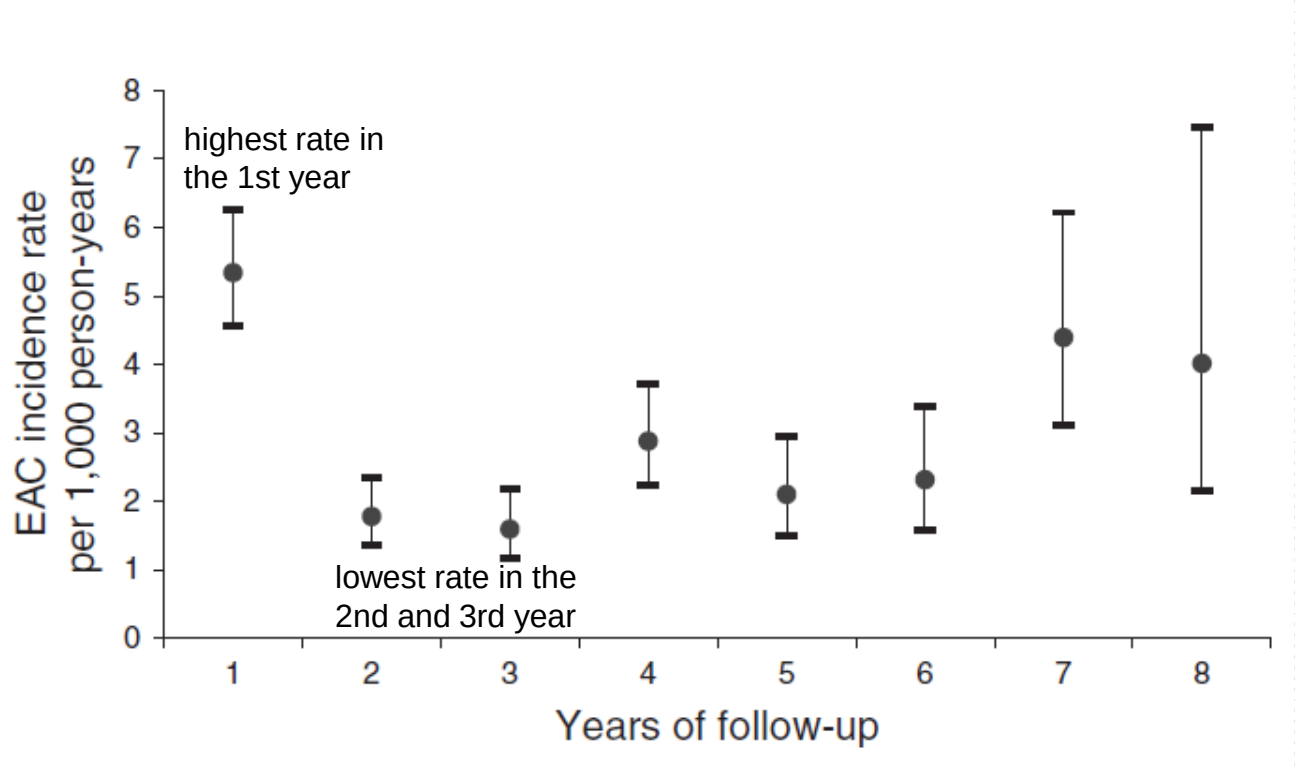
- Cause-specific standardised mortality ratios were elevated for:
  - Ischemic heart diseases by 39%
  - Respiratory system diseases by 51%
  - Digestive system diseases by 120%

Cook MB, Gut 2018

The Annual Risk of Esophageal Adenocarcinoma Does Not Decrease Over Time in Patients With Barrett's Esophagus

28.561 BE patients

significant increase in the incidence rate with increasing years of follow-up



Nguyen T, Am J Gastroenterol 2017

Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement

- Endoscopic screening for BE is not recommended
- Screnning can be considered:
  - Pats. with longstanding GERD symptoms (i.e. > 5 years)
  - and multiple risk factors
    - Age > 50years
    - White race
    - Male sex
    - Obesity
    - First-degree relative with BE or adenocarcinoma of the esophagus

Weusten B, Endoscopy 2017

Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement

Surveillance intervals for nondysplastic BE should be stratified according to the length of the Barrett`s segment

- Irregular Z-line/columnar-lined esophagus < 1cm: No surveillance
- Maximum extent of BE ≥ 1cm and < 3cm: 5 years
- Maximum extent of BE ≥ 3cm and < 10cm: 3 years
- Maximum extent ≥10cm: referred for surveillance to a BE expert center

- pats. reached 75years of age; last surveillance no evidence of dysplasia, no further surveillance endoscopies

Weusten B, Endoscopy 2017

Low Risk of High-Grade Dysplasia or Esophageal Adenocarcinoma Among Patients With Barrett's Esophagus Less Than 1 cm (Irregular Z Line) Within 5 Years of Index Endoscopy.

prospective, multicenter, cohort-study in US and Europe

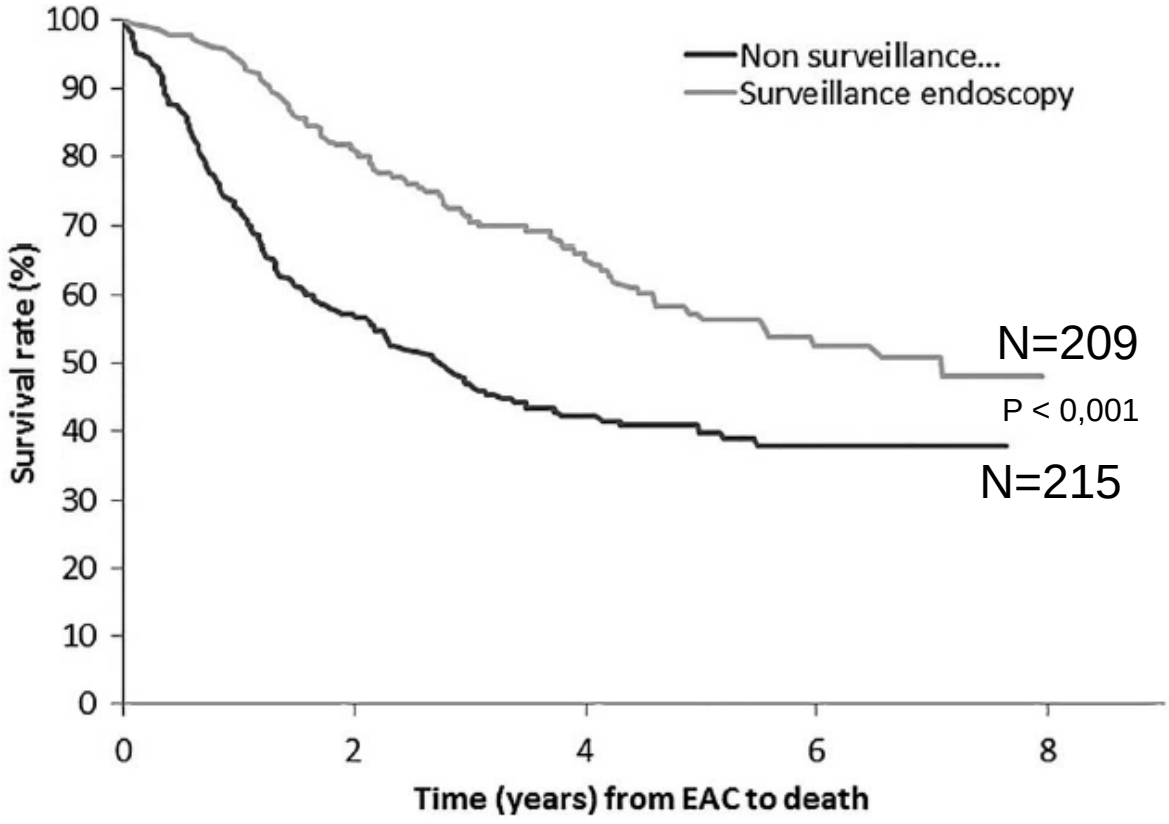
1791 pats. with Barrett , n=167 with „irregular Z-line“ < 1cm, follow-up median 6 years

Variable	Irregular Z line n = 167	BE ≥1 cm n = 1624	*P* value
Presence of hiatal hernia	37 (52.9%)	808 (72%)	<.001
Size of hiatal hernia, *cm*	3 (2, 4)	3 (2, 4)	.52
Visible lesions in BE segment	3 (1.8%)	92 (5.7%)	<.001
Any progression	0 (0.0%)	327 (20.1%)	<.001
Progression to HGD or EAC	0 (0.0%)	71 (4.4%)	.005
Follow-up in years	4.8 (2.3, 8.2)	6.0 (3.2, 8.3)	.545
Number of procedures	3.0 (2.0, 4.0)	4.0 (3.0, 5.0)	<.001

Thota PN, Gastroenterology 2017

Surveillance endoscopy is associated with improved outcomes of oesophageal adenocarcinoma detected in patients with Barrett's oesophagus

Cohort-study; 29.536 pats. with BE; 424 pats. with adenocarcinoma



Surveillance endoscopy:

Early stage: 75% vs 56%

Improved survival: 3,2a vs 2,3a

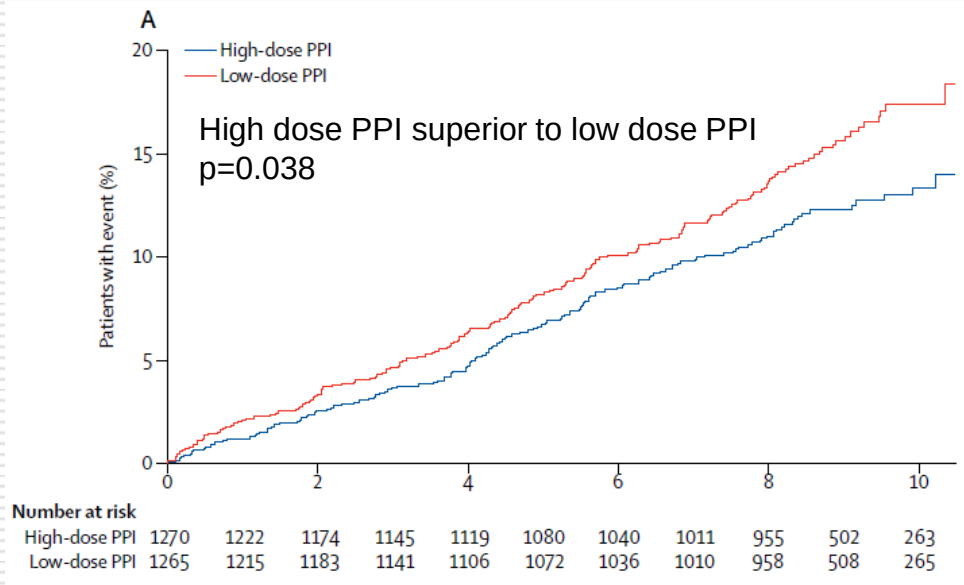
lower mortality: 34% vs 54%

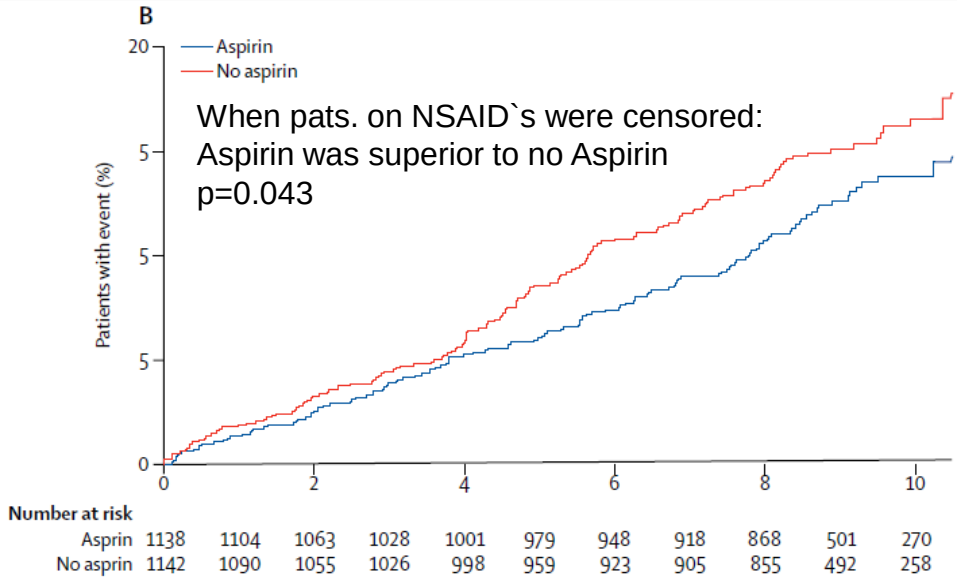
El-Serag HB, Gut 2016

Esomeprazole and aspirin in Barrett's oesophagus (AspECT): a randomised factorial trial

Chemoprevention in Barrett`s metaplasia trial; 2x2 factorial design, 85 centres in UK, Canada
BE > 1cm, high-dose PPI (40mg twice/d) ; low-dose PPI (20mg once/d); Aspirin (300/325mg); no Aspirin for at least 8y; end-point: all cause mortality, esophageal adenocarcinoma or high grade dysplasia

n=2557; median follow up 8,9years





Jankowski J, Lancet 2018

Esomeprazole and aspirin in Barrett's oesophagus (AspECT): a randomised factorial trial

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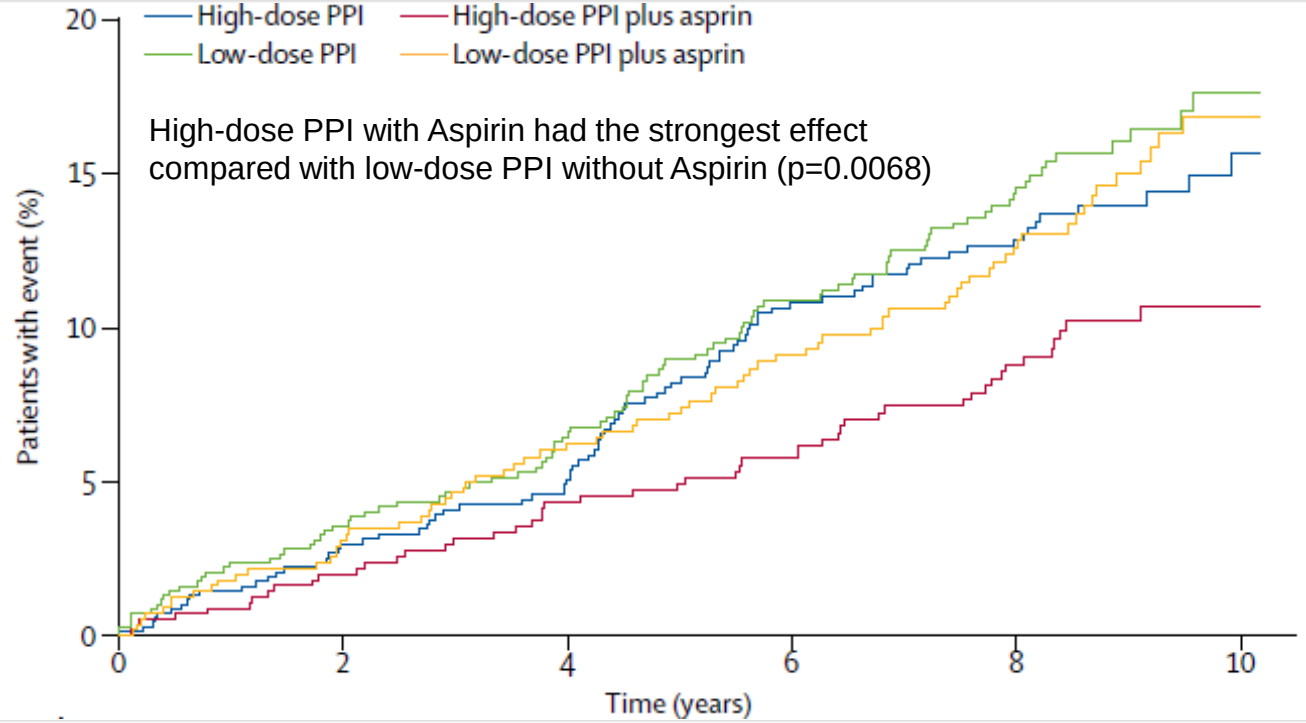


Jankowski J, Lancet 2018

Dexlansoprazole and Esomeprazole Do Not Affect Bone Homeostasis in Healthy Postmenopausal Women

PPI 40mg/d for 26 weeks

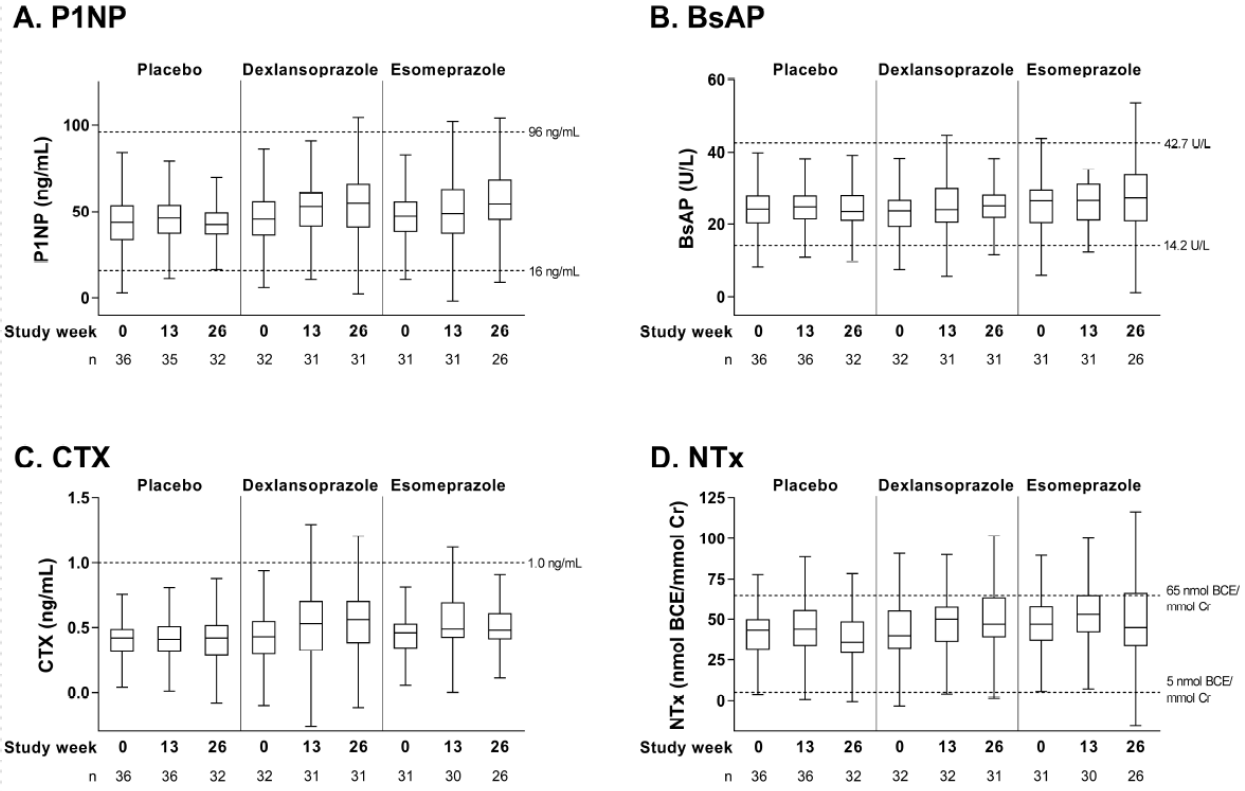


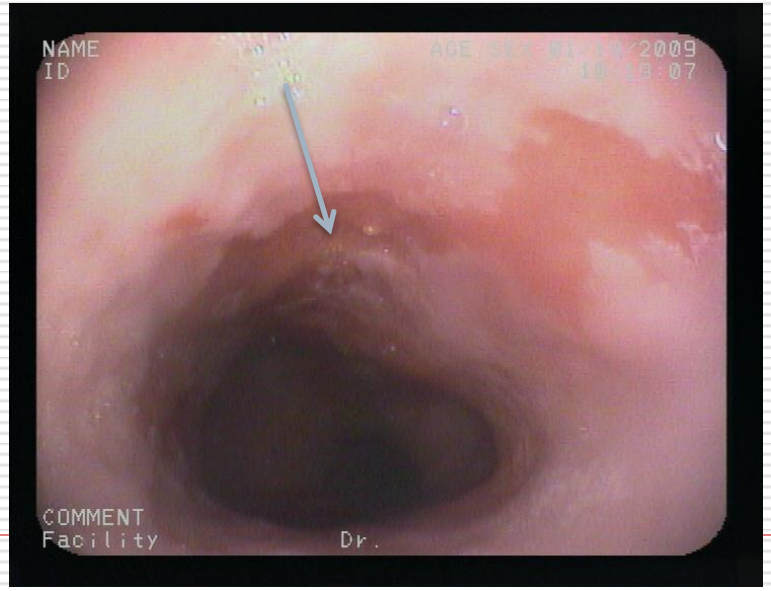
Figure 2. Bone turnover markers. BCE = bone collagen equivalent; BsAP = bone-specific alkaline phosphatase; Cr = creatinine; CTX = C-terminal telopeptide of type 1 collagen; NTx = urine cross-linked N-telopeptide of type 1 collagen; P1NP = procollagen type 1 N-terminal propeptide. Top and bottom of

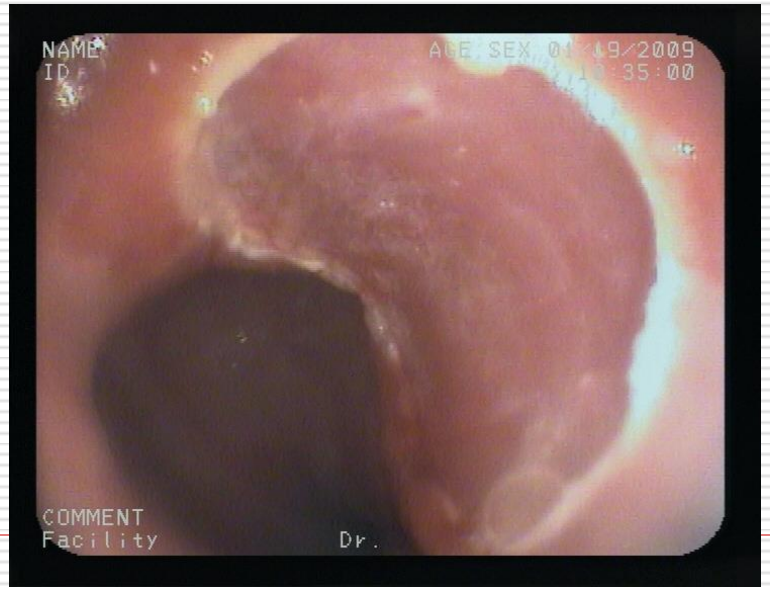
Hansen KE, Gastroenterology 2018 in press

Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement

STATEMENT 11

Patients with visible lesions in BE diagnosed as dysplasia or early cancer should be referred to a BE expert center. All visible abnormalities, regardless of the degree of dysplasia, should be removed by means of endoscopic resection techniques in order to obtain optimal histopathological staging.



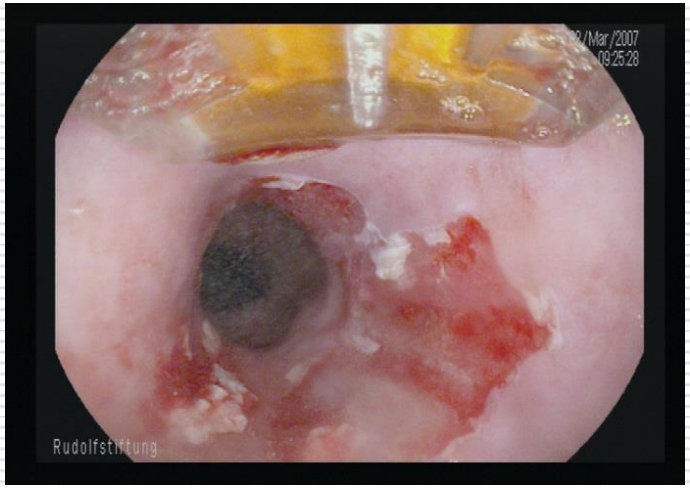


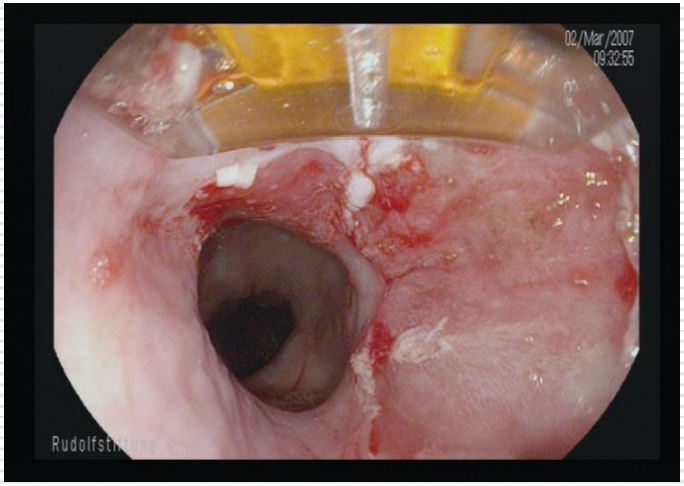
Weusten B, Endoscopy 2017

Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement

Patients with LGD on random biopsies confirmed by a second expert GI pathologist should be referred to a BE expert center. A surveillance interval of 6 months after confirmed LGD diagnosis is recommended.

ii. If a confirmed diagnosis of LGD is found in the subsequent endoscopies, endoscopic ablation should be offered.





Weusten B, Endoscopy 2017

Development of Evidence-Based Surveillance Intervals After Radiofrequency Ablation of Barrett's Esophagus

United States Radiofrequency Ablation Registry (US RFA, 2004 – 2013
United Kingdom National Halo Registry (UK NHR, 2007 – 2015)
3478 pats. – Cox proportional hazard models

Table 2. Recommended Time After Complete Eradication Intestinal Metaplasia of Surveillance Visits to Yield 2.9% Neoplastic Recurrence per Visit or 0.1% Invasive Adenocarcinoma for Patients at Average Risk of Endoscopic Complications

Risk Category	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8
Low-grade dysplasia	1 years	3 years	>5 years[a]	[a]	[a]	[a]	[a]	[a]
High-grade dysplasia or adenocarcinoma in situ	3 months	6 months	1 year	2 years	3 years	4 years	5 years	>5 years[a]

[a]Surveillance times were estimated to a limit of 5 years for the higher 2 risk categories and 7 years for the lower risk categories to avoid extrapolation beyond the data.

Cotton CC, Gastroenterology 2018

Konklusion I: Ösophaguserkrankungen

- **Nicht Reflux-assoziierte Ösophagitis:**
  - Dysphagie, Odynophagie, retrosternaler Schmerz: EoE, Infektionen (Soor), Medikamenten-induziert, M. Crohn, Verätzung
- **Eosinophile Ösophagitis**
  - Neue Europäische Guidelines
  - Steigende Prävalenz
  - Therapie: 3D`s (Drugs, Diet, Dilatation)
  - 1. zugelassene Therapie – orale Budesonid Schmelztablette (2x1mg für 6 Wo)
- **Candida Ösophagitis**
  - Risikofaktoren: PPI/H2A, Topische Steroide, Antibiotika, DM
  - Asymptomatische Patienten müssen nicht zwingend behandelt werden

Konklusion II: Ösophaguserkrankungen

- **PPI Nebenwirkungen:**
  - Dauertherapie 40mg/d für ½ Jahr: Keine negativen Auswirkungen auf Knochen-Homeostase und Knochen-Dichte bei postmenopausalen Frauen

- **Barrett-Ösophagus**
  - Prävalenz in Bevölkerung 1 – 6%, kein Routinescreening
  - Risikofaktor für Adenokarzinom (0,3%/Jahr, Risiko 24x höher)
  - Surveillance Endoskopie verhindert Karzinomentwicklung, verbessert Outcome
  - Aktuelles ESGE Position Statement zur Surveillance (wann und wie)
  - Bei Barrett und Dysplasie: sichtbare Läsionen EMR, ESD, sonst RFA
  - Nach kompletter Eradikation d. intestinalen Metaplasie: Surveillance geht weiter