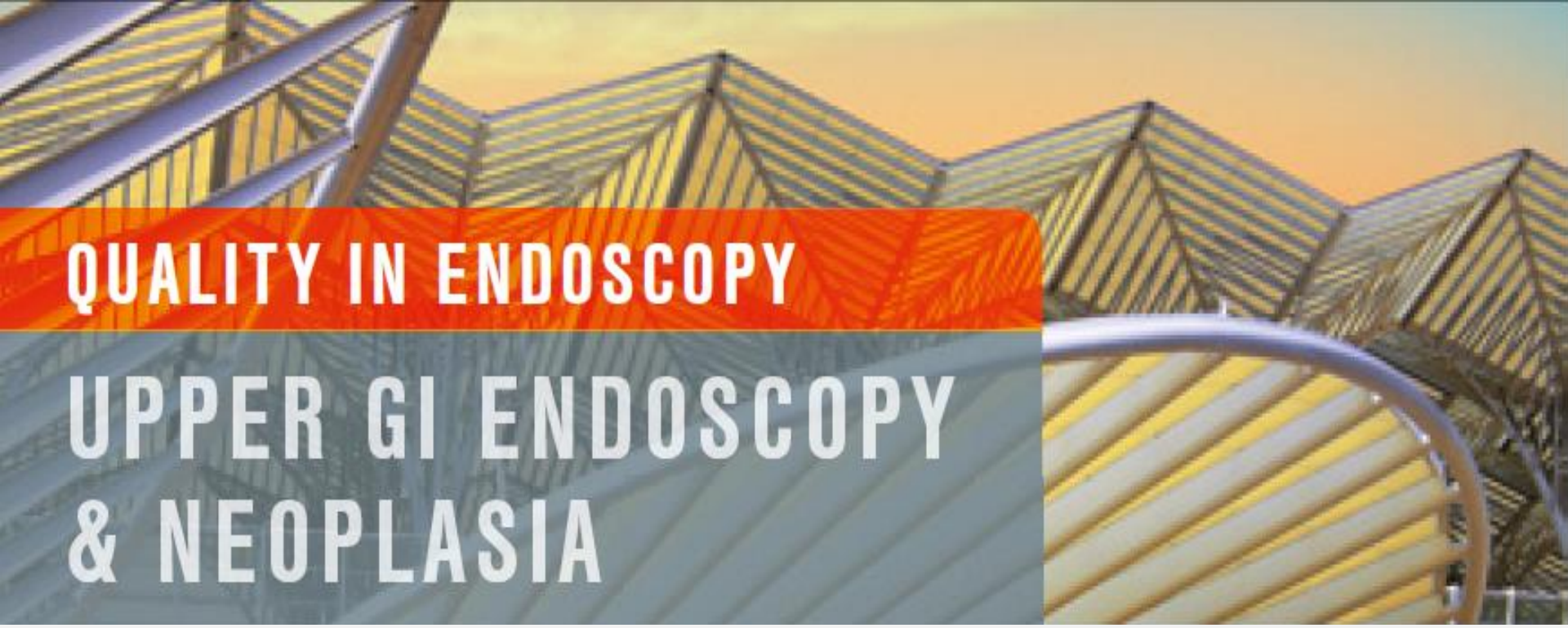


# THE GREAT DEBATE

**Title: How/Should we treat BE with low grade dysplasia?**
CON

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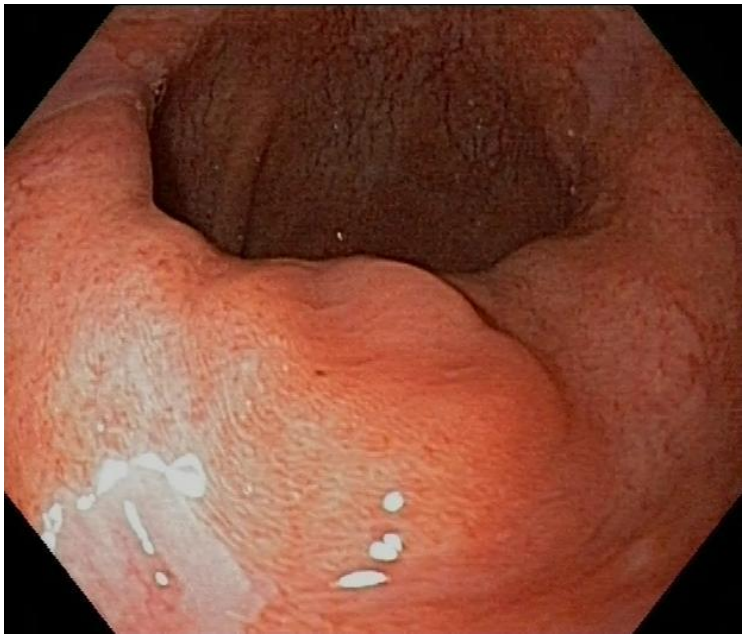
ESGE esdo

# How to treat BE with LGD?

- First should we treat BE with LGD?
- If the answer is no….????
  - The question how is not relevant anymore…



Cliniques universitaires Saint-Luc

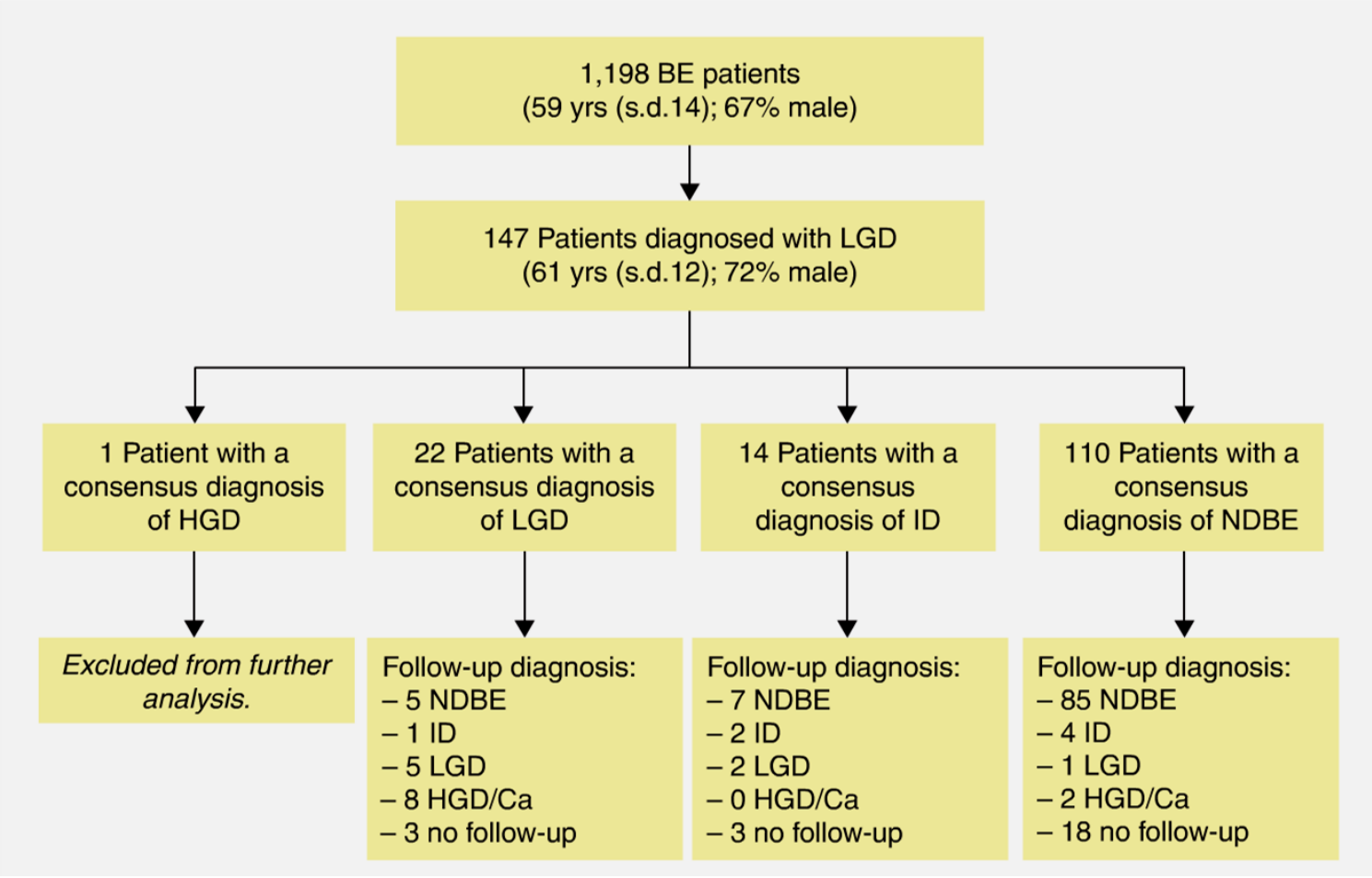
# CON arguments

- LGD itself is not a well-defined diagnosis
- LGD often regresses without intervention
- The risk of progression from LGD to cancer is significantly low
- Follow-up will detect “treatable” HGD and cancer
- Ablative/Resection therapy is not completely harmless
- Ablative/Resection is not 100% efficient
- Follow-up is still needed: cost effectiveness unproven

# LGD itself is not a well-defined diagnosis

- Always doubt the diagnosis of LGD!!!
- The histological features of LGD are nuclear hyperchromasia; nuclear stratification generally confined to the lower half of the epithelium; increased mitotic figures; depleted mucin; and decreased goblet cells, generally in the setting of preserved glandular architecture.
- These features are non-specific and are also seen with inflammation.
- Even expert gastrointestinal pathologists with specific interest in Barrett's esophagus have major disagreements interpreting LGD.

# Well known overdiagnosis of LGD
# 85% downstaged




Curvers WL, et al Gastrointest Endosc 2011;73:195-203
Curvers WL, et al. Low-grade intra-epithelial in Barrett's esophagus: Over-diagnosed but underestimated.AmJ Gastroenterol 2010;105:1523-30.

# LGD can regress without intervention

- Studies on the natural history of LGD are limited because the condition is rare.

- To date, the best data from a multicenter prospective study show that
  - 66% regresses without any intervention
  - and 21% does not progress beyond LGD on long-term follow-up

**So why perform intervention on a benign condition that may disappear without intervention?**

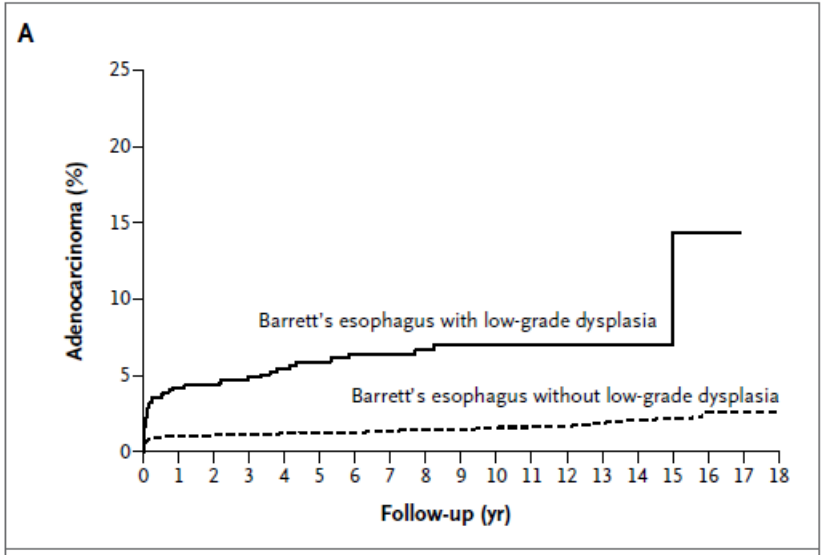
Sharma P, et al. Dysplasia and cancer in a large multicenter cohort of patients with Barrett's esophagus. Clin Gastroenterol Hepatol. 2006; 4:566-572.

# Risk for cancer and cancer related death is very low

- The word “dysplasia” in Barrett’s esophagus induces inordinate fear in our patients and fear should nor be used to motivate behavior!

- The reality is a low risk of progression from LGD to cancer
  - Progression of LGD to cancer is approximately 0.6% /year, not much higher than the 0.12% to 0.5% per patient year risk of progression for non-dysplastic BE
  - Low annual incidence rates of HGD and EAC: EAC, 0.44%/year; HGD, 1.68%/year; and HGD/EAC, 1.83%/year)
  - Moreover no data has proven any survival benefit in treating BE with LGD…

Sikkema M, et al. Am J Gastroenterol 2011:231-8
Wani et al Gastroenterology 2011;141:1179–1186



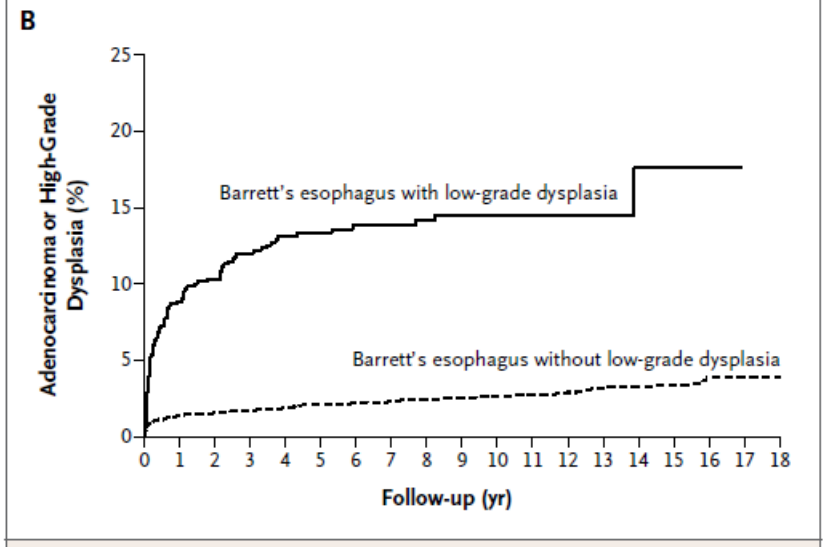




**Figure 2. Cumulative Incidence of Esophageal Adenocarcinoma and of Esophageal Adenocarcinoma or High-Grade Dysplasia.**

Shown is the cumulative incidence of esophageal adenocarcinoma (Panel A) and of esophageal adenocarcinoma or high-grade dysplasia (Panel B) among patients with Barrett's esophagus, according to the presence or absence of low-grade dysplasia on baseline endoscopy. Kaplan–Meier plots include data from the first year after the index endoscopy.

The NEW ENGLAND JOURNAL of MEDICINE

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# Incidence of Adenocarcinoma among Patients with Barrett's Esophagus

Frederik Hvid-Jensen, M.D., Lars Pedersen, Ph.D., Asbjørn Mohr Drewes, M.D., Dr. Med. Sci., Henrik Toft Sørensen, M.D., Dr. Med. Sci., and Peter Funch-Jensen, M.D., Dr. Med. Sci.

Solid evidence that esophageal adenocarcinoma will develop in very few patients with BE

Detection of LGD on the index endoscopy was associated with an incidence rate for adenocarcinoma of 5.1 cases per 1000 person-years (X5).

>>>>> surveillance

# Endoscopic therapy is not completely benign

- Ablative or resection therapy requires repeated sessions
  - RFA average 3.5 treatment sessions and (at times) up to eight
- Patients under surveillance may develop hidden subsquamous cancers after ablative therapy
- Complication rate
  - >6% of patients develop strictures that require dilation, after ablation
  - Long-term safety of ablative therapy?
  - NEJM reported three serious adverse events in 84 BE patients
    - Even one case of serious gastrointestinal hemorrhage is “one case too many” for a benign condition with a low risk of progression to cancer.

**The major reason to avoid ablative/resection therapy is the serious potential for morbidity**

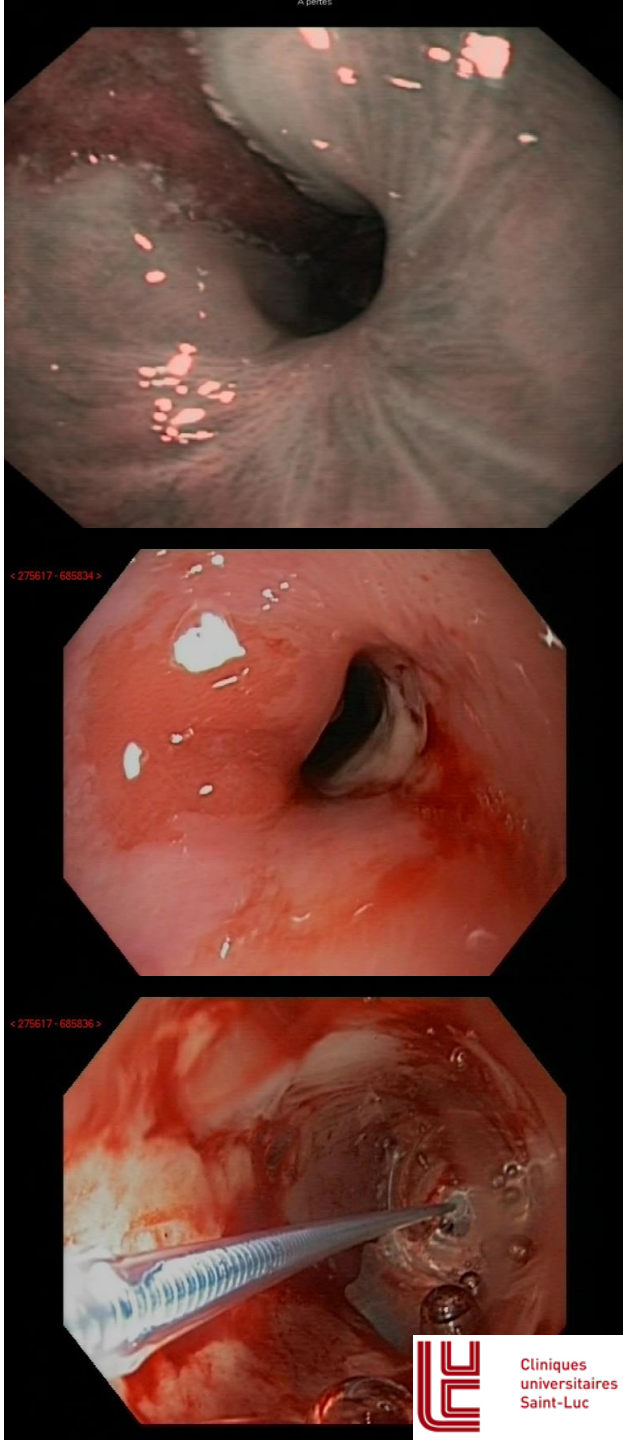
# Complications with ablation

Severe pain 16% of patients

Early complications: 14% of patients
- laceration
- bleeding
- perforation
- pneumonia

Late complications 15% of patients
- severe delayed bleeding
- stenosis
- poor healing
- admission for general symptoms

*Bisschops R, et al. UEGW 2012*



# Co-morbidities

- Most patients with BE and LGD will die from other diseases
- Old patients

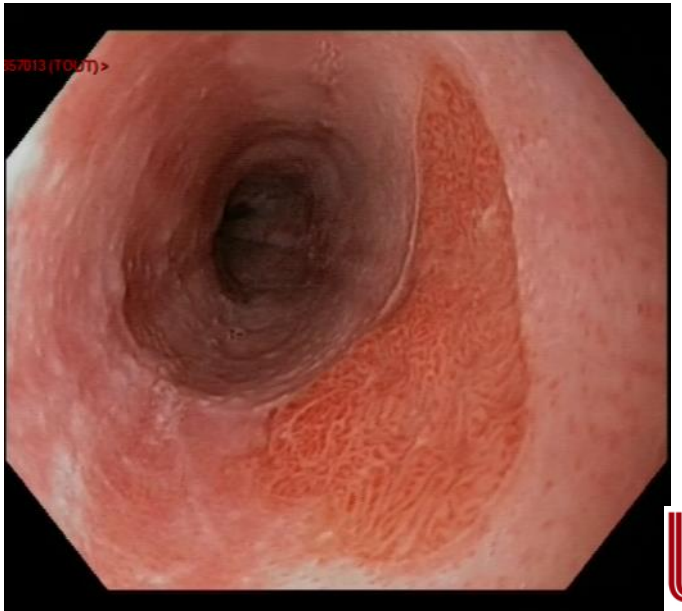
- Exclusion criteria in most studies:
  - active esophagitis or stricture
  - history of esophageal malignancy
  - varices
  - uncontrolled coagulopathy
  - life expectancy of <2 years
  - **Portal hypertension**
  - **Anticoagulation**

*Solaymani-Dodaran et al UEGW OP004*

# Resection and ablation not 100% effective

| Study characteristics | Radiofrequency ablation group | Sham group | *P* value |
|---|---|---|---|
| *n* = 127 Dysplastic Barrett's esophagus patients | 84 | 43 | - |
| Complete regression of intestinal metaplasia | 77.4% | 2.3% | < 0.001 |
| Complete regression of low grade dysplasia | 90.5% | 22.7% | < 0.001 |
| Complete regression of high grade dysplasia | 81.0% | 19.0% | < 0.001 |
| Global progression rate | 3.6% | 16.3% | < 0.05 |
| Progression to cancer rate | 1.2% | 9.3% | < 0.05 |

- In terms of the complete eradication rate of IM, 75-85% may represent a good success, but on the other hand it means that 15-25% of patients have BE left behind.
- Just not good enough!!



Wani S GIE 2010 71:147-166
Shaheen et al GE 2011; NEJM 2009

# Close follow-up still the best option

LGD patients may represent the best BE group for surveillance!!

- Several trials are under way
  - SURF, SURF FR, BOSS, ASPECT, molecular studies
  - With a very strict inclusion of confirmed LGD they may show a 20% risk of HGIN/ADC

- **All of them** diagnosed at an early stage, easily removed or ablated by endoscopic means

- LET'S THEN SURVEIL  SINCE THIS IS ONE BE endoscopic FEATURE THAT NEEDS SURVEILLANCE

# Follow-up still needed
# Cost effectiveness unproven

| BE LGD to EAC, *%/y* | | | |
|---|---|---|---|
| LGD (confirmed and stable) | | | |
| 0.19 | Surveillance, surgery Ca | 24,971 | 16.984 |
| | Surveillance, RFA HGD | 21,135 | 17.034 |
| | Initial RFA LGD | 24,135 | 17.099 |
| 0.5 | Surveillance, surgery Ca | 33,963 | 16.709 |
| | Surveillance, RFA HGD | 26,517 | 16.879 |
| | Initial RFA LGD | 28,486 | 16.987 |
| 0.75 | Surveillance, surgery Ca | 38,810 | 16.516 |
| | Surveillance, RFA HGD | 29,412 | 16.780 |
| | Initial RFA LGD | 31,133 | 16.904 |

Method was simplified by assuming that there were no false positives (eg, indefinite for dysplasia), no regression, and no complication

**The ablation of LGD costs more than continued surveillance with RFA when HGD is found**

Hur et al. Gastroenterology 2012;143:567–575

# Conclusions

My recommendation is therefore not to treat and to wait for appearance of high-grade dysplasia and then intervene (resection or ablation)

This group is in fact the “best” patient group for regular endoscopic surveillance