# 文 献 汇 报

## Refined Criteria for Separating Low-grade Dysplasia and Nondysplastic Barrett Esophagus Reduce Equivocal Diagnoses and Improve Prediction of Patient Outcome

*A 10-Year Review*

Am J Surg Pathol 2018;42:1723–1729

**汇报人：李侠**

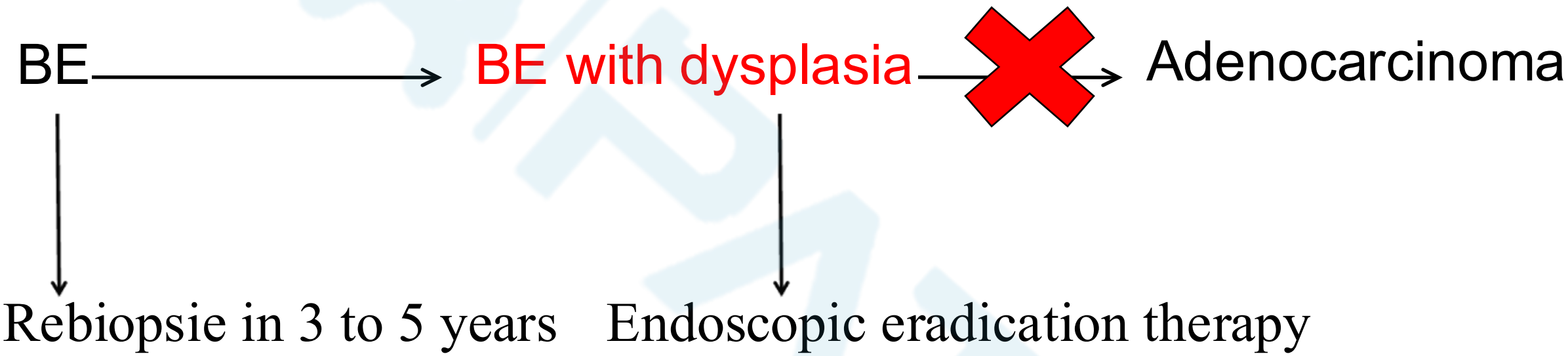
# Backgrounds

Esophageal carcinoma is a common digestive system tumor.

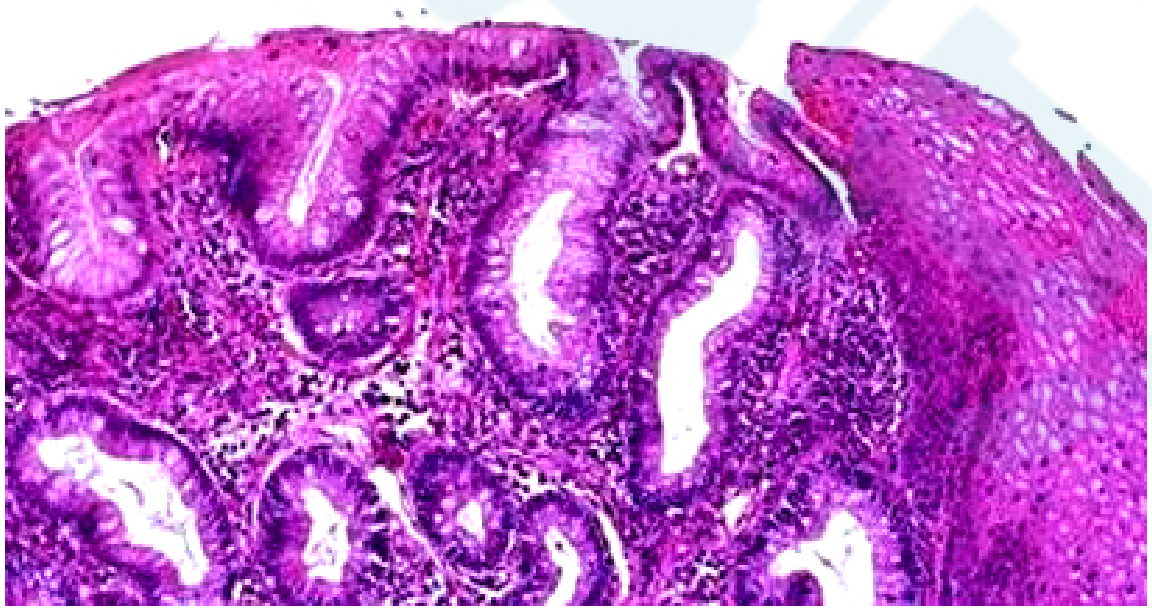
The proportion and overall incidence of esophageal adenocarcinoma (EAC) has dramatically risen over past decades.

Barrett esophagus (BE) is a well-established precursor lesion for EAC.

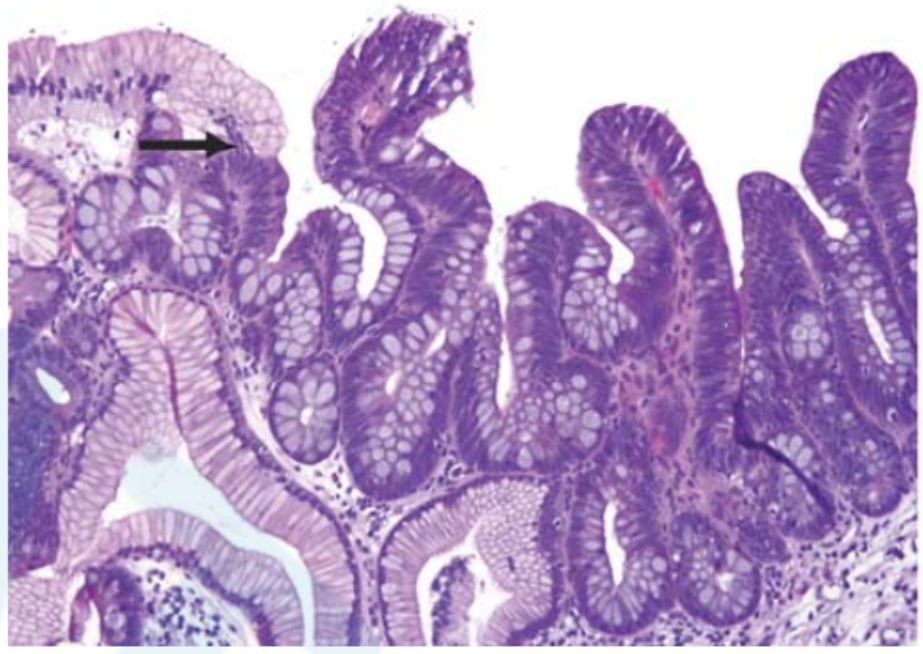
# Backgrounds



# Backgrounds

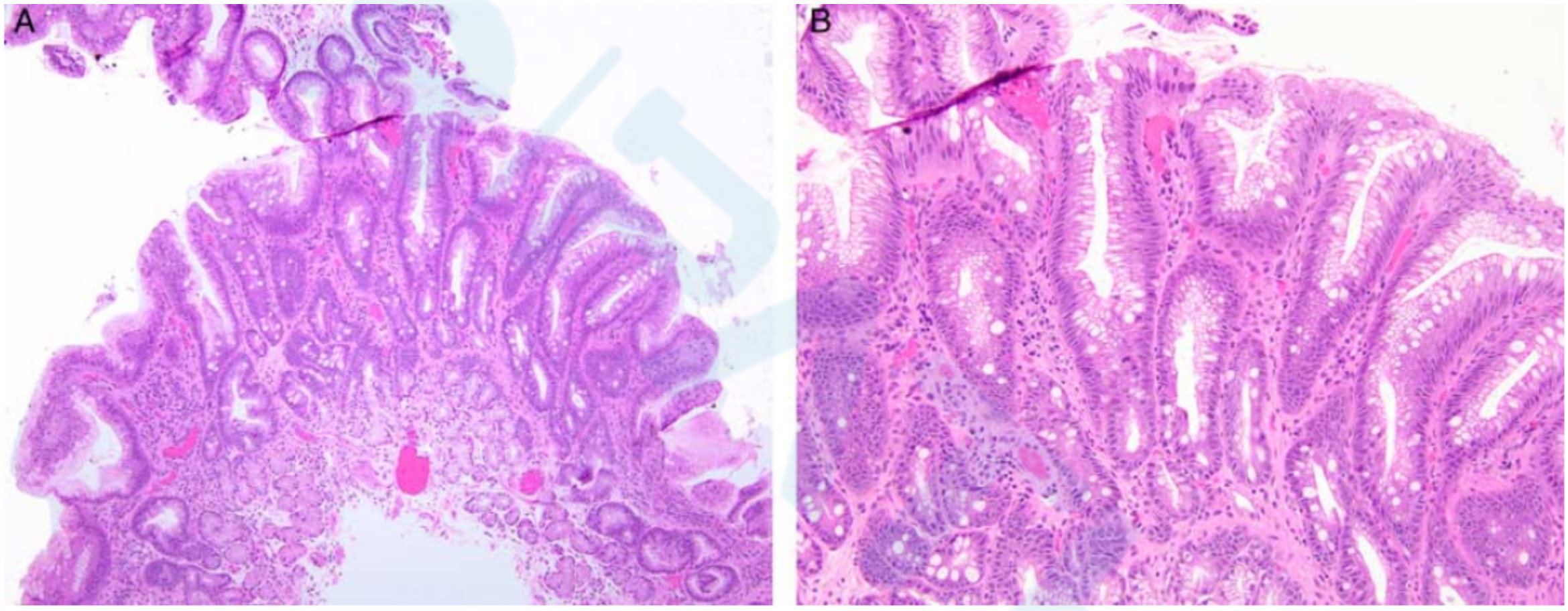


BE



BE with LGD

# Backgrounds




The category of indefinite for dysplasia (IFD) is reserved for challenging cases that are neither unequivocally negative for dysplasia (NFD) nor dysplastic.

# Backgrounds

**Table 2.** Multirater unweighted κ, overall and by category without and with (bold) p53

| | All | | Consultants | |
|---|---|---|---|---|
| Category | No p53 | p53 | No p53 | p53 |
| 1 | 0.56 | **0.63** | 0.58 | **0.66** |
| 2 | 0.08 | **0.08** | 0.1 | **0.06** |
| 3 | 0.23 | **0.31** | 0.26 | **0.37** |
| 4 | 0.65 | **0.63** | 0.66 | **0.7** |
| Combined | 0.42 | **0.48** | 0.45 | **0.52** |

Histopathology. 2009;54:699–712.

# Backgrounds

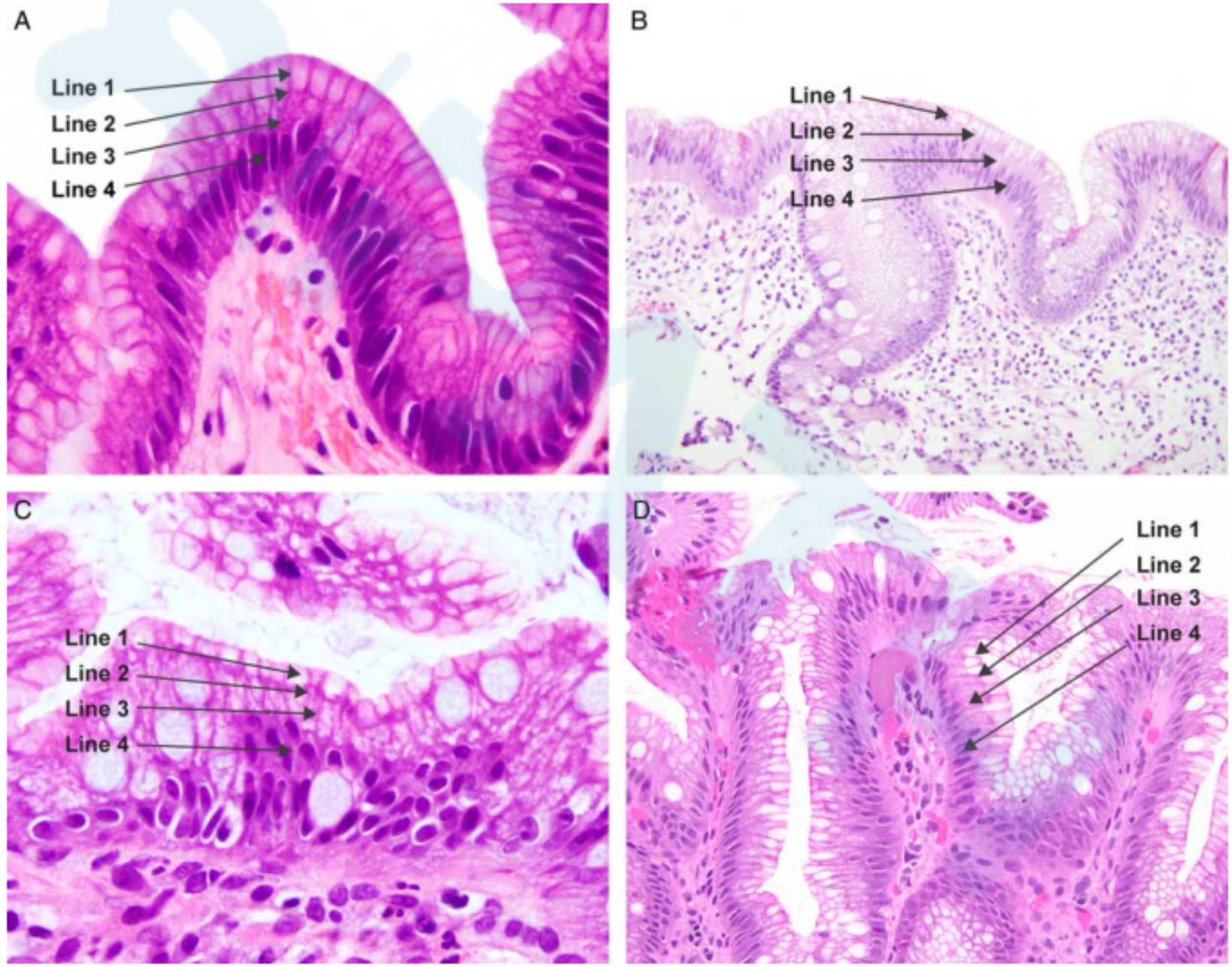



**FIGURE 1.** Photomicrographs showing (A) benign columnar (cardiac) mucosa, (B, C) nondysplastic BE, and (D) nondysplastic BE with moderate nuclear atypia (showing gradual transition on the right side) previously categorized as IFD with maintenance of the "4 lines": line 1—the gastric type mucin vacuole; line 2—the base of the mucin vacuole; line 3—the cytoplasm; and line 4 the nuclei.

# Backgrounds

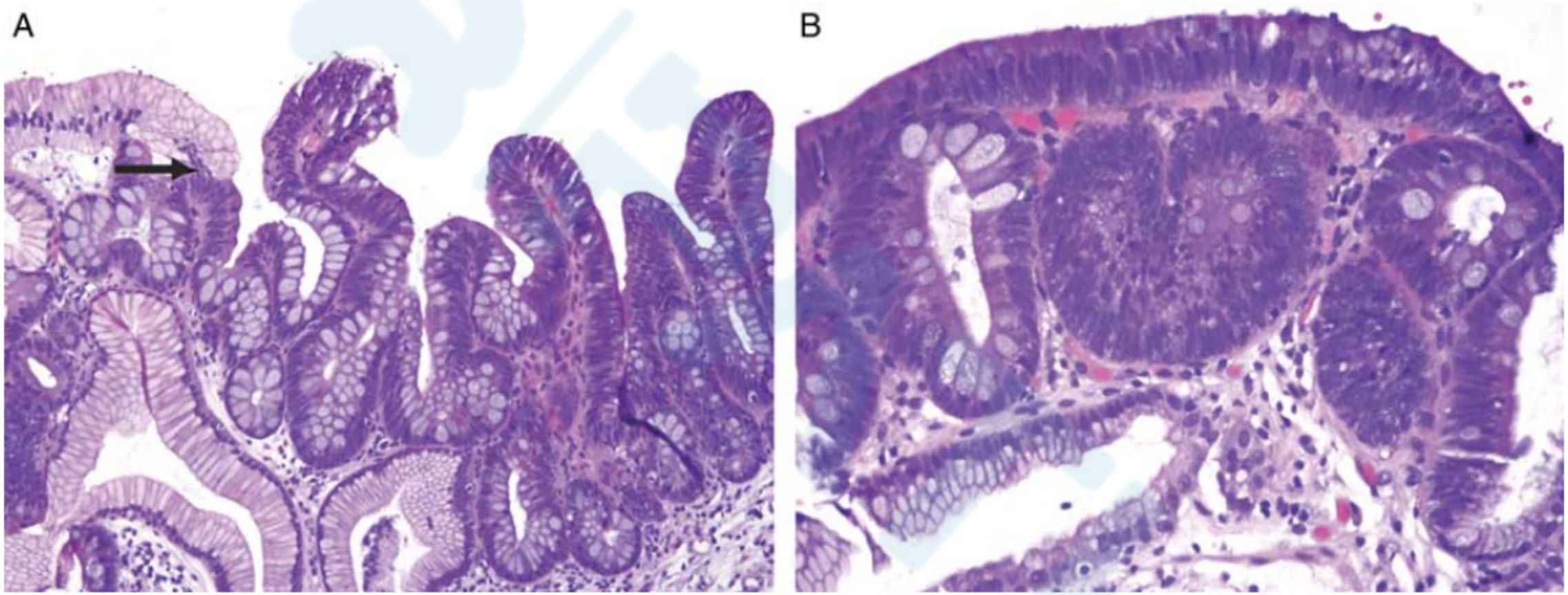



**FIGURE 2.** Photomicrographs (A, B) of BE with LGD showing loss of the "4 lines" of reactive epithelium, atypical hyperchromatic nuclei, and an abrupt transition from nondysplastic to dysplastic epithelium (arrow).

# Backgrounds

In this study we examine how this change to our diagnostic criteria affected the proportion of cases categorized as IFD as well as the short-term follow-up on these cases over a 10-year span from 2007 to 2016.

# MATERIALS AND METHODS

1549 cases from 1130 patients from 2007 to 2016.

2 groups： 2007 - 2011 and 2012 - 2016.

The next biopsy was used as a measure of how frequently patients with IFD had dysplastic BE.

# Demographics and Biopsy Results

TABLE 1. Demographics and Biopsy Results

| | n (%) | | | |
|---|---|---|---|---|
| | Biopsies, 2007-2011 (N = 776) | Biopsies, 2012-2016 (N = 773) | All Biopsies (N = 1549) | *P* |
| Age (mean [SD]) (y) | 63.8 (12.7) | 64.5 (11.8) | 64.1 (12.3) | 0.25 |
| Sex, male (%) | 74.4 | 70.5 | 72.4 | 0.090 |
| Race, white (%) | 84.1 | 85.0 | 84.6 | 0.65 |
| Biopsy results | | | | |
| NFD | 652 (84.0) | 699 (90.4) | 1351 (87.2) | $3.3\times10^{-3}$* |
| IFD | 65 (8.4) | 33 (4.3) | 98 (6.3) | |
| LGD | 30 (3.9) | 19 (2.5) | 49 (3.2) | |
| HGD | 11 (1.4) | 10 (1.3) | 21 (1.4) | |
| ≥IMC | 18 (2.3) | 12 (1.6) | 30 (1.9) | |

*$\chi^2$ test comparing frequencies of the 5 categories between the 5-year periods.

# Results of Next Biopsy of IFD Cases

TABLE 2. Results of Next Biopsy on IFD Cases

| | n (%) | | |
|---|---|---|---|
| | IFD Cases From 2007-2011 (N = 65) | IFD Cases From 2012-2016 (N = 33) | *P* |
| Follow-up biopsy available | 48 (73.8) | 21 (63.6) | 0.30 |
| Results of next biopsy | | | |
| NFD* | 42 (87.5) | 18 (85.7) | 0.081† |
| IFD* | 5 (10.4) | 0 | |
| LGD* | 1 (2.1) | 2 (9.5) | |
| HGD* | 0 | 1 (4.8) | |
| ≥ IMC* | 0 | 0 | |

*Percentage among cases with follow-up biopsy available.

†Fisher exact test comparing frequency of next biopsy with and without definite dysplasia between the 5-year periods.

# Results of Next Biopsy of NFD Cases

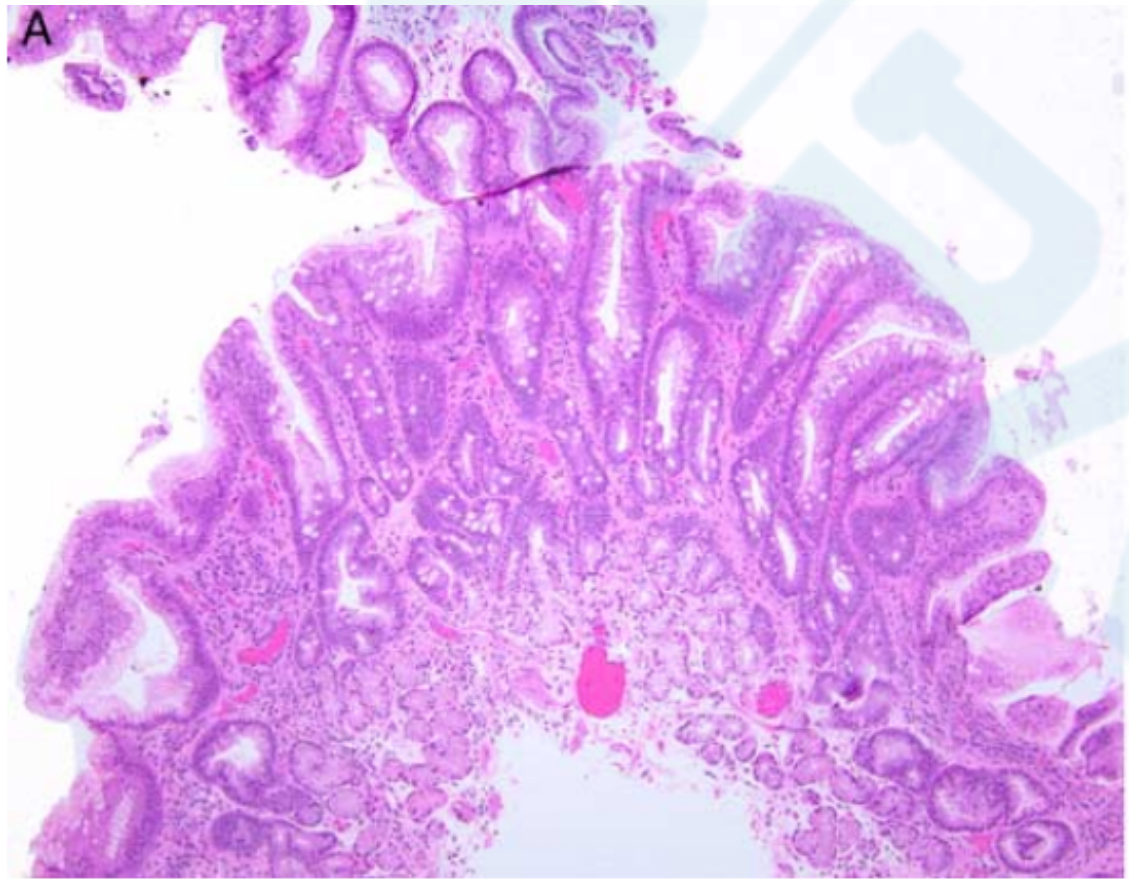
TABLE 3. Results of Next Biopsy on NFD Cases

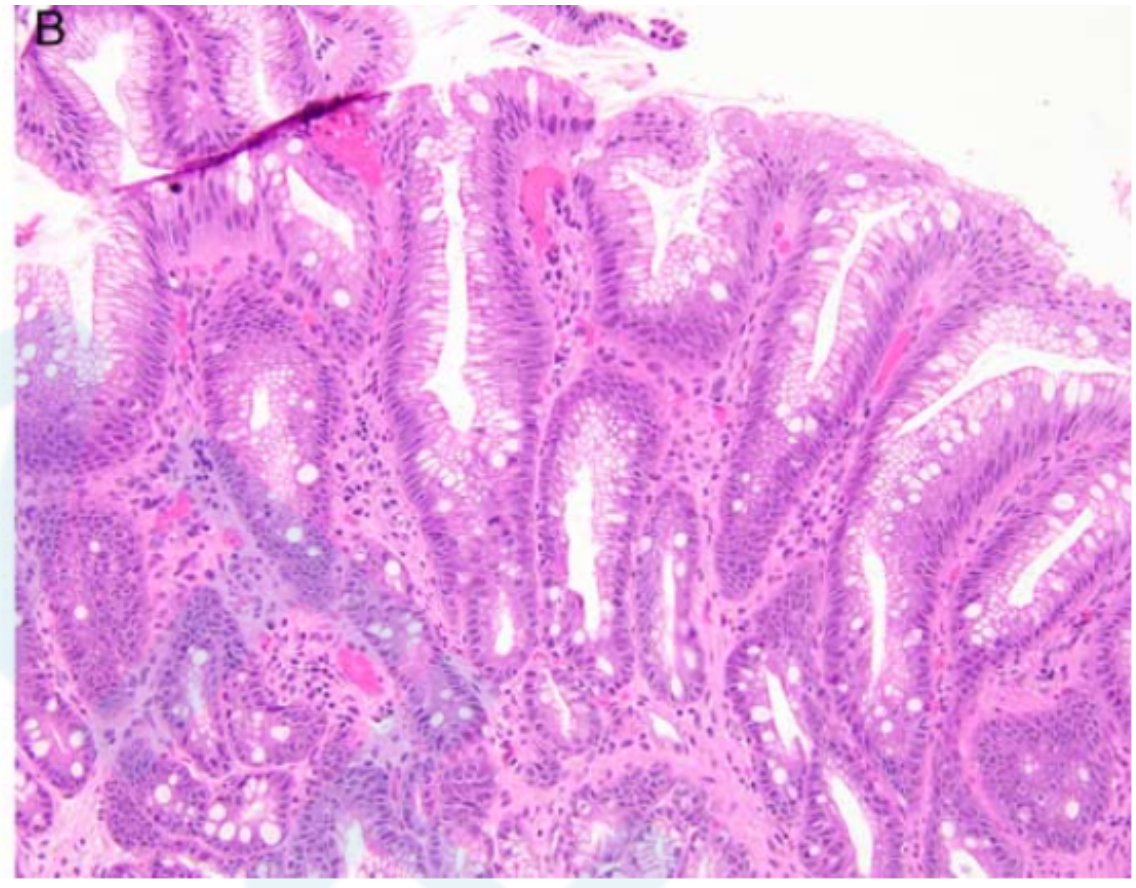
| | n (%) | | |
|---|---|---|---|
| | NFD Cases From 2007-2011 (N = 652) | NFD Cases From 2012-2016 (N = 699) | *P* |
| Follow-up biopsy available | 360 (55.2) | 222 (31.8) | < 0.001 |
| Results of next biopsy | | | |
| NFD* | 319 (88.6) | 207 (93.2) | 0.28† |
| IFD* | 25 (6.9) | 9 (4.1) | |
| LGD* | 14 (3.9) | 4 (1.8) | |
| HGD* | 2 (0.6) | 2 (0.9) | |
| ≥ IMC* | 0 | 0 | |

*Percentage among cases with follow-up biopsy available.

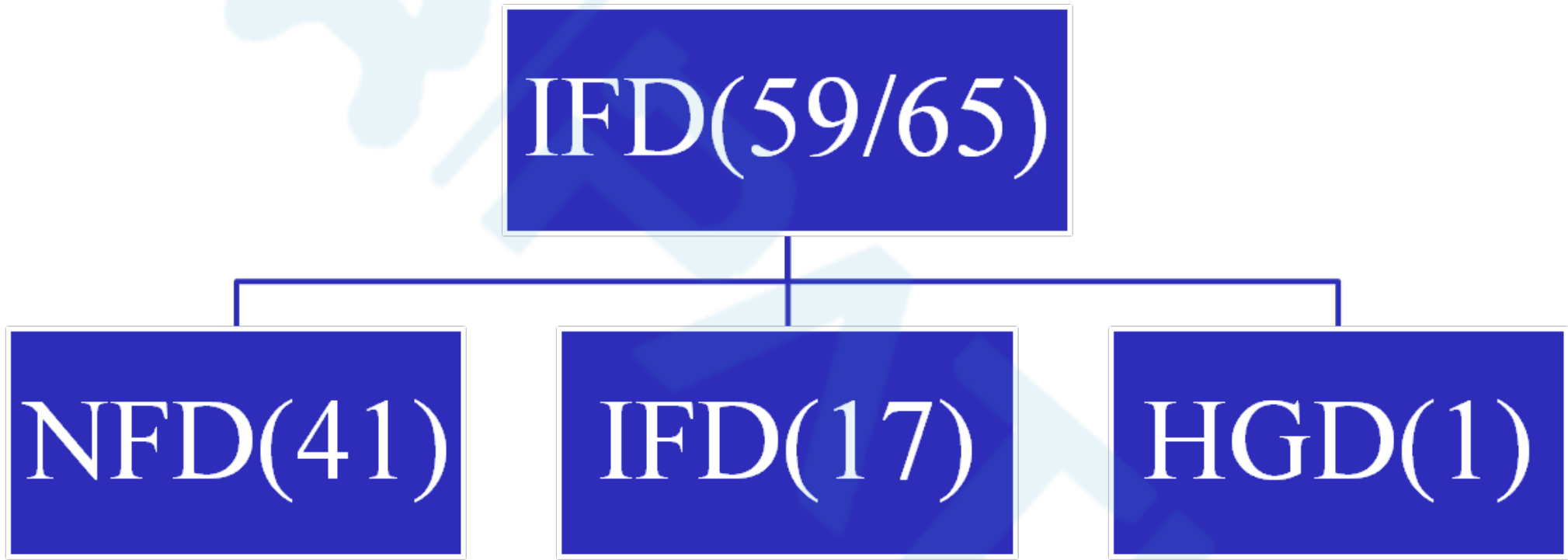
†$\chi^2$ test comparing frequency of next biopsy with and without definite dysplasia between the 5-year periods.

# Rereview of IFD Cases From 2007 to 2011



# Rereview of IFD Cases From 2007 to 2011



# 3 Themes of IFD

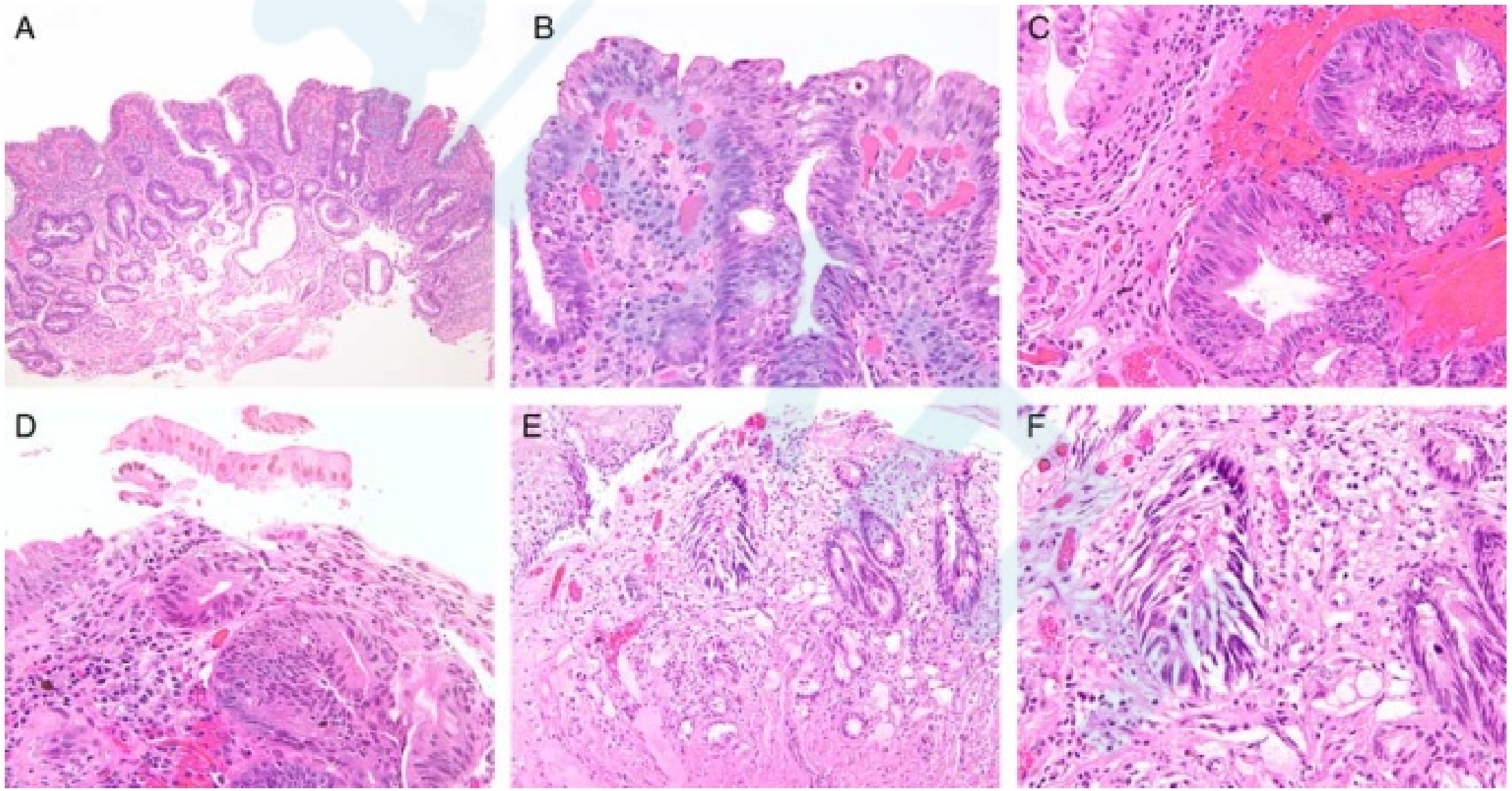



**FIGURE 4.** Examples of cases that are still categorized as IFD showing: (A, B) atypia and partial loss of the "4 lines" with marked confounding acute inflammation; (C, D) atypical basal crypts with mature nondysplastic surface epithelium; and (E, F) cauterized glands where dysplasia cannot be excluded due to technical limitations.

# Conclusions

We successfully decreased the number of equivocal diagnoses by nearly 50% overall.

No increase in the frequency of dysplasia on the next biopsy among the NFD cases.

A stricter diagnostic threshold for IFD is appropriate as it appears that a very small fraction of these biopsies represent true dysplasia.

IFD, LGD, and HGD in any given clinic should be <10%.

# 谢谢…

异型增生的诊断要根据是否存在细胞和结构的不典型性及其程度[2135,2353,2654,2842]。

**无异型增生**：该诊断用于以下情况，病变表现为化生性的柱状上皮，杯状细胞可有可无，并有再生改变。Barrett 食管再生可显示轻度的隐窝增生和分枝、萎缩，甚至囊性变，尤其是邻近溃疡或溃疡下。细胞核可轻度增大、深染，尤其是在隐窝底部，可见明显核仁和核轻度复层。

**不确定的异型增生**："不确定"的概念常用于以下情况：学术上用不典型性解释困难时；病变达到不典型，但还尚未至异型增生，尤其是伴有炎性溃疡性病变，且不典型（异型增生样）改变不出现于表面上皮，只在隐窝基底部时[1889,2353]。然而，近来有报道这是"早期"的异型增生[1889]。总的来看，上皮突然出现由无不典型向不典型转变都提示是真的瘤变。对于炎症相关性不典型病变，推荐进行抗 GORD 治疗，在治疗 3～6 个月后应再取活检，目的是对不典型区域再评估。

**低级别异型增生**：其特点是隐窝结构相对正常或仅轻度紊乱，细胞的不典型性表现为削尖的核位于细胞浆基底部。细胞核拉长、增大、拥挤、浓染，具有不规则的外形，染色质深，伴或不伴有多个不明显的核仁，轻度多形性并轻度失去极向，黏附性差和分裂像增加。

**高级别异型增生**：其诊断特点是显著的细胞异常和明显结构复杂的腺体。高级别异型增生细胞异常包括核多形性明显、失去极向、核浆比增加，隐窝及表面上皮全层呈复层核。高级别病变的结构异常包括隐窝增生、分枝、显著拥挤或绒毛状上皮结构，很少见到管腔内乳头状、桥状或筛状生长方式。

**黏膜内腺癌**：高级别异型增生与黏膜内腺癌很难鉴别，后者定义为可见固有层的浸润。这充其量也就是病理工作者关于区分黏膜内癌和高级别异型增生的一点共识[740]。以前黏膜内腺癌的标准包括：①固有层内出现单个或小簇的紧密排列背靠背的腺体；②筛状或实性的膨胀式生长，邻近的隐窝扭曲变形；③不能通过这里先前存在的腺体解释一个高度扭曲/不规则的腺体增生。腺癌中常可以见到坏死和（或）结缔组织增生，尽管这些特点很少见于局限在黏膜内的癌，事实上，在黏膜下浸润癌中可能也见不到[2409]。有研究