Gastroenterology 2017;153:1492–1495

BRIEF REPORT

# Association of Aneuploidy and Flat Dysplasia With Development of High-Grade Dysplasia or Colorectal Cancer in Patients With Inflammatory Bowel Disease

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**There is controversy over how to best manage patients with inflammatory bowel disease and flat low-grade dysplasia (fLGD) in the colon. We performed a retrospective analysis of formalin-fixed paraffin-embedded colon tissues with fLGD from 37 patients undergoing surveillance colonoscopy for inflammatory bowel disease from 1990 to 2015 at the University of California at San Francisco Medical Center, to determine whether detection of aneuploidy is associated with later development of high-grade dysplasia (HGD) or colorectal cancer. Medical data were collected from the patients for a mean follow-up time of 37 months. Using flow cytometry analysis of paraffin-embedded colon tissue, we detected aneuploidy in 15 of 37 samples with fLGD (40.5%). By comparison, aneuploidy was detected in 14 of 15 samples with flat HGD (93.3%) and 2 of 45 samples that were negative for dysplasia (4.4%). The univariate hazard ratio for subsequent detection of HGD or colorectal cancer in patients with fLGD and aneuploidy was 5.3 (95% CI, 1.542−24.121) within a mean follow-up time of 37 months. The presence of aneuploidy therefore identifies patients with fLGD in colon tissue who have an increased risk for HGD or colorectal cancer and may provide supportive evidence to a morphologic impression or suspicion of flat HGD.**

*Keywords:* IBD; Colon Cancer Risk Factor; Marker; Early Detection.

Inflammatory bowel disease (IBD) is a major risk factor for the development of colorectal cancer (CRC).[1,2] Colonoscopic surveillance aims to reduce CRC incidence by detecting pre-invasive, dysplastic lesions. Patients with endoscopically resectable polypoid dysplasia seem to have a good prognosis,[3] whereas some dysplastic lesions are flat (or "invisible") and thus more difficult to detect and/or resect endoscopically.[4] Although colectomy is recommended for flat high-grade dysplasia (fHGD) due to its strong association with CRC,[5–7] the management of flat low-grade dysplasia (fLGD) remains controversial due to its variable progression rates to HGD or CRC, which range from 0% to >50%.[8,9] Earlier studies that examined a potential correlation between aneuploidy and IBD-related dysplasia failed to analyze DNA content in flat dysplasia or correlate histologic grade of dysplasia with its outcome.[10]

To evaluate whether aneuploidy can aid in the risk stratification of fLGD, flow cytometry was performed on 37 fLGD samples obtained from formalin-fixed paraffin-embedded colon tissues. Demographic characteristics of our cohort are provided in Supplementary Table 1. Fifteen (40.5%) of 37 fLGD samples showed aneuploidy (Figure 1*A* and *B*; Supplementary Figure 1 and Supplementary Table 2), and there was no evidence of HGD or CRC on the H&E recut

**EDITOR'S NOTES**

BACKGROUND AND CONTEXT

The management of flat low-grade dysplasia (fLGD) in patients with inflammatory bowel disease (IBD) remains controversial, although colectomy is typically indicated for flat high-grade dysplasia (fHGD) in the colon.

NEW FINDINGS

The presence of aneuploidy in the setting of fLGD was significantly associated with subsequent detection of HGD or colorectal cancer (CRC). Aneuploidy was also detected in almost all cases of fHGD.

LIMITATIONS

The flow cytometric assessment of aneuploidy as a predictive marker of HGD or CRC in the setting of fLGD will require further validation in a larger, prospective study.

IMPACT

The presence of aneuploidy can identify a subset of fLGD patients who may benefit from early colectomy or increased colonoscopic surveillance, and provide supportive evidence to a morphologic impression or suspicion of fHGD.

***Abbreviations used in this paper:*** **CRC, colorectal cancer; fHGD, flat high-grade dysplasia; fLGD, flat low-grade dysplasia; IBD, inflammatory bowel disease.**

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0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2017.08.031

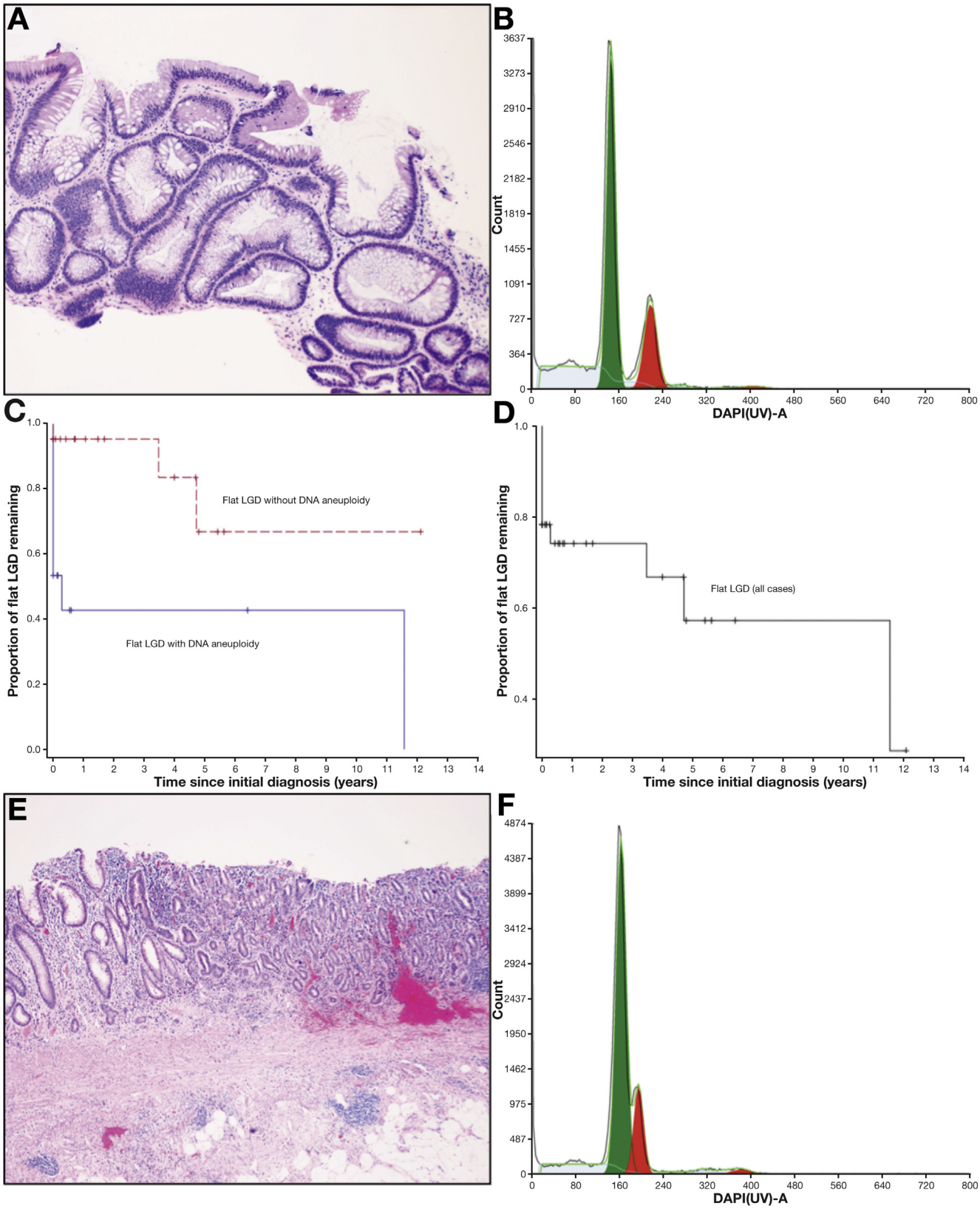


**Figure 1.** (*A*) Flat LGD (H&E, 100×). (*B*) DNA histogram shows a discrete aneuploid peak (*red*) that is visually distinguishable from the normal diploid population (*green*) in this fLGD patient. (*C*) Detection of HGD or CRC in fLGD patients with aneuploidy at baseline. (*D*) Overall detection of HGD or CRC in all fLGD patients. (*E*) fHGD (H&E, 40×). (*F*) A distinct aneuploid population (*red*) is seen in this fHGD patient.