Prevalence of advanced histological features and synchronous neoplasia in patients with flat adenomas CME

Vishnu Naravadi, MD,[1] Neil Gupta, MD, MPH,[1] Dayna Early, MD,[2] Sreenivas Jonnalagadda, MD,[2] Sachin B. Wani, MD,[5] Srinivas Gaddam, MD,[3,4] Prateek Sharma, MD,[3,4] Steven A. Edmundowicz, MD,[2] Ajay Bansal, MD,[3,4] Amit Rastogi, MD[3,4]

Maywood, Illinois; St. Louis, Kansas City, Missouri; Kansas City, Kansas; Aurora, Colorado, USA

Background and Aims: The prevalence of advanced histology in flat adenomas is uncertain. There are limited data on the prevalence of synchronous adenomas in patients with flat adenomas. The aims of this study were to determine whether the flat adenomas harbor advanced histology more than the polypoid adenomas and whether the presence of flat adenomas is an independent predictor of synchronous adenomas.

Methods: A retrospective analysis of data from 3 prospective clinical trials conducted at 2 tertiary care referral centers that included patients undergoing screening or surveillance colonoscopy was performed. The location, size, and morphology of each polyp resected was documented and sent for histopathological examination in a unique specimen jar.

Results: A total of 2931 polyps were removed in 1340 patients. Of the 1911 adenomas (65.2%), 293 (15.3%) were flat and 1618 (84.7%) were polypoid. The prevalence of advanced histology did not differ between flat and polypoid adenomas (1.4% vs 3.1%; $P = .13$). Multivariate analysis confirmed that the presence of at least 1 flat adenoma was a predictor of the presence of a large adenoma ($P < .01$; odds ratio [OR], 2.80; 95% CI, 1.86–4.22), advanced adenoma ($P < .01$; OR, 2.70; 95% CI, 1.80–4.06), and 3 or more adenomas ($P < .01$; OR, 2.44; 95% CI, 1.66–3.59).

Conclusion: Although the prevalence of advanced histology in flat adenomas is similar to that of polypoid adenomas, flat adenomas are associated with increased prevalence of synchronous large and advanced adenomas. Whether these results imply shorter surveillance intervals in patients with flat adenomas needs to be explored in future studies. (Gastrointest Endosc 2016;83:795-9.)

Colorectal cancer is the third most common cancer and one of the leading causes of cancer-related death in the United States.[1] Colonoscopy can prevent colon cancer by removal of adenomatous lesions that are precursors of colorectal cancer.[2] Although the majority of colorectal cancers was thought to develop from polypoid adenomas, recent studies have demonstrated that flat adenomas are also important precursor lesions.[3-5] Few studies have shown a higher incidence of advanced histology such as high-grade dysplasia (HGD) and even early invasive cancer in these flat adenomas compared with polypoid adenomas.[6,7] However, other studies have failed to confirm this finding.[8] In addition, there have been limited previous data about whether patients with flat

Abbreviations: CI, confidence interval; HGD, high-grade dysplasia; OR, odds ratio; VA, Veterans Affairs.

DISCLOSURE: *Dr Gupta has received research support from Cook Medical, CDx Diagnostics, and Cosmo Pharmaceuticals. Dr Jonnalagadda is a consultant for and is on the Advisory Board of Olympus America. Dr Sharma has received a research grant from Olympus, Cook, and Cosmo Pharmaceuticals. Dr Edmondowicz is a consultant for and is on the Advisory Board of Olympus. Dr Rustogi has received research grants from Olympus. All other authors disclosed no financial relationships relevant to this publication.*

See CME section; p. 808.

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2015.08.040

Received March 20, 2015. Accepted August 7, 2015.

Current affiliations: Division of Gastroenterology and Nutrition, Loyola University Medical Center, Maywood, Illinois (1), Division of Gastroenterology, Washington University School of Medicine, St. Louis, Missouri (2), Division of Gastroenterology, Kansas City Veterans Affairs Medical Center, Kansas City, Missouri (3), Division of Gastroenterology, University of Kansas Medical Center, Kansas City, Kansas (4), Division of Gastroenterology and Hepatology, University of Colorado, Anschutz Medical Campus, Aurora, Colorado (5).

Reprint requests: Vishnu Naravadi, MD, Division of Gastroenterology and Nutrition, Loyola University Medical Center, 2160 S First Ave., Building 54, Maywood, IL 60153.

adenomas are at higher risk of synchronous lesions.[8] If this is indeed true across different studies, then the identification and treatment of these lesions assume significant clinical importance and consequence. These flat adenomas are also thought to arise from mechanisms different from those of polypoid adenomas,[9,10] and their significance in terms of prevalence of synchronous adenomas is unclear.

The aim of this study was to estimate the prevalence of advanced histological features in flat adenomas and also determine whether the presence of a flat adenoma is an independent predictor of synchronous adenomas.

METHODS

Setting

This was a post hoc analysis of data from 3 prospective trials investigating the impact of novel imaging techniques on polyp detection and/or polyp histology prediction.[11-13] The studies were conducted at the VA Medical Center in Kansas City, Missouri, and at Washington University in St. Louis, Missouri, between August 2008 and May 2013. All data from the 3 clinical trials were stored in a centralized database. All 3 clinical trials had similar inclusion/exclusion criteria and colonoscopy methodologies and all were approved by the local institutional review boards.

Study population

Patients scheduled for screening or surveillance colonoscopy were prospectively enrolled in 1 of 3 clinical trials[11-13] after providing written informed consent. Inclusion criteria were referral for screening or surveillance colonoscopy and the ability to provide informed consent. Exclusion criteria were previous surgical resection of any part of the colon, a history of colon cancer, a history of inflammatory bowel disease, use of antiplatelet agents or anticoagulants that precluded the removal of the colon polyps, poor general condition or any other reason to avoid prolonged procedure time, history of polyposis syndrome or hereditary nonpolyposis colon cancer, or the inability to give informed consent. Patients in whom the cecum could not be intubated or bowel prep was inadequate were excluded as well.

Colonoscopy procedure

The colonoscopies were performed by 1 of 6 experienced endoscopists by using different Olympus colonoscopes: CF-H180AL, PCF-H180AL, and PCF-160AL (Olympus America Inc, Center Valley, Pa). The EVIS EXERA II CV–180 video processor and the 19-inch high-definition monitor OEV 191H (Olympus) were used in all 3 studies. Each colonoscopy was performed by using either standard-definition white light, high-definition white light (with or without a transparent cap), or narrow-band imaging. In 1 study, all colonoscopies were conducted with the participation of a gastroenterology trainee.[13] After cecal intubation, the location, size, and morphology of each polyp detected during the withdrawal phase was documented.

Bowel preparation was evaluated and graded as previously described.[14] There were 4 categories of bowel preparation: excellent (>90% of mucosa seen, mostly liquid colonic contents, minimal suctioning needed for adequate visualization), good (>90% of mucosa seen, mostly liquid colonic contents, significant suctioning needed for adequate visualization), fair (>90% of mucosa seen, mixture of liquid and semisolid colonic contents that could be suctioned and/or washed), and inadequate (<90% of mucosa seen, mixture of semisolid and solid colonic contents that could not be suctioned or washed).

Polyp description

Flat polyp morphology was characterized by using the classification system described by the Japanese Society for Cancer of the Colon and Rectum, which includes superficially elevated, completely flat, and depressed.[15,16] Polyps were characterized as either neoplastic (adenomas) or nonneoplastic (hyperplastic, no diagnostic abnormality, other benign histology). Serrated adenomas (both sessile serrated and traditional serrated) were included in the neoplastic category. Adenomas were further characterized by the presence of any villous features, HGD, or adenocarcinoma. Advanced adenomas were defined as adenomas greater than or equal to 10 mm or with villous histology or high-grade dysplasia or cancer. Size of the polyp was estimated by comparison with the span of an open biopsy forceps, the sheath of a polypectomy snare or the diameter of an open snare placed against the polyp. Each polyp was then resected, placed in a unique specimen jar, and sent for histopathological evaluation. Location was estimated using the anatomical landmarks. The right side of the colon was defined as the colon proximal to the splenic flexure (cecum, ascending colon, hepatic flexure, and transverse colon). The left side of the colon was defined as the colon from splenic flexure to the rectum.

Statistical analysis

Statistical analysis was performed using Stata/IC 10.1 (StataCorp, College Station, Tex). A P value of <.05 was considered significant. Categorical variables were summarized by using percentages and 95% confidence intervals (CIs) were calculated. Normally distributed continuous variables were summarized by using means and SDs, whereas nonnormally distributed continuous variables were summarized using medians and ranges. Nonpaired categorical and normally distributed continuous data were compared by using the Fisher exact test and an unpaired t test, respectively. Nonnormally distributed continuous variables were compared using the Wilcoxon rank sum test.

To adjust for the effect of potentially confounding variables, odds ratios were adjusted for age, sex, race,