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Agreement in interpreting villous elements and dysplasia in adenomas less than one centimetre in size

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ABSTRACT

Background: Villous elements and dysplasia grade in small adenomas are used in many countries to guide post-polypectomy colonoscopy intervals.
Aims: Measure agreement in interpretation of villous elements and dysplasia in small adenomas.
Methods: Consecutive endoscopically resected adenomas <10 mm in size (203 adenomas less than 6 mm and 149 adenomas 6–9 mm in size) were reviewed by 3 expert gastrointestinal pathologists. Interpretations were compared to routine clinical pathology readings at our institution and to each other.
Results: All pathologists used the same definitions for villous and tubular histology. The overall kappas for villous elements in <6 mm and 6–9 mm adenomas were 0.29 and 0.26, respectively. Interpretation of dysplasia grade had kappas of 0.02 and 0.09 for adenomas <6 mm and 6–9 mm, respectively. Two expert pathologists who used cytologic criteria had much higher fractions of high grade dysplasia compared to the third expert and the pathologists at our centre, who relied on architectural criteria.
Conclusions: Villous elements and dysplasia grade in small adenomas are problematic as determinants of post-polypectomy surveillance intervals. Uniform pathologic criteria for dysplasia grade are needed.

1. Introduction

Interobserver variation between pathologists in the histologic interpretation of colorectal polyps has been the subject of several reports [1–9]. In general, these studies show that pathologists tend to have high levels of agreement with regard to distinguishing adenomas from hyperplastic polyps [1–4], but substantial variation in the interpretation of whether villous elements are present in adenomas and whether adenomas have high or low grade dysplasia [4–9]. These levels of variation have led to calls to dispense with interpreting villous elements and degree of dysplasia in adenomas [10], and to use the percent of villous elements in adenomas as a quality measure in colorectal cancer prevention programmes [11]. Indeed, the British Society of Gastroenterology does not consider either villous elements or degree of dysplasia in its recommendations for post-polypectomy surveillance intervals [12].

In this study we evaluated the magnitude of variation in interpretation of villous elements and high grade dysplasia among pathologists, and methodologic differences between pathologists that may underlie the variation. Our study varies from prior studies in two important regards. First, no prior study evaluated polyps that were exclusively <1 cm in size [4–9]. The clinical relevance of villous elements and high-grade dysplasia (HGD) in adenomas ≥1 cm is, however, diminished because such adenomas are considered advanced based on their size alone. As such, a reading of villous elements or HGD in an adenoma ≥1 cm does not warrant altering the follow-up interval in current U.S. guidelines [13]. On the other hand, a reading of villous elements or HGD in an adenoma <1 cm makes that adenoma advanced and does alter the surveillance recommendation. Because the prevalence of villous elements and HGD is lower in adenomas <1 cm, and the lower prevalence could affect factors such as suspicion bias regarding the presence of advanced histology, we considered that measurement of interobserver variation in interpretation of these elements in adenomas <1 cm was of greater interest than measurement in large adenomas. Finally, unlike most previous studies [4–9], our sample was of consecutive resected adenomas and not selected. Thus, the slides in our series were not selected for being "classic" for any of the features, and none of the features were over represented in frequency [4–9].

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2. Methods

The study was approved by the Institutional Review Board at IUPUI/Clarian Health Partners. We utilized a database of colonoscopies performed at Indiana University Hospital to respectively identify histopathology slides of 352 consecutive conventional adenomas (as interpreted by our general pathologists) less than 1.0 cm in size. Serrated lesions, including hyperplastic polyps, sessile serrated polyps (also called sessile serrated adenomas), sessile serrated polyp with cytological dysplasia, and traditional serrated adenoma were not included in the study. The polyps were identified via an endoscopy database that stores information on all polyps removed by colonoscopy in the unit according to date, polyp size, and histology. The colonoscopies were performed in 2002 for a mixture of indications including colorectal cancer screening, polyp surveillance and diagnostic examinations. Polyp size was determined by the endoscopist. There were 203 adenomas <6 mm in size and 149 that were 6–9 mm. The sample size was estimated based on discussion with our GI pathologists as number of slides that the visiting pathologists could reasonably review during a 2 day visit with 8 h of slide reading per day, assuming that an assistant would hand the pathologist the slide and record the pathologist's interpretation of the histologic findings. We invited three experts in gastrointestinal pathology from outside our institution (M.O., J.G., R.R.) to review the slides. All 3 pathologists were blinded to the original interpretation of the polyps. The pathology reviews were conducted in 2007.

The original purpose of the study was a quality review of pathology interpretations of small adenomas at our institution. Specifically, we were interested in whether our pathologists were over-reading either villous elements or HGD, which would tend to result in patients with small polyps undergoing post-polypectomy surveillance at intervals that were too short [12]. Each of the 3 outside experts travelled to our institution on different occasions to perform the review. Each outside pathologist visited for 2 days and was attended by an assistant (the same individual served as assistant for all pathologists) who provided each slide for review and recorded the interpretation of the pathologist. The same sample of 352 slides was reviewed by each pathologist. One of the outside pathologists did not have sufficient time to complete review of all of the slides and in both of the other cases there were a few slides that the pathologist either did not read, or the assistant did not record the reading, or the assistant recorded an ambiguous result. These cases account for missing data (Table 1).

The outside experts were not provided any criteria for reading the slides, except that they should read villous elements when present and that the degree of dysplasia should be classified as either high or low. After they completed their review, each was asked to define their criteria for villous elements and degree of dysplasia and to cite references supporting their definitions as they deemed appropriate.

After completion of the study and identification of generally low kappa values for interpretation of villous elements and HGD, we found that one of the outside experts used the same definition for HGD as the pathologists at our centre, but the kappa value for agreement between this outside expert and our staff pathologists was still low. Therefore we asked a single expert at our centre (O.C.) to review a subset of the slides, with the goal of determining whether the kappa values would improve when the outside expert who used the definition of HGD used at our institution was compared to our expert rather than to our routine staff pathologists' readings. Kappa values of <0 were considered to represent poor agreement, 0–0.20 slight agreement, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial and 0.81–1.00 almost perfect [14].

Mantel–Haenszel Chi-square tests were used to test for an association between dysplasia grade and the presence of villous elements separately for each pathologist. Generalized estimating equation methodology applied to binary data was used to test for an overall association while accounting for the examination of the slides by multiple pathologists.

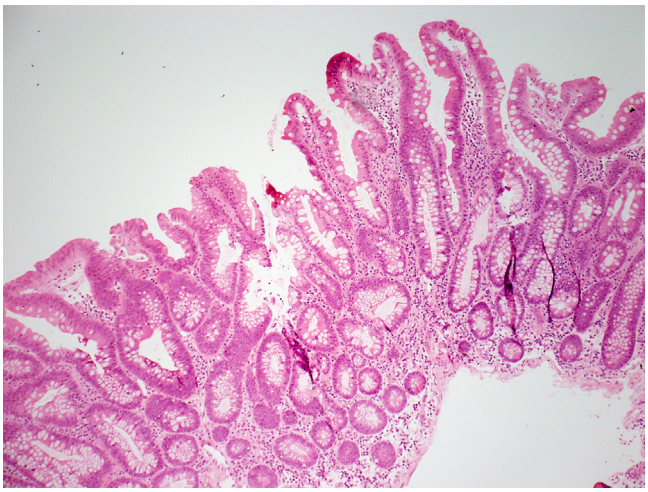

Fig. 1. A 7 mm adenoma that was interpreted as tubular by two pathologists and tubulovillous by two pathologists.

3. Results

The column "IU Interpretation" in Table 1 represents the original clinical interpretation by staff pathologists at Indiana University. Table 1 summarizes the percentage of adenomas read with villous elements and dysplasia grade by our pathologists and the 3 expert outside reviewers.

3.1. Villous elements

Neither our pathologists nor the outside pathologists thought that any of the polyps <6 mm in size was villous, and the outside pathologists found that none of the 6–9 mm polyps was villous. Our pathologists interpreted only 1 adenoma 6–9 mm in size as villous, so tubulovillous and villous are combined in Table 1. There was substantial variation in the percent of adenomas that were called tubulovillous, which ranged from 1% to 4% for adenomas <6 mm and from 1% to 12% for adenomas 6–9 mm in size, with significant differences between IU and outside pathologists and also between outside pathologists (Table 1).

Table 2 shows the kappa values for interpretation of the adenomas. For overall agreement in reading villous elements, the kappa values indicate fair agreement for both <6 mm and 6–9 mm adenomas (Table 2). Kappas were generally as high or higher between the IU reading and the outside pathologists compared to the kappas for agreement between the outside experts. Concordance levels were relatively high for villous elements, reflecting the low prevalence of villous elements in this consecutive sample of small adenomas.

Interview with the outside pathologists after completion of the survey determined that all 3 pathologists used the same criteria for interpretation of villous elements, namely those of the World Health Organization, i.e. the length of glands exceeding twice the length of the normal mucosa, and these features occupying at least 25% of the polyp [15]. Interview with the lead GI pathologists at our centre indicated that our pathologists are advised to use the same criteria. Fig. 1 shows a histologic section from a 7 mm adenoma that was interpreted as tubular by two pathologists and tubulovillous by two pathologists.