Increased Prevalence of Advanced Histologic Features in Small and Diminutive Polyps in Patients Undergoing Surveillance and Diagnostic Colonoscopy

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Objective: Studies addressing small and diminutive polyps and their potential of harboring advanced histologic features (AH) are scarce in Hispanics. We aimed to determine the prevalence of AH in a cohort of Hispanics.

Methods: A retrospective review of medical records of patients who had a colonoscopy from 2005 through 2010. The data collected included demographics, indications, history (personal/family) of colon cancer and/or polyps, and polyp histology. Polyps with high-grade dysplasia, prominent villous component, adenocarcinoma or serrated were classified as having AH.

Results: The population comprised 1884 patients, and 3835 polyps were evaluated; 63.3% were diminutive (1–5 mm), 22.7% small (6–9 mm), and 13.9% large (≥10 mm). The prevalence of AH for small and diminutive polyps were 4.9% and 1.1%, respectively. Of the polyps with AH, 11.9% were diminutive and 19.6% small. Small polyps were 5.04 times more likely to harbor AH than were diminutive polyps. Distal rather than proximal polyps were more likely to harbor AH. Furthermore, AH was >7 times more common in small (6–9 mm) polyps identified during diagnostic or surveillance colonoscopies compared to screening colonoscopies.

Conclusions: The prevalence of AH was significantly associated with size, location (distal), and procedure indication. Although diminutive polyps (<6 mm) were less likely to harbor AH, the risk for non-Hispanics was higher than previously reported. The "resect and discard" strategy for polyps ≤ 1 cm should be used with caution in ethnically diverse cohorts, as the risk for AH may be higher in Hispanics than in non-Hispanic Whites. [*P R Health Sci J 2023;42(2):139-145*]

Key words: Colonic polyps, Colonic neoplasms, Hispanic Americans, Prevalence study

Cancer is the second cause of death in the United States (US) and the first cause of death in Puerto Rico (PR) (1,2,3). According to 2018 national and state population estimates from the US Census, Hispanics represent about 18% of the US population, while Puerto Ricans are about 9.5% (2) of that Hispanic population. In the Hispanic population living in the US, cancer is the most common cause of death at all ages, and the colon is the second leading site of new cancer in both men and women (2). In PR, more specifically, colorectal cancer is the second cause of cancer-related death and the second most common cause of newly diagnosed cancer in men and women (3). Ethnicity-related disparities in colorectal cancer epidemiology may be attributed to biological, environmental, and/or health care system–related factors.

Screening is the mainstay of reducing colorectal cancer mortality (4). Current colorectal screening methods are divided into tests that are geared to detect colon cancer at early stages (stool based) and those that detect colorectal polyps and cancer by direct visualization. The main advantage of the colonoscopy, the most commonly used direct-visualization test for colon cancer, is that it allows for the identification and removal of pre-malignant colorectal polyps at the time of the examination (4). With the advent of higher resolution scopes and the emphasis on high-quality colonoscopy, the detection of small (6–9 mm) and diminutive (1–5 mm) colon polyps has increased significantly over the years (5–8).

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It is well known that most sporadic colon cancers arise from adenomatous or serrated colorectal polyps (9,10). Advanced adenomas are customarily defined as polyps that are at least 1 cm in size; with villous elements, or harboring severe dysplasia. In contrast, small (6–9 mm) and diminutive (≤5 mm) polyps are considered non-malignant (11–20). In 2011, the American Society for Gastrointestinal Endoscopy (ASGE) Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) initiative proposed the strategy of "resect and discard" for diminutive (≤5 mm) polyps (11). Cost analyses have found that this strategy is associated with cost savings and has a low impact on patients' cancer risk (12–15). Few studies on Hispanics have explored small and diminutive polyps and their potential for harboring advanced histologic features or invasive cancer (16,17). The primary aim of our study was to determine the magnitude of association between advanced histologic features and polyp size. In addition, we wanted to determine the magnitude of association between advanced histologic features and polyp size by location in the colon and the clinical indication for colonoscopy.

Methods

The study was a retrospective review of the medical records of consecutive patients who underwent a complete colonoscopy using a high-definition endoscope at the VA Caribbean Healthcare System from October 2005 through September 2010. The investigation was approved by the local Institutional Review Board, and the statistical analysis was supported by the PR Clinical and Translational Research Consortium of the University of PR Medical Sciences Campus as well as the National Institute on Minority Health and Health Disparities and National Institute of Allergy and Infectious Diseases, both being part of the National Institutes of Health, under award number U54MD007587.

The demographic data collected included sex (female/male), age (continuous and dichotomous variable), and indication for colonoscopy (screening, surveillance, or diagnostic). A diagnostic colonoscopy is a colonoscopy done to investigate abnormal gastrointestinal symptoms, or exams, such as having a positive fecal occult blood test. Data regarding personal and/or family history of colon cancer and/or polyps (as recorded in the medical record), polyp size (in millimeters, as documented by a pathology report), histology, and location in the colon (proximal or distal to the splenic flexure) were also collected. All the colorectal polyps that were found were considered for inclusion and were classified according to size to (≤5 mm, 6–9 mm, ≥10 mm). Each polyp was classified as being adenomatous or non-adenomatous (hyperplastic). Polyps with any of the following histologic features: high-grade dysplasia, a prominent villous component (villous or tubulovillous), adenocarcinoma or a serrated histology, were considered as having advanced histologic features. The pathological reports were reviewed by a second gastrointestinal pathologist to confirm the histologic findings.

Eligibility criteria

All the polyps that were removed during a colonoscopy and that had an available histologic examination (from October 2005 through September 2010) were included in the study. The exclusion criteria were having an inflammatory bowel disease and/or a hereditary polyposis syndrome, having more than 6 polyps on the index colonoscopy (suggestive of syndromic polyposis) (21), being older than 89 years of age, having a non-diagnostic histology, and having cancerous polyps

Outcomes

The primary outcome was to determine (based on the pathology report) the prevalences of diminutive (≤5 m), small (6–9 mm), and large (≥10 mm) polyps with advanced histologic features. The secondary outcome was to determine the prevalence of advanced histologic features per each clinical indication for colonoscopy and based on polyp location.

Statistical analysis

Summary statistics were used to describe the profiles of the veterans who underwent screening and surveillance colonoscopies within the VA Caribbean healthcare System in PR. Means and standard deviations were used for quantitative variables, such as age and number of polyps. Frequency distribution was used for categorical variables, such as histology, polyp size, location, and indication for colonoscopy.

Contingency tables (18) were used to describe the associations between advanced histologic features and polyp size, polyp location, and indication for colonoscopy. To assess the statistical significance of this association, the chi-squared distribution was used.

To evaluate our primary aim, a mixed logistic regression model was used to estimate the magnitude of the association (odds ratios [ORs]) with 95% confidence intervals (CIs), between the advanced histologic features and polyp size, adjusting for multiple polyps and polyp location (19). The parameter estimation was performed using the multilevel approach to control for a potential correlation in the presence of multiple polyps extracted from the same patient.

To examine our secondary aims, statistical methods similar to those used for the primary aim were employed, but stratified by colonic polyp location (proximal vs. distal) and colonoscopy indication (screening, diagnostic, or surveillance). Statistical analysis was performed using Stata/SE, ver. 14 (StataCorp LLC. College Station, Texas, USA).

Results

The study population consisted of 1884 patients, of which 1842 (97.7%) were men. The mean age of was 67.2 (±10.10) years. The indications for colonoscopy were as follows: 654 (34.7%) were for screening purposes, 636 (33.7%), diagnostic, and 594 (31.6%), surveillance (Table 1). Overall, a total of 3835 polyps were found, with an average of 2.04 (±1.29; range: 1–6)

polyps per subject. Of these, 63.3% (2429) were diminutive (1–5 mm), 22.7% (872) were small (6–9 mm), and 13.9% (534) were large (≥10 mm). Most of the polyps (2201; 57.4%) were found on the left side of the colon (from the splenic flexure to the rectum). The 2 most common histologic findings were tubular adenomas and hyperplastic polyps, totaling 2725 (71.1%) and 891 (23.2%), respectively (Tables 1 and 2). In 27.8% (61) of the cases the polyps were single (1 polyp per colonoscopy), while in 72.1% (158), there were multiple polyps (synchronous polyps in the colonoscopy). The clinical characteristics of the polyps according to their histologic features are presented in Table 3.

Table 1. Baseline characteristics of patients undergoing screening and surveillance colonoscopy at the Veterans Hospital in Puerto Rico (n = 1884).

Patient characteristic	n (%)
Sex	
Female	42 (2.23)
Male	1842 (97.67)
Age	
Mean ± SD	67.21 ± 10.10
Number of polyps per patient	
Mean ± SD	2.04 ± 1.29
Range (min – max)	1 – 6
Indication	
Screening	654 (34.69)
Diagnostic	636 (33.74)
Surveillance	594 (31.57)

Table 2. Characteristics of polyps removed from patients undergoing screening, diagnostic, and surveillance colonoscopy at the Veterans Hospital in Puerto Rico (n = 3835)

Polyp characteristic	n (%)
Histology	
Tubular adenoma	2725 (71.05)
Tubular adenoma/high-grade dysplasia	24 (0.60)
Tubulovillous	78 (2.03)
Villous	43 (1.12)
Serrated	31 (0.80)
Adenocarcinomas	43 (1.12)
Hyperplastic	891 (23.23)
Size	
≤ 5 mm	2429 (63.34)
6–9 mm	872 (22.74)
≥ 10mm	534 (13.92)
Location	
Right colon	1634 (42.61)
Left colon	1423 (37.11)
Rectum	778 (20.29)
*Multiplicity**	
Single polyp	893 (45.2)
Multiple polyps without HR	2492 (64.98)
Multiple polyps with 1 HR	377 (9.83)
Multiple polyps with at least 2 HRs	73 (1.90)

*Multiplicity refers to patients with more than 1 polyp on the same colonoscopic examination). HR = high risk, which was defined by the presence of high-grade dysplasia, a prominent villous component (villous or tubulovillous), a serrated histology or the presence of adenocarcinoma.

Of the 3835 polyps evaluated in this study, we identified 219 polyps harboring advanced histologic features. Of these, 26 (11.9%) polyps were diminutive (1–5 mm), 43 (19.6%) were small (6–9 mm), and 150 (68.5%) were large (≥10 mm) in size (Table 3). Advanced histologic features were identified in 26 (1.07%), 43 (4.93%), and 150 (28.08%) of the diminutive, small, and large polyps, respectively (P < .001). Small polyps (6–9 mm) were 5.04 times more likely to harbor advanced features compared to diminutive polyps (95% CI: 2.94–8.64). Moreover, large polyps (≥10 mm) were significantly more likely to have advanced histologic features compared to diminutive polyps (OR: 65.8; 95% CI: 35.27–122.70) (Table 3). Polyps with advanced histologic features were more likely to be located in the distal colon (distal to the splenic flexure) than in the proximal colon (OR: 2.48; 95%: CI: 1.75–3.51).

Association of Polyp size with advanced histologic features by Colonoscopy indication

Patients who underwent a diagnostic colonoscopy had a 55% higher likelihood of having polyps with advanced histologic features compared to patients whose colonoscopies were for the purpose of screening or surveillance (OR: 1.55; 95% CI: 1.03–2.32) (Table 3).

A stratified analysis examining the association between polyp size and advanced histologic features by colonoscopy indication was performed (Table 4 a–c). The probability of having advanced histologic features in small polyps (6–9 mm) was much higher when the indication for the colonoscopy was for diagnostic (OR: 7.52; 95% CI: 2.33–24.20) or surveillance purposes (OR: 7.38; 95% CI: 3.23–16.85) rather than for screening. In patients who had screening colonoscopies, large polyps (adjusted OR: 38.85; 95% CI: 14.57–103.63) were significantly more likely to have advanced histologic features compared to small (adjusted OR: 2.14; 95% CI: 0.74–6.18) or diminutive polyps (Table 4a).

Discussion

Small and diminutive colon polyps have been described in the literature as having very low risk for advanced histologic features compared with polyps larger than 1 cm. In the present study, we report increasing prevalences of advanced histologic features with increasing polyp size, the location of the polyp(s) (distal to the splenic flexure), and colonoscopy indication. Overall, small polyps were 5 times more likely to have advanced histologic features than were diminutive polyps, even after adjusting for age and having a personal/family history of colorectal cancer (OR: 5.04; 95% CI: 2.94 - 8.64). In the literature, the reported prevalences of advanced histologic features for small and diminutive polyps range from 0.2% to 1.7% for diminutive polyps (1–5 mm) and 1.5% to 6.6% for small polyps (5–9 mm in size) (12,13,16,20). Our reported prevalence was higher than were those of these studies, with advanced histologic features seen in 1.1% and 5% of diminutive and small polyps,

Table 3. Clinical characteristics of advanced versus non-advanced polyps for the complete cohort (n = 3835)

Variable	Advanced histology n = 219 n (%)	Non-advanced histology n = 3,616 n (%)	Crude OR (95% CI)	Age-adjusted OR (95% CI)*
Size				
≤ 5 mm	26 (11.87)	2403 (66.45)	Reference	Reference
6–9 mm	43 (19.63)	829 (22.93)	5.13 (3.00–8.80)	5.04 (2.94–8.64)
≥10mm	150 (68.49)	384 (10.62)	66.51 (35.62–124.17)	65.78 (35.27–122.70)
Indication				
Screening	60 (27.40)	1178 (32.58)	Reference	Reference
Diagnostic	97 (44.29)	1238 (34.24)	1.60 (1.07–2.40)	1.55 (1.03–2.32)
Surveillance	62 (28.31)	1200 (33.19)	1.00 (0.65–1.54)	0.96 (0.62–1.48)
Polyp location				
Proximal	57 (26.03)	1577 (43.61)	Reference	Reference
Distal	162 (73.97)	2039 (56.39)	2.36 (1.67–3.34)	2.48 (1.75–3.51)

OR: odds ratio. All ORs were calculated using mixed model logistic regression; distal colon: located distal to the splenic flexure.

respectively. This observed difference might be a result of biological and/or environmental factors associated with our studied population, which consisted mostly of Hispanic men. There are several well-studied factors associated with advanced histologic features, including being of an older age, being a male, suffering from obesity and smoking. Nevertheless, specific risk factors for the development of advanced histologic features in diminutive and small polyps have not been extensively studied (1,3,4,12–17,20). Some investigators have suggested that polyp size (small rather than diminutive), age (>65 years), and sex (male) are independent factors (20). In our study, we did not observe an association of advanced histologic features with age (>65 years).

Recent publications about our Puerto Rican Hispanic population reiterate the fact that there are patterns of ethnic and sex-related disparities when it comes to colorectal neoplasia, and that these differences are also present when our population is compared with others in the US that are composed of (non-Puerto Rican) Hispanics (22). Although there has been a decrease in colorectal cancer incidence and mortality in White males, this decrease is not reflected in the Hispanic male population. In addition, Hispanic men are more likely to have a higher proportion of distal colonic tumors compared to White males (23). In a study by Cruz-Correa et al., the overall prevalence of colorectal neoplasia, in a cohort of asymptomatic individuals undergoing screening colonoscopies in PR, was 25.1%, and 4% of the patients had advanced colorectal neoplasia (defined as lesions ≥1 cm with high-risk colonic adenomas with or without high-risk features). Furthermore, the investigators demonstrated that advanced histologic features were associated with distal colonic location. In our study, the prevalence of advanced histologic features in polyps of 1 cm or greater was much higher. This could be due to the fact that, in contrast with our current study, the Cruz-Correa et al. study included only patients undergoing screening colonoscopies and had a higher number of women. Similarly, we also found a higher risk of advanced histologic features in distal compared to proximal colonic polyps (OR: 2.48; 95% CI: 1.75–3.51).

One of the most important findings of our investigation was the higher proportion of advanced histologic features in small polyps found in patients undergoing either diagnostic or surveillance colonoscopies. Thus, the increased risk of having advanced histologic features in small polyps found during non-screening colonoscopies would support, in this context, resecting all small polyps and submitting them for pathologic evaluation. In 2011, the PIVI program of the ASGE evaluated the "resect and discard" strategy for dealing with diminutive polyps (11). This strategy relies on the ability of the endoscopist to predict a given polyp's histology by using advanced endoscopic technologies such as narrow-band imaging (NBI) (11,14) and optical chromoendoscopy. The strategy was proposed as a cost-containment measure based on 4 major factors (15). The first was that at least 1 polyp would be identified in 1 of every 2 colonoscopies; the second was that most of the polyps found would be no more than 5 mm in size; the third was that the estimated cost of a histologic examination is similar to that of a colonoscopy; and the fourth was that there would be an additional financial burden associated with the follow-up visit to communicate results (14). According to the PIVI recommendations, this strategy should be applied only when the concordance with pathology-based decisions about assigning post-polypectomy surveillance intervals is greater than 90% and the histology of the identified polyp is predicted in real time using advanced endoscopic techniques (11). A 2015 review and meta-analysis established that the initial thresholds for the real-time assessment of diminutive polyps with NBI optical biopsy were met and the post-polypectomy surveillance intervals were appropriate, thus supporting the use of the "resect and discard" strategy for adenomas that are 5 mm or smaller (24). Although our study confirmed that the majority (63.3%) of the polyps identified through colonoscopy were diminutive, it also identified the potential risk of failing to identify advanced histologic features in 1.1% of these polyps and, as a consequence, assigning incorrect surveillance intervals. Moreover, a third of all the polyps with advanced histologic features were less than 9 mm in size, thus highlighting the importance of incorporating other factors, such as sex, polyp location, and ethnicity and/or race, into the clinical assessment of diminutive and small polyps.

The present study has several strengths, including the independent evaluation of high-risks polyps by 2 pathologists, the use of a large cohort of patients and polyps, and a well-characterized Hispanic population (Puerto Rican Hispanics

Table 4a. Association of polyp size and advanced histologic features in individuals undergoing screening colonoscopy (n = 1238)

Variable	Screening			
	Advanced histology n = 60 n (%)	Non-advanced histology n = 1178 n (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Size				
≤ 5 mm	9 (15.00)	770 (65.37)	Reference	Reference
6–9 mm	7 (11.67)	268 (22.75)	2.16 (0.77–6.08)	2.14 (0.74–6.18)
≥10 mm	44 (73.33)	140 (11.88)	37.92 (14.80–97.14)	38.85 (14.57–103.63)

Table 4b. Association of polyp size and advanced histologic features in individuals undergoing diagnostic colonoscopy (n = 1335)

Variable	Diagnostic			
	Advanced histology n = 97 n (%)	Non-advanced histology n = 1238 n (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Size				
≤ 5 mm	10 (10.31)	846 (68.34)	Reference	Reference
6–9 mm	20 (20.62)	261 (21.08)	7.29 (3.16–16.83)	7.38 (3.23–16.85)
≥10 mm	67 (69.07)	131 (10.58)	74.63 (27.90–199.65)	62.18 (23.97–161.31)

Table 4c. Association of polyp size and advanced histologic features in individuals undergoing surveillance colonoscopy (n = 1262)

Variable	Surveillance			
	Advanced histology n = 62 n (%)	Non-advanced histology n = 1200 n (%)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Size				
≤ 5 mm	7 (11.29)	787 (65.58)	Reference	Reference
6–9 mm	16 (25.81)	300 (25.00)	7.82 (2.40–25.49)	7.52 (2.33–24.20)
≥10 mm	39 (62.90)	113 (9.42)	138.57 (28.80–666.67)	140.70 (29.43–672.52)

OR: odds ratio. All ORs were calculated using mixed model logistic regression. *Adjusted for sex (female vs. male), age (as a continuous variable), polyp location (distal vs. proximal), and familial history of polyp cancer (no vs. yes).

living in PR). Another strength is the use of pathologists' measures of polyp sizes. Several studies have addressed the discordance between the estimates of polyp size made by endoscopists and the actual measurements made by the pathologists measurements. Using the pathologists' measurements allowed us to reduce the size estimate bias of the endoscopists (25,26). Our study has several limitations, including its retrospective nature, the limited analysis of confounding factors, and the temporality of exposures. In addition, the nature of the study population, consisting mostly of male patients, limits the generalizability of our findings.

Our study reported a higher prevalence of advanced histologic features in diminutive and small polyps than did studies in non-Hispanic cohorts. Most importantly, the risk of having advanced histologic features increased for polyps identified during diagnostic and/or surveillance colonoscopies. To our knowledge, this specific association for small and diminutive polyps has not been previously reported, as data regarding advanced histologic features are usually grouped irrespective of colonoscopy indication. Based on our findings, we thus support removing small and diminutive polyps for histologic examination, especially polyps identified during diagnostic and/or surveillance colonoscopies. Until new advanced imaging techniques are properly validated and widely available and endoscopists are properly trained in their use, applying the guidelines on "resect and discard" is premature for populations with a high risk of advanced histologic features including Puerto Rican Hispanics, diabetics, individuals who are obese, and those with a family history of colorectal cancer (27). Prior to the implementation and dissemination of the "resect and discard" strategy, several ethical, liability-related, quality control–related, and economic factors need to be taken into consideration. In this era of high-quality colonoscopy, the adenoma detection rate (ADR) has become the most important measure of the quality of the colonic mucosa inspection (6,7). The endoscopist's ADR is based upon validation through a histologic examination of the resected specimen. In the absence of a histologic examination of diminutive polyps, if the "resect and discard" strategy is implemented, the endoscopist's ADR will depend solely on self-reported and unconfirmed adenoma detection, not validated by histologic confirmation. This may impose an additional challenge not envisioned at the time that the "resect and discard" strategy was proposed. Hence, developing and exploring additional endoscopic imaging and validation methods for correctly classifying small and diminutive polyps is warranted before the extensive implementation of the "resect and discard" strategy across diverse populations.

In summary, our study demonstrated an association between advanced histologic features and polyp size, distal colonic location, and the indication for a given colonoscopic procedure (diagnostic or surveillance-related). Although polyps of less than 6 mm were less likely to harbor advanced histologic features than larger polyps, the prevalence was higher than what has

been previously reported for non-Hispanic cohorts (12). Based on our findings, the "resect and discard" strategy for small and diminutive polyps should be used with caution in individuals of certain ethnic and racial backgrounds, as the prevalence of advanced neoplasia in small colorectal polyps might be higher than previously reported.

Resumen

Objetivo: La población hispana cuenta con pocos estudios que evalúen la presencia de histologías avanzadas (HA) en los pólipos colónicos pequeños y diminutos. Nuestra meta fue determinar la prevalencia de HA en una población Hispana. Metodología: Se estudiaron retrospectivamente los expedientes médicos y colonoscopias realizadas durante el 2005 al 2010. Se recolectó información demográfica, indicaciones, historial (familiar/personal) de cáncer de colon y/o pólipos, y la histología. Aquellos pólipos con displasia de alto grado, vellosos, serrados o adenocarcinoma se consideraron como HA. Resultados: Se evaluaron 3835 pólipos en 1884 pacientes; 63.3% diminutos (1-5 mm), 22.7% pequeños (6-9 mm) y 13.9% grandes (≥10 mm). La prevalencia de HA en pólipos pequeños y diminutos fue 4.9% y 1.1%, respectivamente. Entre los pólipos con HA, 11.9% eran diminutos y 19.6% eran pequeños. Los pólipos pequeños tenían 5.04 veces más riesgo que los diminutos; al igual que los más distales comparados con los proximales. La HA resultó ser >7 veces más común en pólipos pequeños identificados en estudios diagnósticos o de vigilancia en comparación con los de cernimiento. Conclusión: La prevalencia de la HA en pólipos <1cm resultó estar significativamente asociada al tamaño, la localización distal y la indicación. Los pólipos diminutos se asociaron con una baja probabilidad de desarrollar histología avanzada; sin embargo, el riesgo fue mayor al reportado en poblaciones no hispanas. La estrategia de "remover y descartar" pólipos pequeños se debe utilizar con cautela dentro de grupos étnicamente diversos ya que el riesgo de histología avanzada puede ser mayor.

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