Relationship between Sporadic Hyperplastic Polyps and Colorectal Neoplasia in Hispanic Veterans

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Objective: Hyperplastic polyps (HP) traditionally have been regarded as having no malignant potential. Some studies have suggested that HP in the distal colon may predict presence of adenomatous polyps in the proximal colon. Other studies have failed to show this relationship. The purpose of this study was to evaluate for the first time in our Hispanic veterans population if there was a relationship between the presence of sporadic HP and colorectal neoplasia (CRN) and to evaluate if proposed risk factors for CRN are also risk factors for sporadic HP.

Methods: The study consisted of a retrospective review of all the medical records of patients who underwent a colonoscopy for the first time during the calendar year 2005 and had a pathologic diagnosis of HP, tubular adenoma (TA), tubulovillous adenoma (TVA), villous adenoma (VA) and/or colon adenocarcinoma at the VA Caribbean Healthcare System. Patient's age, BMI, smoking and alcohol use history, presence of DM, cholesterol and triglyceride levels, use of aspirin and the size and location of the lesions were recorded. Records with incomplete data and patients with a prior colonoscopy were excluded.

Results: 861 patient records were reviewed of which 405 met the inclusion criteria. Most patients (99%) of the patients were males, mean age 67.5 (range 36-87). The total number of colonic lesions was 1,065 (240 hyperplastic, 825 CRN). Histologic evaluation of lesions revealed: 121 patients who had HP, 331 with TA, 33 with TVA, 12 with VA, 13 with serrated adenomas and 61 patients had adenocarcinoma. Univariate analysis revealed that patients with HP appeared to have a lower likelihood of having TA (p<0.001), adenocarcinoma (p=0.002), and CRN in general (P<0.001) as compared to patients without HP. Multivariate analysis with logistic regression revealed that patients with HP had a significantly lower likelihood of having TA (adjusted OR = 0.21; 95% CI 0.12 - 0.37), and adenocarcinoma (adjusted OR = 0.33; 95% CI 0.15 – 0.73) compared to patients without HP. No correlation was found between DM, use of alcohol, smoking, or aspirin use and the presence of sporadic HP.

Conclusion: The present study suggests that the presence of HP is not associated with CRN in our veteran population. None of the risk factors proposed for CRN appear to be also risk factors for developing HP. The results of this study support current colon cancer guidelines in which surveillance for HP is not recommended. [*P R Health Sci J 2010;4:372-376*]

Key words: Polyps, Neoplasia, Adenocarcinoma

Colorectal carcinoma affects more than 150,000 patients per year in the United States, causing more that 50,000 cancer related deaths per year, a rate second only to lung cancer (1-2). Similarly, CRC accounts for 13% of all cancer deaths in PR affecting approximately 1,500 individuals every year (Puerto Rico Central Cancer Registry Data, 2004). Screening and surveillance colonoscopy regimens recommended by medical professional societies can decrease the morbidity and

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mortality by removal of premalignant polyps, and early detection of colon cancer at a curable stage (2).

A colon polyp is an abnormal growth of tissue along the lining of the colon. It may be characterized by its gross appearance according to the presence or absence of a stalk and its size, but regardless of the macroscopic features, specific definition is based on the histologic characteristics (1).

Colon polyps can be divided into two large groups, neoplastic and non-neoplastic. Histologically, adenomas have a glandular architecture making evident their neoplastic nature. Tubular adenomas are the most common subgroup, followed by tubulovillous and villous adenomas. By definition, all adenomas are dysplastic, and therefore, carry a potential of malignant transformation. Tubular adenomas are usually small with mild degree of dysplasia whereas villous adenomas are often larger and with a severe degree of dysplasia. The potential for malignant transformation increases with size and villous morphology.

The most common non-neoplastic lesion in the colon is the hyperplastic polyp. Hyperplastic polyps are usually small (typically <5mm in diameter), with a prevalence of 10-35% in Western populations (2). The characteristic microscopic feature of a hyperplastic polyp is the serrated or saw-tooth configuration of the crypt epithelium. Traditionally, hyperplastic polyps have been regarded as to having no malignant potential. Some studies have suggested that the presence of hyperplastic polyps in the distal colon may predict the presence of adenomas in the proximal colon, whereas other studies have failed to show this relationship in asymptomatic, average-risk subjects (3-4). Current guidelines from American College of Gastroenterology, American Gastroenterology Association, World Health Organization, American Society for Gastrointestinal Endoscopy, and the American Cancer Society recommend follow up colonoscopies at the same interval as for normal colonoscopies do not recommend surveillance colonoscopy following the removal of hyperplastic polyps alone (5) .

Recent studies have shown that hyperplastic polyps may exhibit a number of genetic alterations associated with colon cancer, including DNA microsatellite instability (MSI), activating mutations in K-ras or BRAF, TGF beta RII, and loss of heterozygosity (LOH) of chromosome 1p (6-8). Some studies have shown that the prevalence of hyperplastic polyps is similar to the incidence of colorectal cancer than is the prevalence of adenomatous polyps, in both high and low-risk populations (3). Hyperplastic polyps can develop as sporadic hyperplastic polyps and as a particular syndrome known as hyperplastic polyposis syndrome. Evidence is accumulating that there may be a link between the presence of hyperplastic polyps and colorectal neoplasia, particularly in the case of hyperplastic polyposis (3, 6). Hyperplastic polyposis syndrome is a clinical entity characterized by multiple and/or large hyperplastic polyps throughout the colon, in coexistence with serrated adenomas, traditional adenomas and mixed polyps (5). The proposed definition of hyperplastic polyposis include the following criteria: at least 5 histopathologically diagnosed hyperplastic polyps proximal to the sigmoid colon, of which 2 are greater than 10 mm in diameter; any number of hyperplastic polyps occurring proximal to the sigmoid colon in an individual who has a first degree relative with hyperplastic polyposis; and more than 30 hyperplastic polyps of any size, but distributed throughout the colon (3).

The serrated appearance of hyperplastic polyps may also be seen in two other entities: serrated adenomas and mixed polyps. Serrated adenomas comprise crypts that simultaneously demonstrate the saw-tooth appearance of hyperplastic polyps and the epithelial dysplasia of adenomas. Mixed polyps (also known as admixed polyps) show a combination of discrete hyperplastic and adenomatous components. Hyperplastic polyps, serrated adenomas and mixed polyps are known collectively as serrated polyps. Recent advances in the knowledge of the molecular basis of colorectal carcinoma have set the foundation for the development of a proposed alternate mechanism of developing colon cancer known as the serrated polyp neoplasia pathway (3, 5).

Several environmental factors have been proposed to influence the development of colorectal neoplasia. High fat diet, alcohol consumption, diabetes mellitus, obesity, sedentary lifestyle and cigarette smoking have been associated as being risk factors for the development of colon cancer (1, 3, 9-10). A low body mass index, and use of ASA/NSAID's, has been proposed as protective factors against the development of colorectal cancer (1, 11-12).

The Puerto Rico Veteran population is composed predominantly by males, above 50 years old, which as recommended by the American Gastroenterology Association Guidelines for Colorectal Cancer Screening and Surveillance, are offered the alternative of screening colonoscopy as a preventive measure. We conducted a retrospective study analyzing pathology reports from colonoscopies with polypectomies, in an attempt to determine if there was a relationship between the presence of hyperplastic polyps and colorectal neoplasia. The relationship of the location of hyperplastic polyps and the presence of colorectal neoplasia was evaluated. Lastly we analyzed if proposed environmental factors considered to influence colorectal cancer, play a role in the development of hyperplastic polyps in our studied population.

Methods

A computer search was done for pathology diagnoses of hyperplastic polyps, tubular adenomas, tubulovillous adenomas, villous adenomas and colon adenocarcinoma using VISTA computerized medical record. The search was done starting from January 1, 2005 through December 31, 2005. After obtaining the results, colonoscopy reports were reviewed to determine the location of the polyps and/or cancer. Computerized Patient Record System (CPRS) was also reviewed to determine patient's age, body mass index (BMI) at the time of the colonoscopy,

smoking history, alcohol use history, presence of diabetes mellitus, cholesterol and triglyceride levels, and use of aspirin.

Index colonoscopy was defined as the first colonoscopy done in each patient included in this study as documented in the CPRS medical record. Polyps localized in the proximal colon were defined as those polyps found in the cecum, ascending colon and transverse colon as described in the colonoscopy report. Polyps localized in the distal colon were defined as those polyps found in the splenic flexure, descending colon, sigmoid colon and rectum. The presence of diabetes mellitus was established by having the diagnosis on the CPRS medical record Problem List or as having a blood glucose level ≥ 200 mg/dL in two separate days or as having a fasting blood glucose level ≥ 126 mg/dL in two separate days. Hypercholesterolemia was defined as having a total cholesterol level above 200mg/dL. Hypertriglyceridemia was defined as having a triglyceride level above 200mg/dL. Use of aspirin was established as having this medication prescribed in the medication profile of the CPRS medical record for at least one year prior to the index colonoscopy.

Specimen pathologic reports were used to categorize lesions into two major groups: hyperplastic polyps and colorectal neoplasia. Size and morphology was tabulated based on pathology reports. Lesions corresponding to the colorectal neoplasia group were further classified into: tubular adenoma, tubulovillous adenoma, villous adenoma, serrated adenoma, and adenocarcinoma.

Inclusion criteria

All patients who underwent a complete colonoscopy for the first time, for any indication (including average risk screening, family history of colon cancer or polyps, changes in bowel habits, abdominal pain, weight loss, positive fecal occult blood test, chronic diarrhea, anemia, rectal bleeding, melena with negative EGD, and abnormal imaging study) as documented in the CPRS medical record that were found with a pathologic diagnosis of hyperplastic polyp, tubular adenoma, tubulovillous adenoma, villous adenoma and colon adenocarcinoma from January 1, 2005 through December 31, 2005 were included.

Exclusion Criteria

All patients with a colonoscopy prior to the study period, incomplete studies, studies with poor bowel preparation, and records with incomplete data were excluded from the analysis.

Statistical Analysis

A sample size of 382 subjects was determined to be representative of the population of Hispanic veterans in Puerto Rico assuming a disease prevalence of 50%. The main outcome of the study was to determine if there was a relationship between the presence of sporadic hyperplastic polyps and colorectal neoplasia. Tests statistics to observe association between variables (presence of hyperplastic polyps, presence of neoplastic polyps, diabetes mellitus, BMI, use of NSAID's, etc.) was measured with Pearson's Chi square and multivariate analysis with logistic regression was performed to calculate OR's to determine the association of the mentioned variables with the presence of hyperplastic polyps as compared to not having hyperplastic polyps. Statistical significance was established when p value was < 0.05.

Results

A total of 861 records were reviewed using both the VISTA and CPRS electronic medical records. Four hundred and fifty six records had to be excluded from the analysis due to incomplete data or because the subject had a colonoscopy done prior to the study period. Four hundred five records met the inclusion criteria. Four hundred one patients were males (99%), four females (1%) with a mean age of 67.5 (from 36 to 87 years old). Refer to Table 1 for patient characteristics and indications for colonoscopy.

Table 1. Patient Characteristics

Patient Characteristics	N = 405
Age (mean ± SD) [years]	67.5 ± 10.26
Male (%)	401 (99%) 4 (1%) 176.6 ± 32.46
Female (%)	
Weight (mean ± SD) [lbs]	
Height (mean ± SD) [in]	69.1 ± 2.85
BMI (mean ± SD) [kg/m2]	27.2 ± 4.32
Smokers (%)	139 (34.3%)
Alcohol (%)	188 (46.3%)
Diabetes mellitus (%)	155 (38.3%)
High cholesterol (%)	260 (64.2%)
High triglycerides (%)	188 (46.4%)
Aspirin use (%)	272 (67.2%)
Indication for colonoscopy (%)	
FOBT (+)	143 (35.3%)
Abnormal imaging study	75 (18.5%)
Screening colonoscopy	66 (16.3%)
Hematochezia	41 (10.1%)
Anemia	30 (7.4%)
Changes in bowel habits	16 (4.0%)
Family history of colon cancer/polyps	11 (2.7%)
Constipation	8 (2.0%)
Melena with negative EGD	6 (1.5%)
Abdominal pain	5 (1.2%)
Weight loss	3 (0.7%)
Abnormal rectal exam	1 (0.3%)

FOBT: Fecal occult blood test; EGD: Esophagogastroduodenoscopy

The total number of colonic lesions was 1,065 (240 hyperplastic polyps, 825 colorectal neoplasias). Of the 405 patients included in the study, 40 (9.9%) only had hyperplastic polyps, 284 (70.1%) only had colorectal neoplasia, and 81 (20%) had both hyperplastic polyps and colorectal neoplasia. One hundred twenty one (29.8%) patients had hyperplastic polyps, 331 (81.7%) patients had tubular adenomas, 33 (8.1%) patients had tubulovillous adenomas, 12 (2.9%) patients had

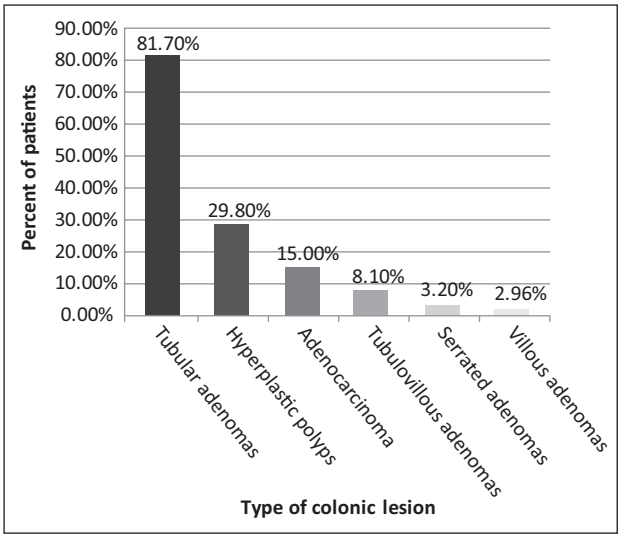

Figure 1. Distribution of Identified Colorectal lesions

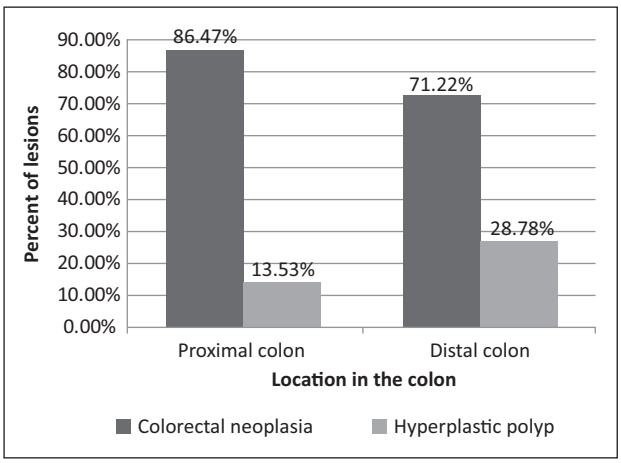

Figure 2. Distribution of Hyperplastic Polyps and Colorectal Neoplasia by Location

villous adenomas, 13 (3.2%) patients had serrated adenomas and 61 (15.0%) patients had adenocarcinoma (Figure 1).

The geographic distribution of lesions in the colon was as follows: colorectal neoplasia in the proximal colon: 377 (46%); colorectal neoplasia in the distal colon: 448 (54%); hyperplastic polyps in the proximal colon: 59 (24.5%); and hyperplastic polyps in the distal colon: 181 (75.5%) (Figure 3). There were a total of 194 polyps or lesions ≥ 1cm in size of which only 6 of them were hyperplastic polyps. No cases of hyperplastic polyposis syndrome were detected.

Univariate analysis using Pearson Chi-Square revealed that patients with hyperplastic polyps appeared to have a lower likelihood of having tubular adenomas ($p<0.001$), adenocarcinoma ($P=0.002$), and colorectal neoplasia in general ($P<0.001$) when compared to patients without hyperplastic polyps. Multivariate analysis with logistic regression revealed that patients with hyperplastic polyps had a significantly lower likelihood of having tubular adenomas (adjusted OR = 0.21; 95% CI 0.12 - 0.37), and adenocarcinoma (adjusted OR = 0.33; 95% CI 0.15 – 0.73) compared to individuals without hyperplastic polyps. No correlation was found between diabetes mellitus, use of alcohol, smoking, or aspirin use and the presence of sporadic hyperplastic polyps.

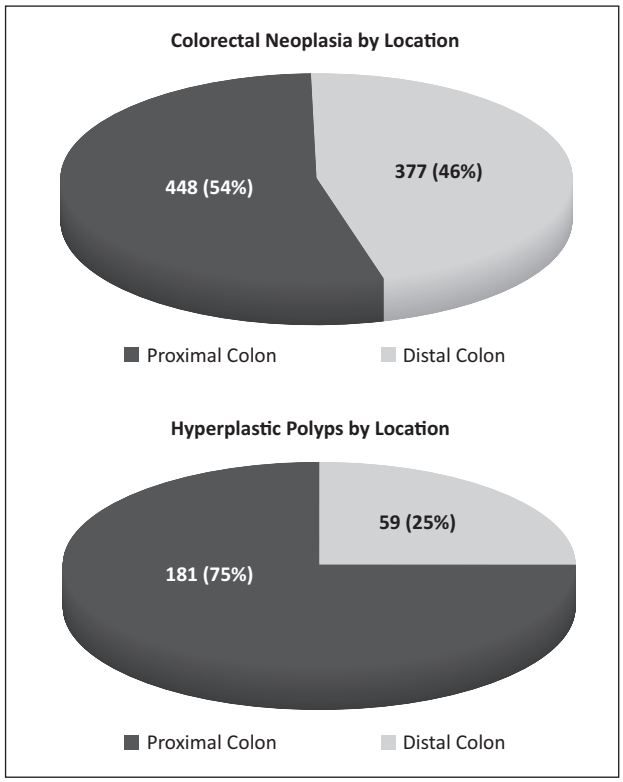

Figure 3. Lesions by Location

Discussion

The present study suggests that the presence of hyperplastic polyps is not associated with an increased risk for developing colorectal neoplasia in the selected Hispanic veteran population in Puerto Rico. On the contrary, our study suggests that the presence of hyperplastic polyps is associated with a lower likelihood of harboring colorectal neoplasia. To our knowledge this is the first study that attempts to establish a relationship between hyperplastic polyps and colorectal neoplasia in a Hispanic population.

The results of this study support the hypothesis that colorectal neoplasia and hyperplastic polyps have different developmental carcinogenic pathways. The distribution of hyperplastic polyps and colorectal neoplasia throughout the colon correlate with that previously described in the literature. None of the proposed risk factors for colorectal neoplasia such as diabetes mellitus, hyperlipidemia, smoking or alcohol use, appear to play a role in the development of hyperplastic polyps in our studied population. The results of this study support current colon cancer guidelines in which surveillance for hyperplastic polyps is not recommended.

We find particularly interesting that a high percentage of our patients who had a first colonoscopy and had a neoplastic colonic lesion, with adenocarcinoma identified in 15% of patients. Although our population consists mostly of elderly patients, this finding may suggest that our current screening program for colon cancer should be reinforced, perhaps to target patients at a younger age, to detect colorectal neoplasia at an earlier stage.

Serrated adenomas have an increased malignant potential. These polyps show a predilection for the proximal colon and are usually sessile. These lesions differ from hyperplastic polyps showing epithelial dysplasia, exaggerated serrations, crypt dilation, and increased mucin secretion. Although the identification of large right sided hyperplastic polyps in our study may suggest underdiagnosis, this could not be corroborated since the pathology slides were not reviewed by a single blinded pathologist. The identification of serrated polyps in 3.2% of the patients included in the study, suggests that the pathologists involved in the interpretation of these histological slides were knowledgeable about this entity, therefore unlikely to have been underestimated.

We acknowledge that our study is retrospective, and therefore had some limitations. For example we could not quantify smoking or alcohol use. The compliance with the use of aspirin could not be corroborated. And finally, more than half of the screened patients had to be excluded and may have limited the generalizability of the analysis; however, the study sample size was determined to be representative of the population based on the prevalence of colorectal neoplasia among a screening VA population.

Resumen

Objetivo: Tradicionalmente se ha pensado que los pólipos hiperplásicos (PH) no tienen ningún potencial de transformarse en malignidad. Hay estudios que sugieren que PH en el colon distal pudieran predecir la presencia de pólipos adenomatosos en el colon proximal. Otros estudios no han demostrado esta relación. El propósito de este estudio fue evaluar por primera vez, en nuestra población de veteranos hispanos, si existe una relación entre la presencia de pólipos hiperplásicos esporádicos (PHS) y neoplasia colorectal (NCR), y también evaluar si los factores de riesgo para el NCR son también factores de riesgo para PHS. Métodos: El estudio consistió en una revisión retrospectiva de todos los registros médicos de pacientes que fueron sometidos a una colonoscopia por primera vez durante el año calendario 2005 y tuvieron un diagnóstico patológico de PH, adenoma tubular (AT), adenoma tubulovelloso (ATV), adenoma velloso (AV) y adenocarcinoma de colon en el VA Caribbean Healthcare System. Se obtuvo información sobre el paciente, la edad, IMC, historial de uso de tabaco y alcohol, presencia de DM, los niveles de colesterol y triglicéridos, uso de aspirina y el tamaño y la ubicación de las lesiones. Se excluyeron los registros con datos incompletos y los pacientes con colonoscopias previas. Resultados: Se revisaron 861 registros de pacientes, de los cuales 405 cumplieron los criterios de inclusión (intervalo de confianza de 95%). 99% de los pacientes eran varones, edad promedio de 67.5 (36-87). 121 pacientes tuvieron PH, 331tuvieron AT, 33 tuvieron ATV, 12 tuvieron AV, 13 tuvieron adenomas serrados y 61 pacientes tuvieron adenocarcinoma. El número total de lesiones del colon encontradas fue 1.065 (240 hiperplásicas, 825 NCR). Análisis de univariable utilizando la prueba de estadística de independencia revelo que los pacientes con PH parecían tener una menor probabilidad de tener AT ($p < 0.001$), adenocarcinoma ($P = 0.002$) y NCR en general ($P < 0.001$) en comparación con los pacientes sin PH. Análisis multivariable de regresión logística reveló que los pacientes con PH tuvieron una probabilidad significativamente menor de tener AT (RP ajustado = 0.21; 95% IC 0.12 – 0.37) y adenocarcinoma (RP ajustado = 0.33; 95% IC 0.15 – 0.73) en comparación a los pacientes sin PH. No se encontró correlación entre DM, uso de uso de alcohol, fumar, o uso de aspirina y la presencia de PHS. Conclusión: El presente estudio sugiere que la presencia de PH no está asociada con NCR en nuestra población de veteranos. Ninguno de los factores de riesgo propuestos para NCR parecen ser también, factores de riesgo para el desarrollo de PH. Los resultados de este estudio apoyan directrices actuales de cáncer de colon en las cuales no se recomienda la vigilancia para PH.

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