

PREVALENCE OF HIGH-GRADE DYSPLASIA AMONGST VETERAN MEMORIAL MEDICAL CENTER PATIENTS WITH SUBCENTIMETER COLORECTAL POLYPS ON COLONOSCOPY

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ABSTRACT

Significance: Colorectal cancer (CRC) is a major cause of morbidity and mortality throughout the world and most of which arise from adenomatous polyps. Early recognition and use of polypectomy reduces the occurrence of CRC. However, controversy exists as to the likelihood that small and diminutive adenomas harbor significant advanced histology which increases risk for CRC. The prevalence of advanced histology in such polyps has become a crucial issue in optimizing CRC screening strategies. This study aims to determine prevalence of high grade dysplasia amongst Veteran Memorial Medical Center patients with subcentimeter colorectal polyp on colonoscopy

Methodology: This is a cross-sectional study which involved retrieving previous colonoscopy records from January 2012 to December 2016. Patients with polyps less than 1 cm were included and histopathologic reports were retrieved.

Results: Majority of patients found to have subcentimeter polyps with high-grade dysplasia were male with an average age of 69 ± 12 years. The prevalence of high-grade dysplasia amongst patients with subcentimeter polyps was at 31.6%. Majority of them were diminutive with an average diameter of 0.5 cm. Most of which were located distally (72%) particularly at the sigmoid colon (38%).

Conclusion: We noted higher prevalence of subcentimeter polyps with high-grade dysplasia among elderly Filipino patients compared to previous international studies. This strengthens our advocacy of promoting screening colonoscopy since patients with high-grade dysplasia will have an earlier follow-up colonoscopy after 3 years. We conclude that subcentimeter polyps are clinically significant and should not be easily ignored.

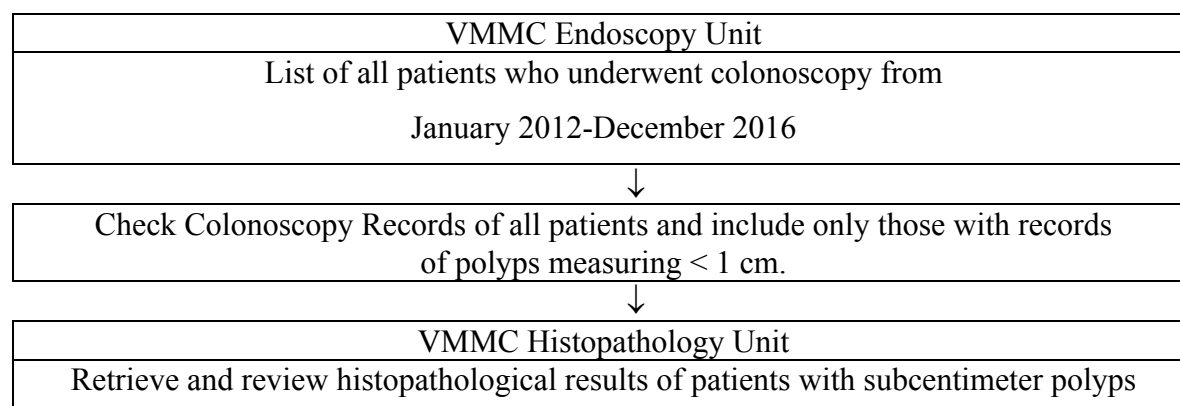
Keywords: High Grade Dysplasia, Subcentimeter polyps

INTRODUCTION

Colorectal cancer (CRC) is a major cause of morbidity and mortality throughout the world. It accounts for over 10% of all cancer incidence. It is the third most common cancer worldwide and the fourth most common cause of death. It affects men and women almost equally. It now is generally accepted that most (95%) colorectal cancers arise from benign, neoplastic adenomatous polyps. Colonic adenomatous polyps are premalignant lesions. Early recognition and use of polypectomy for these polyps can reduce the occurrence of colorectal cancer. The prevalence of polyps in average-risk, asymptomatic persons is at least 20%–30%. The majority of these polyps will be 10 mm or smaller. However, controversy exists as to the likelihood that small and diminutive adenomas harbor significant advanced histology (defined as high-grade dysplasia, carcinoma, or villous elements). Such advanced histology found in any polyp generally is considered to pose a risk for colorectal cancer.⁵ The prevalence of advanced histology in small polyps has become a crucial issue in optimizing colorectal cancer screening strategies. Yamaji et al. presented that the proportion of malignant neoplasms among lesions <20 mm was 0.21%, 0.31%, and 0.75% in the young, middle, and old age groups, respectively, showing a significant increasing trend with age.²⁰ The aim of this study is to determine the prevalence of high grade dysplasia amongst VMCC patients with subcentimeter colorectal polyp and show their clinical relevance in terms of malignant potential hence the need for polypectomy regardless of size.

METHODOLOGY

This is a retrospective cross-sectional study. Currently, there are no local data available regarding prevalence of dysplasia or malignancy among subcentimeter colorectal polyps in the Philippines hence retrospective study was chosen. A total of 5-year data review was done. Data obtained will hopefully be used as baseline data for further prospective studies. Computed Sample Size via OpenEPI is at least 46 patients based on prevalence of 0.75% study from Yamaji *et al.* (2006) that the proportion of malignant neoplasms among sub-centimeter polyps at old age is 0.75%. The medical records of VMMC patients (both inpatient and outpatient) who underwent colonoscopy with polypectomy from January 2012-December 2016 were reviewed. Inclusion Criteria: 1) Polyp < 1 cm 2) Histopathologic result released by VMMC Histopathology Section. Patient characteristics, and polyp sizes, gross morphologies, locations, and histopathologic report were evaluated.



RESULTS

There was a total of 272 polyps reviewed and analyzed from 239 patients with subcentimeter polyps on colonoscopy in 2012 to 2016. Table 1.0 depicts the baseline characteristics of the patients enlisted in the study.

Table 1.0 Baseline Characteristics of Patients with Subcentimeter polyps on Colonoscopy (2012-2016) in Veterans Memorial Medical Center

Characteristics	Total (N)	239 patients
Age	Average Age (years)	66 ± 11 years
	Maximum	94
	Minimum	33
Gender	Male	172 (72%)
	Female	67 (29%)
Indication for Colonoscopy	Screening	187 (78.24%)
	Episode of Hematochezia	21(8.79%)
	Chronic Constipation	31(12.97%)
Number of polyps	1	207 (86.61%)
	2	30 (12.55%)
	3	2 (0.84%)

We evaluated patients referred for colonoscopy between January 2012 to December 2016. Majority (72%) were male with average age of 66±11 years old. There was an average of 1 polyp obtained with screening purpose as the most common indication for the colonoscopy.

Majority of the polyps obtained were diminutive (81%), located at the sigmoid colon (38%) and with histopathologic diagnosis of Tubular Adenoma with Low-Grade Dysplasia (61.76%). There was a lower prevalence of adenocarcinoma among subcentimeter polyps at 0.74% but with substantial proportion of which have high grade dysplasia at 31.6% (Table 2.0 and Table 3.0).

Table 2.0 Baseline Polyp Characteristics and Histopathologic Diagnosis

Characteristics	N= 272 polyps
Size	
<i>Diminutive (</5 mm)</i>	221 (81%)
<i>Small (6-10 mm)</i>	51 (19%)
Location	
<i>Rectum</i>	58 (21.32%)
<i>Sigmoid</i>	104 (38.24%)
<i>Descending Colon</i>	36 (13.24%)
<i>Transverse Colon</i>	31 (11.40%)
<i>Ascending Colon</i>	34 (12.50%)
<i>Cecum</i>	9 (3.30%)
Histopathology	
<i>Chronic Non-specific Inflammation</i>	16 (5.88%)
<i>Tubular Adenoma with Low Grade Dysplasia</i>	168 (61.76%)
<i>Tubular Adenoma with High Grade Dysplasia</i>	79 (29.04%)
<i>Tubulovillous Adenoma with High Grade Dysplasia</i>	6 (2.21%)
<i>Villous Adenoma with High Grade Dysplasia</i>	1 (0.37%)
<i>Adenocarcinoma</i>	2 (0.74%)
<i>Schistosomiasis</i>	1 (0.37%)

Table 3.0 Profile of Patients with Subcentimeter Polyps with Adenocarcinoma on Histopathology

Patient Number	Age	Sex	Indication of Colonoscopy	Size (cm)	Description	Location
#22	66	M	screening	0.3	Sessile	Ascending Colon
#102	57	M	screening	0.5	Sessile	Rectum

A total of 86 subcentimeter polyps with high-grade dysplasia (31.6%) were recorded. Table 4.0 shows the profile of patients from which these polyps were obtained. Majority of which were from male patients (78%) with an average age of 69 ± 12 years seen on screening colonoscopy and with an average number of 1 polyp.

Table 4.0 Profile of Patients with Subcentimeter Polyps with High-grade Dysplasia on Histopathologic Report

Characteristics	Total (N)	78 patients
Age	Average Age (years)	69 ± 12 years
	Maximum	94
	Minimum	43
Gender	Male	61 (78%)
	Female	17 (22%)
Indication for Colonoscopy	Screening	55 (71%)
	Episode of Hematochezia	12 (15%)
	Chronic Constipation	11 (14%)
Number of polyps	1	71 (91%)
	2	6 (7.7%)
	3	1 (1.3%)

Table 5.0 shows the characteristics of those subcentimeter polyps with high-grade dysplasia. Majority of them were noted to be diminutive (73%) and were located distally (72%) with the most common morphology being sessile (93%) and location being the sigmoid colon (38%). One out of three of those with subcentimeter polyp with adenocarcinoma was located in the ascending colon (Table 3.0) hence strengthening the value of colonoscopy over sigmoidoscopy as a screening tool for colon cancer.

Table 5.0 Characteristics of Subcentimeter Polyps with High-grade Dysplasia on Histopathologic Report

Characteristics	Total (N)= 86 polyps
Description	
Size	
<i>Diminutive (</5 mm)</i>	63 (73%)
<i>Small (6-9 mm)</i>	23 (27%)
Morphology	
<i>Sessile</i>	80 (93%)
<i>Pedunculated</i>	6 (7%)
Location	
<i>Rectum</i>	13 (15%)
<i>Sigmoid</i>	33 (38%)
<i>Descending Colon</i>	16 (19%)
<i>Transverse Colon</i>	11 (13%)
<i>Ascending Colon</i>	11 (13%)
<i>Cecum</i>	2 (2%)

DISCUSSION

Our findings were consistent with a prospective Korean study which evaluated medical reports of all patients undergoing total colonoscopic examination over a 12-month period. Three hundred thirty nine small colorectal polyps, removed during colonoscopy, have been analyzed. All adenomas were categorized into two groups: Group I, < or =5 mm diameter (diminutive polyp), Group 2, 6 to 10 mm diameter (small polyp). Results showed that the most common age group was also in the sixth decade. Majority was also male with male-to-female ratio at 2:1.¹³

Our results were quite similar with the study of Lee et al. Among small colorectal polyps obtained from the study, 180 (53.1%) were adenomatous, 32 (10.0%) were hyperplastic, 119 (34.9%) were chronic nonspecific inflammation, 3 (0.9 %) were lymphoid hyperplasia, and 4 (1.1%) were cancerous. The most frequent sites of these lesions were also at the rectum and sigmoid (60.2%).¹³

Prevalence of adenocarcinoma among subcentimeter polyps were consistent with previous studies. The prevalence of cancerous polyps in series of endoscopically removed polyps is between 0.2% and 11%. Nowadays, the number of cases in which malignant polyps are removed is increasing due to screening programs. In an asymptomatic population of people over 50 years old who underwent direct colonoscopy, there was a 0.8% prevalence of adenocarcinoma of which 50% were carcinoma “*in situ*” or in stage I. During screening programs, adenocarcinomas have been detected in between 3% and 4.6% of those who undergo colonoscopy following a positive immunological fecal occult blood test result.⁴

Prevalence of high-grade dysplasia was higher compared to previous international studies. In the previous US National Polyp Study, a careful pathological analysis of 572 adenomas 5 mm in diameter removed by expert colonoscopist investigators showed that only 0.9% contained high-grade dysplasia.³ In a study by Toll et al., eighty-three patients treated between 1999 and 2007 for high-grade dysplasia (HGD) in a colorectal adenoma were identified. Adenomas with high grade dysplasia did not appear to have a particular endoscopic appearance. They were distributed throughout the colon, and although most were > 1 cm, 17% were < 1 cm.¹⁹ Another Chinese study also showed 17% of the 1,272 polyps <1 cm were classified as advanced adenoma.¹⁸ A European study by Gschwantler et al. analyzed a total of 7590 adenomas removed from 4216 patients. In the class of adenomas with diameter < 0.5 cm, no invasive carcinoma was found, but 3.4% of adenomas had high-grade dysplasia.⁹

Our population consists mainly of elderly male patients. According to a Korean study by Yo Han Jeong et al. Male sex and an age of > 65 were found to be independent risk factors of advanced adenoma. An advanced age has been previously associated with advanced histology amongst polyps of < 10 mm.²³

All adenomas have variable degrees of dysplasia ranging from low-grade to high-grade. Classically, it is believed that the malignant potential of adenomas correlates with type of polyp, size, and degree of dysplasia. Higher grades of dysplasia, increasing percentage of villous tissue within the polyp, and polyps greater than 1 cm in diameter are associated with increased risk of malignancy. A polyp is considered malignant when cancer cells within the neoplasm have extended to the submucosa via penetration through the muscularis mucosal layer.⁷ Size,

histological type, location and age are independent risk factors for advanced pathologic features in colorectal adenomas.⁹

Similarly, in a study from Brazil by Silva et al. 91.9% of polyps <0.5 cm in size were also sessile. Conversely, those larger than 1 cm were mostly pedunculated (67.7%). It is well known that polyps <5 mm, also known as minute polyps, are rarely stalked.¹⁸

Based on a systematic review by Vleugels et al. which explored the natural history of diminutive and small colorectal polyps, some 1- 9-mm adenomas progress to advanced adenomas within 2 to 3 years. However, no information on long-term Colorectal Carcinoma transition rates was found.²² In a previous study in which 858 malignant polyps were analyzed, in 89 patients (10%), there was residual disease or recurrent carcinoma. In malignant polyps with unfavorable histology, the risk of relapse or residual lesions ranges between 10% and 39%.⁴

According to European Society of Gastrointestinal Endoscopy (ESGE), in the high-risk group (patients with adenomas with villous histology or high grade dysplasia or ≥ 10 mm in size, or ≥ 3 adenomas), the ESGE recommends surveillance colonoscopy 3 years after the index colonoscopy and then every five years after the first negative exam (Colucci et al.). Epidemiological studies have indicated that the high-risk group is at increased risk of Colorectal Cancer compared with the general population. Patients stratified into the high-risk group who were followed for 14 years (without endoscopic surveillance) had a 3.6 to 6.6- fold increase in Colorectal Cancer risk, compared with the general population. Another study found that patients with advanced adenomas who did not undergo endoscopic surveillance had a 4.26 times greater risk for Colorectal Cancer. (ESGE).¹⁰

CONCLUSION & RECOMMENDATIONS

Our findings showed that there is a substantial proportion of subcentimeter polyps on colonoscopy noted to have high-grade dysplasia (31.6%) as compared to previous international studies. We therefore highly recommend emphasizing screening colonoscopy among our patients. Those found to have subcentimeter polyps with high-risk dysplasia would require an earlier follow-up of every three years because these set of patients have an increased risk of developing Colorectal Cancer compared to the general population.

Our population consists mainly of retired male veteran patients with average age of $>/65$ years old hence it does not truly represent our population. Recent guidelines of the American Cancer Society recommended that screening should begin at age 45 for people at average risk instead of 50 years old. Multi-center studies on the prevalence of high risk dysplasia among subcentimeter polyps among patients 40 years old and above is recommended to be able to establish local data in the Philippines and to check if the recent guidelines is applicable in our country as well.

Our study is limited by its retrospective nature hence prospective studies are recommended to ascertain risk factors and association for this condition. It would also be interesting for new prospective studies to be carried out to evaluate the progress of such patients and to establish the most suitable treatment and follow up regimens for them.

We conclude that subcentimeter polyps are clinically significant and should not be easily ignored.

REFERENCES

- 1) Aktekin, N. et al. Rate and Risk Factors of Advanced Adenomas among Diminutive Polyps. 2015.
- 2) Barret M. et al. Factors Associated with Adenoma Detection Rate and Diagnosis of Polyps and Colorectal Cancer during Colonoscopy in France: Results of a Prospective, Nationwide Survey. 2013. PLoS ONE 8(7): e68947
- 3) Bond, J. Polyp Guideline: Diagnosis, Treatment, and Surveillance for Patients With Colorectal Polyps. American Journal of Gastroenterology. 2000. Vol. 95, No. 11
- 4) Bujanda et al. Malignant Colorectal Polyps. World Journal of Gastroenterology. 2010 July 7; 16(25): 3103-3111
- 5) Butterfly et al. Prevalence of clinically important histology in small adenomas. Clin Gastroenterol Hepatol 2006; 4:343-8.
- 6) Church, J. Clinical Significance of Small Colorectal Polyps. Diseases of the Colon and Rectum. 2004 Apr;47(4):481-5.
- 7) Colucci et al. Colorectal Polyps. Clinical Medical Research. 2003 Jul; 1(3): 261–262.
- 8) Eshgi et al. A retrospective study of patients with colorectal polyps. Research Institute for Gastroenterology and Liver Diseases. 2010.

- 9) Gschwantler et al. High-grade dysplasia and invasive carcinoma in colorectal adenomas: a multivariate analysis of the impact of adenoma and patient characteristics. *European Journal of Gastroenterology and Hepatology*. 2002 Feb;14(2):183-8.
- 10) Hassan, C. et al. Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. 2013.
- 11) Hassan, C. et al. Systematic review: distribution of advanced neoplasia according to polyp size at screening colonoscopy. *Aliment Pharmacol Ther*. 2010 Jan 15;31(2):210-7
- 12) Laudico et al. Cancer Incidence and Survival in Metro Manila and Rizal Province, Philippines. 2010 *Japanese Journal of Clinical Oncology*.
- 13) Lee, S. et al. Clinicopathologic Features and Clinical Significance of Small and Diminutive Colorectal Polyps. *Journal of the Korean Society of Coloproctology*. 2005 Feb;21(1):6-12
- 14) Mohammad et al. A retrospective study of patients with colorectal polyps. 2011. Research Institute for Gastroenterology and Liver Diseases.
- 15) Paris Workshop Participants. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon. *American Society for Gastrointestinal Endoscopy*. 2003. Volume 58, No. 6
- 16) Rex, D. and J. Goldblum. Should HGD or Degree of Villous Changes in Colon Polyps Be Reported? *American Journal of Gastroenterology* 2008;103:1327–1333
- 17) Sano, Y. et al. A multi-center randomized controlled trial designed to evaluate follow-up surveillance strategies for colorectal cancer: the Japan Polyp Study. *Digest Endo* 2004;16:376–8.
- 18) Silva et al. Influence of patient age and colorectal polyp size on histopathology findings. *Arq Bras Cir Dig* 2014;27(2):109-113
- 19) Toll et al. Prognostic significance of high-grade dysplasia in colorectal Adenomas Volume 13, Issue 4, April 2011, Pages 370-373.
- 20) Tsai, F. and W. Strum. Prevalence of advanced adenomas in small and diminutive colon polyps using direct measurement of size. *Digestive Diseases and Sciences*. 2011 Aug;56(8):2384-8
- 21) Unal et al. Malignancy risk of small polyps and related factors. *Digestive Diseases and Sciences*. 2007 Oct;52(10):2796-9.
- 22) Vleugels, J. et al. Natural history of diminutive and small colorectal polyps: a systematic literature review. 2017 Jun;85(6):1169-1176.
- 23) Yo Han Jeong et al. Risk Factors of Advanced Adenoma in Small and Diminutive Colorectal Polyp *J Korean Med Sci* 2016; 31: 1426-1430
- 24) Yamaji, Y. et al. The Malignant Potential of Freshly Developed Colorectal Polyps According to Age. *Cancer Epidemiol Biomarkers Prev* 2006;15:2418-2421.