

## **Adenoma, Sessile Serrated Polyps and Colorectal Cancer in patients $\geq 50$ years old and $< 50$ years old: a Retrospective Study**

### **Introduction**

Colonoscopy is the preferred screening for Colorectal Cancer (CRC) according to the American College of Gastroenterology (ACG)<sup>1</sup>. Screening for colonic polyps start at age 50 years old, however ACG recommends earlier screening on black patients, starting at age 45 years old<sup>1</sup> because of high incidence and mortality compared to other racial groups<sup>2-3</sup>.

Overall, there is a decrease in age-adjusted CRC incidence rates between 1975 and 2010 of 0.92%<sup>4</sup>. In a study done by Taggarshe et al published in 2013 wherein they noted that incidence of CRC in patients aged  $< 50$  years old increased from 6.8% (1982 to 1990) to 8.5% (2000-2010).<sup>5</sup> Colon cancer in the young incidence increased 17% and rectal cancer rose up to 75%.<sup>6</sup> The decrease in CRC incidence in older age group (above 50 years old) is largely attributed to the increase in screening colonoscopies. With the changes in incidence, there is a shift towards early detection in the young. The lack of screening for the younger patients delay diagnosis hence leads to a more advance disease and poor outcome.

Most colorectal cancer arise from adenomas, which is the most common and comprises two-thirds of all colonic polyps<sup>8-9</sup>. Adenomas histologically are described as tubular, tubulo-villous and villous. Pathogenesis is based on the adenoma-carcinoma sequence, wherein the formation of a neoplastic process requires multiple cumulative genetic alterations<sup>10-12</sup>. Sessile Serrated Adenomas/Polyp (SSA/P) had been noted to be a significant contributor of interval colorectal cancers, comprising greater than 30%<sup>13-14</sup>. SSA/P frequently exhibits dysplasia, according to Longacre, in 110 SSA/P, 37% showed foci of significant dyplasia and 11% contained areas of intramucosal carcinoma<sup>15</sup>. Tumors from SSA/P precursor is associated with high frequency of methylation of some CpG islands (CpG island hypermethylation phenotype [CIMP]-positive) and *BRAF* mutation leading to DNA instability.<sup>16-18</sup> Studies show early detection and removal of these CRC precursor lesions will decrease cancer related mortality<sup>19-20</sup>.

In the Philippines, there is no published data available regarding the incidence of the different histologic subtype of colorectal polyps and colorectal cancer in patients  $< 50$  years old compared to patients seen  $\geq 50$  years old.

### **Objectives**

To compare the incidence and histological subtype of colorectal polyps and colorectal cancer in patients undergoing colonoscopy before age 50 years with patients aged 50 years and older.

1. To describe the baseline characteristics of all patients who underwent colonoscopy at Manila Doctors Hospital
  
2. To compare the incidence of the colorectal polyps in patients

- 2.1 Age <50 years old
- 2.2 Age ≥ 50 years old
- 3. To compare the histologic subtype of colorectal polyps in patients
  - 3.1 Age <50 years old
  - 3.2 Age ≥ 50 years old
- 4. To compare the incidence of colorectal cancer and histologic subtype seen in patients
  - 4.1 Age <50 years old
  - 4.2 Age ≥ 50 years old

**Methods**

This is a retrospective cross sectional study done on all colonoscopies performed at Manila Doctors Hospital from January 1, 2016 to December 31, 2016. The endoscopy reports were retrieved. Information that was collected include: age, gender, indication and colonoscopic findings.

All corresponding pathology reports of excised lesions were retrieved from Manila Doctors Hospital Pathology Laboratory. Lesion subtype will be recorded on per colonoscopy findings. Patients with incomplete colonoscopic report and histopathology reports were excluded from the study.

**Statistical analysis**

The characteristics of patients, indications for colonoscopy and findings were compared between the two groups (<50 vs ≥50 years) using z-test for two proportions. All statistical association tests were performed using Stata SE version 12.0. Two-tailed statistics were used throughout with a significance level of P-value <0.05.

**Results**

A total of 1,647 reports were retrieved. We excluded 16 cases with incomplete data in their endoscopy reports and 10 cases with no histopathology done at Manila Doctors Hospital Pathology Laboratory. Out of all the reports retrieved, 486 patients were aged<50 years old and 1,135 patients were ≥50 years old. The mean age of all patients who underwent colonoscopy was 57.86 which range from 22 years old to 95 years as shown in Table 1 and Table 2.

Table 1 Characteristics of all patients who underwent colonoscopy in Manila Doctors Hospital

	All	<50 y/o	≥50 y/o
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Totals	1621	486	1135
Mean Age	57.86	39.43	63.28
Median Age	59	41	62
Age Range	22-95	22-49	50-95
Gender			
Male	342	85	257
Female	283	57	226

Table 2. Indications of ALL patients who underwent colonoscopy

Indication (n, %)	<50 (%)	≥50 (%)	p value
Abdominal pain	81 (16.67)	121 (10.66)	<b>0.0008</b>
Changes in bowel movement	55 (11.32)	111 (9.78)	0.3497
Family History of CRC	48 (9.88)	77 (6.78)	<b>0.0325</b>
Personal History of CRC	22 (4.53)	51 (4.49)	0.9763
Personal history of polyps	39 (8.02)	171 (15.07)	<b>0.0001</b>
Anemia	23 (4.73)	160 (14.10)	<b>&lt;0.0001</b>
Lower gastrointestinal bleeding	145 (29.84)	195 (17.18)	<b>&lt;0.0001</b>
Screening	73 (15.02)	249 (21.94)	<b>0.0014</b>

The polyps were detected in 572 patients (35.29%) and colorectal cancer in 52 patients (3.27%) of all the colonoscopies done (Table 3). Adenomas (tubular adenoma, tubulovillous and villous adenoma) were observed in 11.52% in patients <50 years old and 26.08% in patients ≥50 years old. (p value <0.0001). Sessile serrated adenomas/polyps were seen in 1.23% in <50 years old and 1.94% in ≥50 years old, which showed no significant difference between the two groups. (see Table 4)

The most common indication in patients age <50 years old was lower gastrointestinal bleeding, whereas patients ≥50 years old was anemia. (p value <0.05) see Table 2. Most common indication for younger patients includes abdominal pain (p value 0.0008) and family history of colorectal cancer (p value 0.0325). Those patients aged ≥50 years old do colonoscopy for screening (p value 0.0014) and if they have personal history of colorectal cancer (p value 0.0001). Colonoscopy indications are listed in Table 2.

Table 3 Polyps and CRC of all patients in Manila Doctors Hospital

	All	%	<50 y/o	%	≥50 y/o	%	P value
<b>Polyps (all types)</b>	<b>572</b>	<b>35.29%</b>	<b>130</b>	<b>26.75</b>	<b>442</b>	<b>38.94</b>	<b>&lt;0.0001</b>
CRC	52	3.27%	11	2.27	41	3.61	0.236

Table 4. Adenomas and Sessile serrated polyp in each age group

		<50 y/o	%	≥50 y/o	%	p value
Adenomas	352 (21.67%)	56	11.52	296	26.08	<0.0001
SSA/P	28 ( 1.72%)	6	1.23	22	1.94	0.3190

When adenomas are analysed by subtypes, there is no significant difference between the two age group. (p value 0.05) Table 4

Table 4. Adenoma histologic subtype

Subtype of adenoma	<50	%	≥50	%	P value
Tubular adenoma	66	82.5	405	83.85	0.7621
Tubulovillous adenoma	6	7.5	50	10.35	0.4299
Villous adenoma	2	2.5	6	1.24	0.3786

Incidence of colorectal cancer is 2.26% in <50 years old and 3.6% in ≥50 years old. (p value 0.236). Poorly differentiated carcinoma is more common in those patients aged <50 years old with a prevalence of 27.7%. Adenocarcinoma well differentiated was seen in 75.6% of patients aged ≥50 years old. Mucinous was seen in one patient in the ≥50 years old age group. (see table 5)

Table 5 Colorectal Cancer histopathology subtype

Colorectal Cancer Histopathology Subtype	<50 n=11	%	≥50 n=41	%
Adenocarcinoma moderately differentiated	2	18.18	6	14.63
Adenocarcinoma well differentiated	6	54.55	31	75.61
Carcinoma poorly differentiated	3	27.27	3	7.32
Mucinous Adenocarcinoma	0	0	1	2.44

## Discussion

In a study by Taggarshe et al, the most common symptoms were rectal bleeding and abdominal pain, similar to the symptoms seen in our study. Our results show that adenomas are significantly seen in patients age ≥50 years compared to those in <50 years old, which was the same in studies which show that prevalence of colorectal adenomas range from 25 to 30% at age 50<sup>21-22</sup>. The prevalence of colorectal adenomas increases with age, especially at age 50 years old<sup>23</sup>. However it should be noted that in terms of histologic subtype: tubular adenoma, tubulovillous, villous and sessile serrated adenoma/polyp; there was no significant difference between the two age groups. This is in contrast with a study that shows that tubulovillous and advanced tubular adenoma were more prevalent in the older age group<sup>24</sup>. The prevalence of sessile serrated polyps was 1.72% in this study. It is less compared to studies wherein the prevalence rate is 8.1 to 8.2%<sup>25-26</sup>. In a study by Wong et al they noted that SSA/P prevalence was higher in patients aged under 50 in a routine colonoscopy service<sup>24</sup>.

Colorectal cancer incidence in this study showed no significant difference between the two age groups that despite increasing awareness of patients regarding screening at age 50, there seems to be an equal detection of CRC in the younger age group <50 years old. Several studies show that CRC incidence rates increased for younger patients<sup>4-7</sup> (20-49 yrs old). Cooley et al<sup>27</sup> found that colorectal resection for cancer increased in patients younger than 50 years old from 11.8% to 13.3.% (1998 to 2005). Davis et al.<sup>28</sup> emphasized that although people older than 50 had decreased incidences of CRC, there is a higher incidence across 20-49 age group in 2006 than 1987 (17.9 per 100,000 in 2006 vs 10.7 per 100,000 in 1987). Most of the younger age group has symptoms which prompted investigation hence colonoscopy was done. Two studies noted that early onset CRC tend to have advanced disease at presentation: stage III (32 to 40%) and stage IV (20 to 34%).<sup>5, 17</sup> In our study poorly differentiated cancer comprises most of the colon cancers seen in patients age <50 years old comprising 27.27% as opposed to well differentiated carcinoma being the most common (75.61%) in the older age group. Poorly differentiated cancer of the colon tends to grow and spreads quickly hence early diagnosis is important. The delay in the diagnosis leads to a delay also in treatment of this early onset CRC. Patients younger than 50 years old without the risk factors have no recommended screening. With the current recommendations, Tagarshe deduced that 8% of patients younger than 50 years old would have missed a diagnosis of CRC.<sup>5</sup> In Europe due to the match rising mortality in young patients, they changed their recommendation to start screening at age 45 years old.<sup>29</sup>

This study has several limitations including its retrospective nature, patients clinical presentation, family history and indications for the colonoscopy was based solely on the database hence they were not personally verified. Additional studies could include outcomes of early onset CRC and to determine possible risk factors in the increasing trends of CRC in this young age group.

## Conclusion

In 2016, the incidence of adenomas who underwent colonoscopy in Manila Doctors Hospital were significantly higher in patients  $\geq 50$  years old but histologic subtype are the same in both age groups. The incidence of sessile serrated polyp/adenomas showed no difference between the two age groups. Colorectal cancer incidence had no significant difference between the two age group. A histopathology of poorly differentiated colorectal cancer is mostly seen in the young age group while well differentiated adenocarcinoma is mostly seen in patients above 50 years old.

Reference:

1 Screening for Colorectal Cancer. US Preventive Services Task Force. JAMA June 21, 2016 Volume 315, Number 23.

2 Laiyemo AO, Doubeni C, Pinsky PF et al Race and colorectal cancer disparities: health-care utilization vs different cancer susceptibilities. J Natl Cancer Inst. 2010 Apr;102(8):538-46. Epub 2010 Mar 31.

3 Schroy PC, Coe A, Chen CA, O'Brien MJ, Heeren TC. Prevalence of advanced colorectal neoplasia in white and black patients undergoing screening colonoscopy in a safety-net hospital. Ann Intern Med. 2013;159(1):13.

4 Bailey CE, Hu CY, You YN, Bednarski BK, Rodriguez-Bigas MA, Skibber JM, et al. Increasing disparities in the age-related incidences of colon and rectal cancers in the United States, 1975-2010. JAMA Surg. 2015;150(1):17-22.

5 Taggarshe D, Rehil N, Sharma S, Flynn JC, Damadi A. Colorectal cancer: are the "young" being overlooked? Am J Surg. 2013;205(3):312-6.

6 O'Connell JB, Maggard MA, Liu JH, Etzioni DA, Livingston EH, Ko CY. Rates of colon and rectal cancers are increasing in young adults. Am Surg. 2003; 69(10):866-72.

7 Dozois EJ, Boardman LA, Suwanthanma W, et al. Young-onset colorectal cancer in patients with no known genetic predisposition: can we increase early recognition and improve outcome? Medicine 2008;87: 259-63.

8 Carlsson G, Petrelli NJ, Nava H, Herrera L, Mittelman A. The value of colonoscopic surveillance after curative resection for colorectal cancer or synchronous adenomatous polyps. Arch Surg. 1987;122(11):1261.

9 Tefik Solakoğlu et al Analysis of 2222 colorectal polyps in 896 patients: A tertiary referral hospital study. Turk J Gastroenterol 2014; 25: 175-9.

10 Shussman, N and Wexner, S. Colorectal polyps and Polyposis syndromes. Gastroenterology Report 2 (2014) 1-15.

11 Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. Cell. 1990;61(5):759.

12 Leslie, A., Carey, F. A., Pratt, N. R. and Steele, R. J. C. (2002), The colorectal adenoma-carcinoma sequence. Br J Surg, 89: 845-860.

- 13 Leggett B, Whitehall V. Role of the serrated pathway in colorectal cancer pathogenesis. *Gastroenterology* 2010;138:2088-100.
- 14 Arain MA, Sawhney M, Sheikh S, et al. CIMP status of interval colon cancers: another piece to the puzzle. *Am J Gastroenterol* 2010;105: 1189-95.
- 15 Longacre TA, Fenoglio-Preiser CM. Mixed hyperplastic adenomatous polyps/serrated adenomas. A distinct form of colorectal neoplasia. *Am J Surg Pathol.* 1990;14(6):524.
- 16 Noffsinger AE. Serrated polyps and colorectal cancer: new pathway to malignancy. *Annu Rev Pathol.* 2009;4:343.
- 17 Spring KJ, Zhao ZZ, Karamatic R, et al. High prevalence of sessile serrated adenomas with BRAF mutations: a prospective study of patients undergoing colonoscopy. *Gastroenterology* 2006;131: 1400-7.
- 18 Chan TL, Zhao W, Leung SY, Yuen ST, Cancer Genome Project. BRAF and KRAS mutations in colorectal hyperplastic polyps and serrated adenomas. *Cancer Res.* 2003;63(16):4878.
- 19 Citarda, F; Tomaselli, G, Capocaccia, R et al Efficacy in standard clinical practice of colonoscopic polypectomy in reducing colorectal cancer incidence. *Gut.* 2001 Jun; 48(6): 812–815.
- 20 Corley, D; Jensen, C Marks, A et al Adenoma Detection Rate and Risk of Colorectal Cancer and Death. *N Engl J Med* 2014; 370:1298-130
- 21 Heitman SJ, Ronksley PE, Hilsden RJ, et al. Prevalence of adenomas and colorectal cancer in average risk individuals: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2009; 7:1272-8.
- 22 Rex DK, Lehman GA, Ulbright TM, et al. Colonic neoplasia in asymptomatic persons with negative fecal occult blood tests: Influence of age, gender, and family history. *Am J Gastroenterol* 1993; 88: 825-31.
- 23 Pendergrass CJ, Edelstein DL, Hyland LM, et al. Occurrence of colorectal adenomas in younger adults: an epidemiologic necropsy study. *Clin Gastroenterol Hepatol* 2008; 6: 1011-5.

24 Wong, S., Lidums, I, Rosty C et al Findings in young adults at colonoscopy from a hospital service database audit. BMC Gastroenterology (2017) 17:56

25 Ijspeert J et al Prevalence, distribution and risk of sessile serrated adenomas/polyps at a center with a high adenoma detection rate and experienced pathologists. Endoscopy. 2016 Aug;48(8):740-6.

26 Abdeljawad K et al Sessile serrated polyp prevalence determined by a colonoscopist with a high lesion detection rate and an experienced pathologist. Gastrointest Endosc. 2015 Mar;81(3):517-24.

27 Cooley EK, McPhee JT, Simons JP, et al. Colorectal neoplasia screening before age 50? Current epidemiologic trends in the United States. Dis Colon Rectum 2009;52:222-9.

28 DM, Marcet JE, Frattini JC, Prather AD, Mateka JJ, Nfonsam VN. Is it time to lower the recommended screening age for colorectal cancer? J Am Coll Surg. 2011;213(3):352-61

29 Karsenti, D. et al (2017), Adenoma detection rate according to age: colonoscopy screening should start at 45 years old, Presented at the 25th UEG Week Barcelona, October 30, 2017.

**ADENOMA, SESSILE SERRATED POLYPS AND COLORECTAL CANCER IN PATIENTS  $\geq$ 50 YEARS OLD AND  
<50 YEARS OLD: A RETROSPECTIVE STUDY**

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## Manila Doctors Hospital

**Introduction:** Most colorectal cancer arise from adenomas and sessile serrated adenomas/polyps. In the Philippines, there is no published data regarding the prevalence and histologic subtype of colorectal precursor polyps and colorectal cancer. The aim of the study is to compare the incidence and histological subtype of colorectal precursor polyps and colorectal cancer in patients undergoing colonoscopy before age 50 years with patients aged 50 years and older.

**Methodology:** This is a retrospective cross sectional study done using all patients who underwent colonoscopy at Manila Doctors Hospital from January 1,2016 to December 31,2016. Age, gender and indication and histopathology reports were retrieved with colorectal polyps and colorectal cancer. Z-test for two proportions was done to analyse the data.

**Results:** Adenomas which include tubular adenoma, tubulovillous and villous adenoma were observed in 11.52% in patients <50 years old and 26.08% in patients  $\geq$ 50 years old. (p value <0.0001) When adenomas were analysed by subtypes, there is no significant difference between the prevalence between the two age group. (p value 0.05). Incidence of sessile serrated adenomas/polyps are equally seen in both age groups. Colorectal cancer incidence in this study showed no significant difference between the two age groups despite increasing awareness of patients regarding screening at age 50. Poorly differentiated was mostly seen in the younger age group at 27.7%, while well differentiated is predominantly seen in those above the age 50 years old.

**Conclusion:** In 2016, the incidence of adenomas who underwent colonoscopy in Manila Doctors Hospital were significantly higher in patients  $\geq$ 50 years old but histologic subtype are the same in both age groups. The incidence of sessile serrated polyp/adenomas showed no difference between the two age groups. Colorectal cancer incidence had no significant difference between the two age group. A histopathology of poorly differentiated colorectal cancer is mostly seen in the young age group at while well differentiated adenocarcinoma is mostly seen in patients above 50 years old.

**Keywords:** adenoma, sessile serrated adenoma/polyp, colorectal cancer, incidence