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Clinicopathological features colon polyps from African-Americans

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Abstract

Background & Aims—Among the ethnic groups age standardized incidence rate of colorectal cancer (CRC) is highest among African-Americans. The majority of CRC arise from preexisting adenoma. It is shown that 30% of the US adult population has adenomas. The potential risk of malignant transformation in adenomas differs by specific pathologic and clinical characteristics that we aimed to study in AAs.

Material and Methods—All pathologic reports (150,000) in Howard University Hospital from 1959 to 2006 were reviewed manually. Those pathology reports compatible with the colorectal polyps were carefully reviewed and selected by a GI pathologist. All cases with cancer then excluded from the list. Data then were entered into excel and checked for missing data and duplications. Differences in right side and left side polyps for sex, histology, clinical symptoms were assessed by chi-2 test.

Results—A total number of 5013 colorectal polyps were diagnosed in this period that include 47% male, with mean age (SD) of 63 (12). Half of cases were diagnosed in 2001–2006. Tubular adenoma was the most frequent pathology (73%). The highest frequency of right sided polyps was observed in 1990's (56%). Left sided polyps were younger (P<0.000), more hyperplasic (23% vs. 5%; P<0.000) and more frequent in female (56% vs. 52%; P=0.02) compared to right sided. The frequency of right sided adenoma significantly increases from 18% in 60's to 51% in the period of 2001–2006 (P<0.000). The most frequent symptom in both sides was GI bleeding (21%).

Conclusion—There was a ratio of 9:1 for neoplastic to hyperplastic polyps in our study which is more than what has been reported in Caucasians (7:1). Our data shows a shift in polyps from the left side to the right side of the colon in recent years. This data is consistent with the lack of a reduction in the incidence of colon cancer in African Americans. Screening is thus very important in AA to reduce the incidence of colon cancer.

Keywords

Colon; polyp; African American

Introduction

Colon cancer is the third common cancer in the United States. African-Americans have the highest incidence rate of colorectal cancer among different races [1]. Colon carcinogenesis is believed to be a process taking several years to be completed. A majority of colorectal

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cancers are expected to arise through a multistep pathway. Which include initial hyperproliferation of normal epithelial cells, formation of adenomas and finally the transition to invasive carcinomas [2, 3]. Interruption of adenoma-carcinoma sequence with colonoscopy and polypectomy reduces the incidence of CRC by as much as 90% [4].

The study of adenoma prevalence began in 1947 with examining the total colon in autopsies [5] including the autopsies surveys that have been conducted worldwide (For a complete review refer to Neugut et al. [6]). Colorectal polyps are frequent in the general population. The reported prevalence of colonic polyps varies widely between different geographical areas. It was estimated that 30% of the Western population have colonic polyps while a lower rate (10–15%) is noted in Asia and Africa [7, 8]. Results from previous studies have shown that colonic polyps are more common in men than in women and increase in frequency with increasing age in most of these studies; in some older age groups the prevalence rate exceeds 50% [9–15]

Colorectal polyps are classified histologically mainly as adenoma (neoplastic) or hyperplastic (non-neoplastic) [16]. The majority of polyps are small, non-neoplastic lesions that are found during screening or when procedures are performed for other diagnostic reasons. Surveys have generally shown that the prevalence of hyperplastic polyps varies in different population, as well as adenomas. Autopsy studies reported a 12–52% prevalence of hyperplastic polyps and a 10–40% prevalence of adenomas [17–20]. In screening colonoscopy studies, the corresponding figures were 9–34% and 24–48%, respectively [21–23].

The anatomic distribution of adenoma is shown to be different between different geographical area and races too [24, 25]. Unlike the hyperplastic polyp the adenoma are more prevalent in right side colon and are strongly associated with age [26]. The sub site distribution of colorectal adenomas removed by autopsy or colonoscopy procedures over a 20-year period was found to have a “shift to the right”, similar to that reported for colorectal carcinoma [27–30].

Whereas there is some of information relating to the epidemiology of CRC in African-Americans, much less known about adenomas in this group. The aim of this study was to determine the clinical and pathological characteristics of colon polyps in African-American population and define the risk profile of neoplastic polyps at the main hospital in the district of Colombia in last fifty years.

Material and Methods

Patients

Howard University Hospital (HUH) is located in District of Columbia (Washington DC). It was established in 1959 to serve DC area, mainly African-American population of Capital. More than 90% of HUH cases in this study are now from African-American population. Gastroenterology division at department of medicine is responsible for handling gastrointestinal (GI) diseases, including lower GI diseases and colorectal cancer screening. Cases of colorectal polyps are diagnosed through endoscopy or surgery in hospital. Then all biopsy (polyps) were sent for diagnosis in Department of Pathology. From 1959–2006 more than 150,000 pathologic reports are archived in this department. A team of health professionals were trained to review the pathologic reports (with approval from Howard University Institutional Review Boards). They reviewed all pathologic reports manually and selected the diagnosis compatible with colorectal polyps for further review. Any cases with colorectal cancer diagnosis were excluded from the study. A database in Excel was developed to store the clinical and pathological data. The selected reports were then

abstracted and entered into database. Histological diagnosis, clinical and demographical data were entered into data base. Then the data were rechecked for any missing data and duplication. Year of diagnosis were categorized into five decades. Polyps location was categorized into five sites (ascending, transverse, descending, rectosigmoid and multiple/undefined location). Polyp diagnosis was categorized into six categories (tubular adenoma, tubulovillous, villous, hyperplastic polyp, mixed (hyperplastic and adenoma) and other). A further neoplastic category defined the adenomas. Different categories of symptoms or reason for referral then categorized into eight categories.

Statistical Analysis

Distribution of variables was explored by table of frequency or Mean (SD). Hypotheses were tested by Chi-2. A logistic model was then developed to assess the independent risk factors of neoplastic vs. hyperplastic polyps' diagnosis. In this model the age, gender, anatomic site (proximal/distal) treated as independent risk factors. P value less than 0.05 considered as significant. Data analysis was performed in SPSS 15.0 (Chicago, IL).

Results

Adenoma history at HUH

For the period of 1959–2006, a total number of 5013 colorectal polyps were diagnosed at HUH. Fifty three percent (2650) were female. Mean age (SD) for cases was 63.2 (12.4) years, with the median of 63 years. The number of cases increases continuously with time and fifty percent (50%) of cases were diagnosed after 1999 (Figure 1). Polyps were mostly Tubular adenoma (72.6%) followed by hyperplastic polyp (10.6%) and tubulovillous (8.3%). Two hundred forty one polyps (4.8%) were mixed polyps (hyperplastic and adenoma; Table 1). The ratio of neoplastic to hyperplastic polyps were 8.

Polyps were mainly located in descending (28.9%) and ascending colon (26%). In 645 (12.9%) the location was multiple and in 856 (17.1%) the location was not defined well. Polyps were mostly proximal (51.4%) than distal (48.6%) to splenic flexure. The frequency of hyperplastic polyps was 5.3% in proximal colon and 23.3% in distal colon ($p<0.0001$)

Trend of Location and subtypes by time

The proportion of hyperplastic polyps dramatically increased during the last fifty years. The first hyperplastic polyp cases were diagnosed in 1990's and in period of 2000–2006 peaks at 19.2%. In this period the rate of neoplastic to hyperplastic polyps decreased to 4 ($p<0.0001$) (Table 2). Meanwhile the proportion of right sided polyps increased significantly from 18.2% in 1960's to 55.9% in 1990's and decreased in period of 2000–2006 to 50.7% ($p<0.0001$) (Figure 2). Trend of hyperplastic polyp is more significant in left sided polyps. It peaks to 8.6% (in 2000–2006) in proximal location and in distal colon it peaks at 36.6% at the same period (Figure 3).

Polyp location and subtypes by sex and age

Cases with neoplastic polyps were older than hyperplastic polyp ($p<0.001$). The mean age (SD) was 64.0 (12.4) and 57.7 (10.7) years in neoplastic and hyperplastic polyp, respectively. The ratio of neoplastic to hyperplastic polyps increases steadily with age peaks to 18 in the age over 70 years ($p<0.0001$) (Table 3). The hyperplastic polyp was more frequent in females than male (12.6% vs. 8.4%) ($p<0.0001$).

Proximal cases were older than distal significantly ($p<0.0001$). After stratifying for polyp diagnosis, this difference is shown to be limited to neoplastic polyps. The mean age (SD) was 64.7 (12.1) and 61.2 (12.2) in proximal and distal neoplastic polyps ($p<0.0001$; Table

4). The proportion of distal polyps in female is significantly higher than male (50.4% vs. 46.5%;p<0.02).

Factor affecting the polyp diagnosis

Logistic multivariate model revealed that older age, males and proximal location increases the risk of neoplastic diagnosis significantly. This model has a sensitivity of 99.5% in predicting the risk of neoplastic diagnosis (Table 5)

Symptom distribution in patients

The main reason (or symptom) for referral was defined in 3922 (78.2%) cases. Among them GI bleeding (26.6%), Screening (19.2%) and abdominal pain (3.7%) were the leading symptoms. Frequency of screening increased from 3% in 1959–1970 to 24% in 2000–2006 (p<0.001). Among the 752 cases with screening 438 (58%) had positive guiage test, and 314 (42%) had underwent other screening methods, among them 99% found after 1980. The N/H ratio is 5 in cases referred fro screening while it is 8 in other cases (p<0.001). There is no statistically significant difference between two groups of patients in sex, age and anatomic location.

Discussion

Polyp surveillance accounts for more that 15% of 1.7 million colonoscopies performed each year in the United States [31]. One of the major rationales underlying this surveillance is that 30–60% of patients with adenoma develop metachronous neoplasia within the first three years following index polypectomy [32, 33]. Furthermore, it is estimated that 30% to 40% of adults of ages >60 years have prevalent colorectal adenomatous polyps and individuals with a history of adenoma are at increased risk of colorectal cancer, even with routine colonoscopy exams [34, 35]. We analyzed the data of 5013 cases with polyp diagnosis in last half century from HUH. We found that more than 83% of polyps in AAs in this period were adenoma. The number of polyp cases is almost ten folded from 1980 in this hospital with a shift to right colon in our series. Our data is one of the largest colorectal polyp series have ever been analyzed that include a collection of 50 years of adenoma data from AAs serving hospital. To our knowledge there is no other paper addressing the colon polyps in AA with this large sample size. Many of cases are diagnosed through endoscopy. The chance of bias introduced in autopsy papers is little in our series. All cases were diagnosed by histological methods with highest accuracy level. As a hospital based series, we acknowledge the possible limitation of our study. These included the missing information and biases as results of referral pattern. This data may not represent an entire AA population living in the US but indicates important clues of current situation of polyp distribution in AA population.

The prevalence of colon polyps shows marked international variation. In Hawaiian Japanese, who have a high risk of colon carcinoma, the prevalence of adenoma is shown to be more than 60% [18]. In contrast, Japanese people living in Japan have a low risk of colonic polyp and malignancy. The lowest rate of polyps is reported from Iran (1.6%) [36] with one of the lowest reported rate of colonic malignancy [37]. The reported prevalence of colonic polyps varies widely due to differences in geography, in structure of the studies, and sensitivities of the test used to define prevalence [21].

In the United state it is estimated that 30–40% of age 60+ populations have colonic polyps [33]. Polyp distribution is dissimilar among different ethnic groups in the United States [38]. Though the highest rate of colon cancer is reported in African-American [1], data for colonic adenoma in this population is very scarce. Thorton et al. reviewed more 46000

colonoscopies between 2002–2003 and found that colon polyps are more proximal, bigger in size and younger in age in African-American compare to Whites [39]. The rate of neoplastic to hyper plastic polyps in our series is 8. This ratio is different across the studies. Surveys from United state [40], Spain [41], Indian [8] and Canada [42] reported a ratio of 6 or more for neoplastic to hyperplastic polyps. This ratio is near 1 as reported from Sweden [43] and Australia [44]. In England [45] and New Zealand [46] this ratio is reported to be less than one. Khan et al [42] reported a ratio of 8 for neoplastic to hyperplastic polyps very close to our study (Table 6).

The difference is N/H ratio is unexplainable. Most recent studies show a higher rate of neoplastic polyps. We found a reverse time trend in our study; with higher rate of hyperplastic polyps in recent years for HUH. African-American population, especially in DC area is now experiencing dramatically changes in health status. CRC screening rate increased by 15% from 1997 to 2006 in this area [47]. More than 85% of District Colombia population were insured and had access to health cares in 2006 [48]. The number of colonoscopies in HUH has increased on a yearly basis. HUH has appointed a new GI pathologist from 2004. We indicated a 10 fold rise in screening procedure, mainly from increasing the number of screening colonoscopy in this period. An increasing of medium risk population undergone for colonoscopies together with a better diagnosis of hyperplastic polyp in HUH may explain rising number of hyperplastic polyp in recent years. Lack of robust criteria for hyperplastic polyp diagnosis, or under diagnosis of hyperplastic can predict part of observed time trend in N/H ration in this study.

Hyperplastic is usually considered as inconsequentional and is not described as part of adenoma-carcinoma pathway. Some reports currently describe large hyperplastic polyp as occurring on the right-side in association with colorectal cancer (CRC), and showing a malignant potential [49, 50]. Wynter et al., reported a two variants of hyperplastic with Kras or BRAF mutation and CIMP high with significant malignant potential [51].

Serrated adenomatous polyps of the colon were diagnosed as a variant of hyperplasic polyps. Hyperplasic polyps considered as innocuous and benign lesions without playing a significant role in carcinogenesis [52]. But recently some authors consider Sessile Serrated Adenoma (SSA) as aggressive hyperplastic polyp and precursor of colonic cancer [53, 54]. We found no serrated polyps in our latest series. However, we would like to reevaluate hyperplastic polyp for presence or lack of SSA.

Tubular and tubulovillous (TV) adenoma account for 87% and 10% of neoplastic polyps in our series. This rate for TV is varied across studies. It is more than 45% in Chinese [25] as a low risk population for colon cancer, about 20% in Swiss [55] and less than 5% in some Asian population [7]. TV polyps are believed to have more potential for recurrence and metachronous cancer. Agreement on diagnosis for adenoma histology subtypes is shown to be moderate or low. Kappa for TV diagnosis is reported to be 0.15 between different pathologists [56]. This high disagreement is a main source for variation between different studies for the frequency of TV in adenoma. Discrepancies between the rate of TV and colon cancer rate in different population should be studied more.

The frequency of neoplastic polyps increased with age reaching to more than 90% in ≥70. This is in agreement with other studies showing that prevalence of neoplastic polyps increases with age while prevalence of HYPERPLASTIC POLYP does not change with age [7, 19, 42]. The male gender increases the risk of neoplastic polyps to 50%. This is in agreement with other studies showing a higher chance of neoplastic polyps in males [7, 25]. The observed effect of sex and age on neoplastic polyps is independent and remained in multivariable model.

The anatomic location of polyps varies internationally. Colonoscopies survey from China [25] and India [8] indicated a frequency of left side polyps more than 60%. A study from Germany indicated a 55% of distal colon adenoma [57]. Colon rectal neoplasm is shown to be more proximal in AAs than US Caucasian [24, 38, 58]. Our study indicated a frequency of right sided polyps as much as 51%, not far from the results in North American Caucasian Jass [42, 46]. Thronton found that 57% of colon polyps are right sided in African-American [39]. Previous colonoscopy survey from 1993–1999 at HUH indicated that colon adenoma in AAs are mainly left sided [59]. Neugut et al. have reviewed different aspect of colorectal polyps. They have indicated an increase in right sided polyps from 1969 to 1990 [6]. Whereas in colonoscopy survey of 1969, less than 30% of polyps were in right side in 1990 this rate increase to 69%. We observed a 30% increase in frequency of right sided polyps in our case during last 50 years. This right sided shift increases the importance of colonoscopy as an effective CRC screening strategy in our AAs, especially in older patients.

The most attractive reason for right sided shift in colon cancer is the role of CRC screening (sigmoidoscopy) in detection of left sided adenomas. This reason may not explain the shift of polyps in our data. We observed the shift is mainly affects neoplastic polyps and not hyperplastic polyp while the percentage of hyperplastic polyps remained almost stable in right side, in left side it increased about 50% in 50 years. We propose this shift is mainly affected by the life style change; i.e. smoking, less physical activity, diet (higher animal meat and fat consumption), and environmental factors. The role of other factors such as change in bacterial flora of large intestine should be considered as well.

In this study the right sided polyps had 5 times more risk to be neoplastic compare to left side. The left sided predominance in hyperplastic polyp is observed in Japan [50], as well as India [8] and USA [42, 60]. Distal adenoma polyps is shown to increase the risk of advanced proximal neoplasm as to 7 folds [60] while there are inconclusive results for the effect of distal hyperplastic polyp on the advance proximal findings from no increase in risk to OR as much as 4 [50]. Recent meta-analysis by Otto et al indicated no increased risk of proximal neoplasia subsequent to a distal hyperplastic polyps [61].

This study is a retrospective data collection. Medical charts and pathologic reports were the main sources of our data. This sort of data has some inherent limitation. Any change in diagnosis criteria, pathologist expertise, colonoscopy policies in hospital, and catchments population may factitiously affects the trend. This limitation should be considered in interpreting the findings. Statistically significant results should be distinguished from clinical importance given the high sample size and power of study.

In conclusion, we found that neoplastic polyps in African-American population outnumber the hyperplastic polyps. The adenoma are shifting to right sided, more seen in higher risk groups for cancer, including older ages (>65) and men. This finding seeks a clear strategy for polyp prevention and removal in African-American population. Male and older ages may benefit more from colonoscopy in our population.

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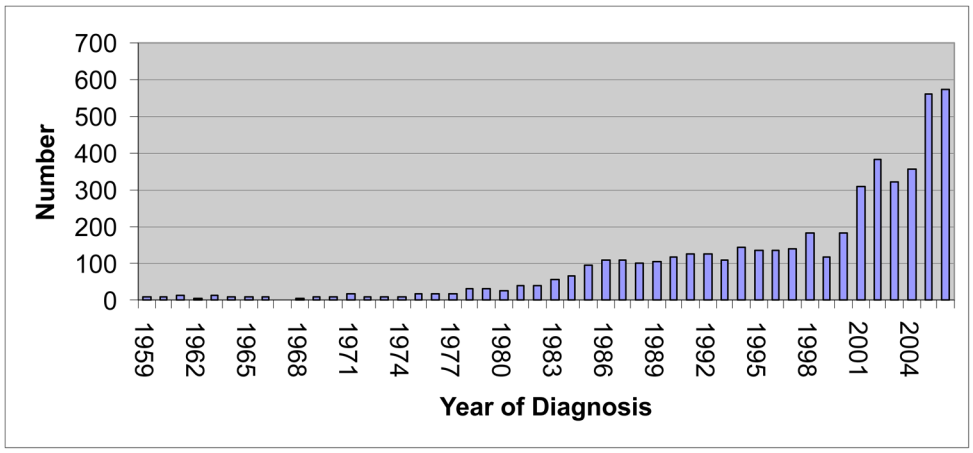

Figure 1.
The frequency of cases by year of diagnosis

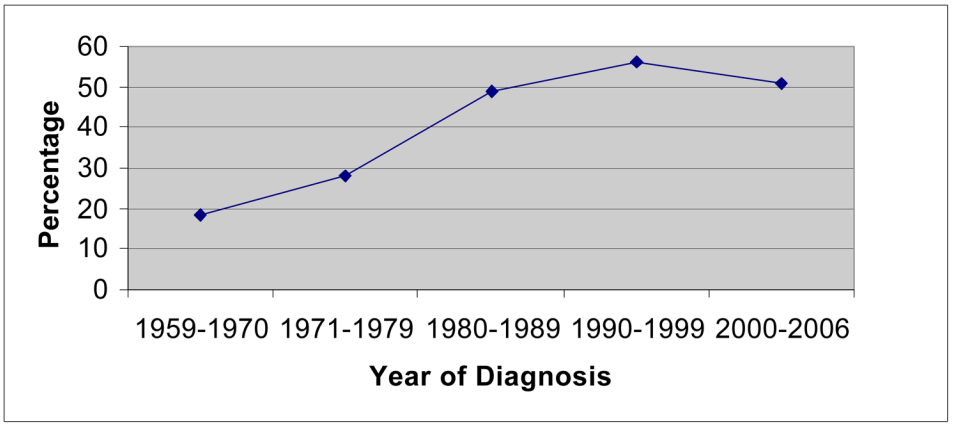

Figure 2.
The percentage of right sided polyps by the year of diagnosis

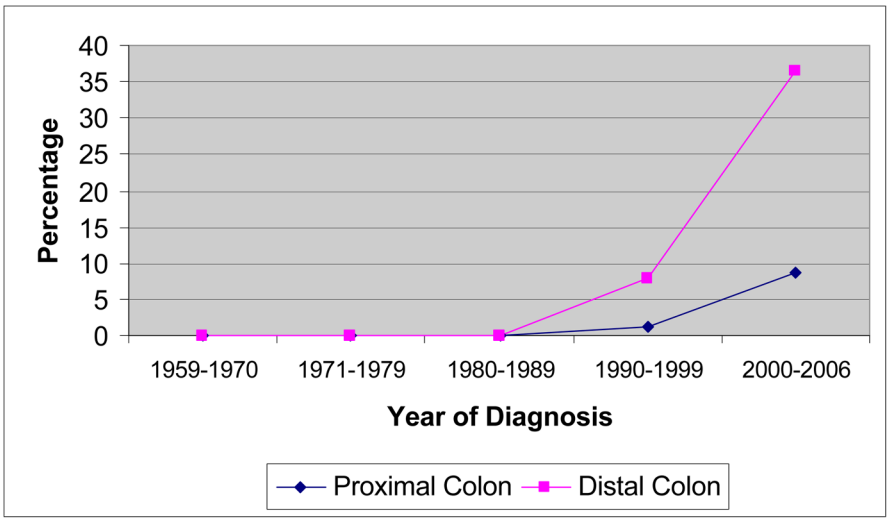

Figure 3.
The percentage of hyperplastic diagnosis in proximal and distal colon by year of diagnosis

Table 1

Histologic diagnosis and Location of Polyps

Diagnosis	Frequency	Percent
Tubular Adenoma	3641	72.6
Tubulovillous	414	8.3
villous	151	3.0
Hyperplastic	533	10.6
Mixed	241	4.8
Others	22	0.4
Undefined	11	0.2
Total	5013	100.0
Location		
Ascending colon	1302	26.0
Transverse	504	10.1
Descending	1450	28.9
Rectosigmoid	256	5.1
Multiple	645	12.9
Undefined	856	17.1
	5013	100.0

Table 2

Distribution of Hyperplastic diagnosis by year of diagnosis

	Diagnosis			
Year	**Neoplastic**	**Hyperplastic**	**Mixed or others**	**Total**
1959–1970	90 (92.8)	0	7 (7.2)	97 (100)
1971–1979	178(96.7)	0	6(3.3)	184(100)
1980–1989	813(97.5)	1(0.1)	22(2.6)	836(100)
1990–1999	1266(91.0)	50(3.6)	75(5.4)	1391(100)
2000–2006	1859(74.2)	482(19.2)	164(6.5)	2505(100)
Total	4206(83.9)	533(10.6)	274(5.5)	5013(100)

Table 3

Distribution of polyp diagnosis by age groups

Age	Neoplastic	Hyperplastic	Mixed or others	Total
≤50	572(76.9)	136(18.3)	36(4.8)	744(100)
51–60	1030(78.8)	192(14.7)	85(6.5)	1307(100)
61–70	1261(86.3)	134(9.2)	67(4.6)	1462(100)
71≤	1316(90.0)	71(4.9)	75(5.1)	1462(100)
Total	4179(84.0)	533(10.7)	263(5.3)	4975(100)

Table 4

Age distribution in proximal and distal polyps by diagnosis

Mean age (SD)	Proximal	Distal	p
Neoplastic	65.1(12.1)	62.5(12.5)	P<0.0001
Hyperplastic	59.0(11.8)	57.4(10.3)	0.2
Other	65.1(11.1)	61.0(12.0)	0.31
Total	64.8(12.1)	61.2(12.2)	P<0.0001

Table 5

Multivariate model for risk of neoplastic diagnosis in colon polyps

	OR	95% CI	P
Age (years)	1.04	1.03–1.05	0.0001
Sex (male/Female)	1.53	1.24–1.88	0.0001
Location (Proximal/Distal)	5.07	4.0–6.4	0.0001

Chi-2 for Hosmer and Lemeshow test= 17.79 (p=0.02)

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Table 6

Distribution (%) of Neoplastic and Hyperplastic polyps in different studies

Reference	Year	No. of Polyps	Location	Neoplastic	Hyperplastic	Others
Autopsy						
Eide and Stalsberg [62]	1978	483	Norway	58	17	25
Vatn and Stalsberg [19]	1982	687	Norway	50	26	24
Williams et al. [45]	1982	843	UK	29	68	3
Bombi [41]	1988	122	Spain	73	2	25
Cood et al. [7]	1985	200	Hong Kong	62	31	7
Jass et al. [46]	1992	406	New Zealand	38	62	0
Colonoscopy						
Granqvist et al [43]	1979	300	Sweden	37	39	24
Tedesco et al. [63]	1982	329	USA	49	37	14
Isbister [44]	1986	803	Australia	59	39	14
O'Brein et al. [40]	1990	5066	USA	67	11	22
Khan et al. [42]	2002	1050	Canada	83	12	5
Tony et al. [8]	2007	122	India	81	9	10
Present study		5013	USA	84	11	4