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OCCURRENCE OF COLORECTAL ADENOMAS IN YOUNGER ADULTS: AN EPIDEMIOLOGIC NECROPSY STUDY

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Abstract

Background and Aims—The colorectal adenoma is the precursor lesion in virtually all colorectal cancers. Occurrence of colorectal adenomas has been studied in older adults but analysis in younger adults is lacking.

Methods—The prevalence by age, sex, race, and location, and the number of colorectal adenomas detected was investigated using epidemiologic necropsy in 3558 persons aged 20–89 autopsied from 1985 to 2004 at the Johns Hopkins Hospital. Results were standardized to the general population. Younger adults 20–49 years old were compared to older adults 50 to 89 years old.

Results—The prevalence of colorectal adenomas in younger adults increased from 1.72% to 3.59% from the 3rd to 5th decade of life and then sharply increased after age 50. In younger adults, adenomas were more prevalent in men than women (RR= 1.09, CI 1.07–1.11) and whites than blacks (RR=1.28, CI 1.26–1.31). Overall, both younger and older adults had predominately left-sided adenomas, but blacks in both age groups had more right-sided adenomas. Occurrence of two or more adenomas in younger adults and five or more in older adults was greater than 2 standard deviations from the mean.

Conclusions—Colorectal adenomas infrequently occur in younger adults and are more prevalent in the left colon. Irrespective of age, blacks have more right-sided adenomas suggesting need for screening the entire colorectum. Two or more adenomas in younger adults and five or more in older adults represents polyp burden outside the normal expectation.

INTRODUCTION

Colorectal cancer is a major American health problem. In the United States, estimates reveal that 153,760 persons will be diagnosed with and 52,180 individuals will die of colorectal cancer

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in 2007(1). Each American citizen has a 6% life time risk of colorectal cancer, and this tumor is the second leading cause of cancer-related death after lung cancer. When colorectal cancer is diagnosed at an early stage, 5-year survival rates are about 90%. However, less than 40% of patients present at early stage (2). Consequently, public health officials have focused on colorectal cancer prevention spending considerable resources in the design and implementation of colorectal cancer screening programs.

The colorectal adenomatous polyp is the premalignant precursor lesion for almost all colorectal cancers (3). This appears true for noninherited (sporadic) colorectal malignancies and also for the inherited forms including hereditary nonpolyposis colorectal cancer, familial adenomatous polyposis (FAP) and other variants (attenuated FAP and MYH associated polyposis). Importantly, persons with inherited colorectal cancer syndromes develop colorectal cancer at younger age, often have multiple adenomas, and can have an accelerated adenoma to carcinoma sequence (4). Consequently, understanding the natural occurrence of colorectal adenomas, especially in younger adults, is important to development of colorectal cancer prevention strategies. Although this data could be obtained through colonoscopic evaluation of asymptomatic, average risk, young adults, this approach is problematic. An alternative methodology is epidemiologic necropsy.

Epidemiologic necropsy is a study design utilizing data incidentally found in autopsies performed for unrelated illnesses (5). Hence, this methodology attempts to avoid referral bias due to the nature of the hospitalized or clinic population investigated. Furthermore, through adjustment for demographics by standardization, selection bias from composition of an autopsy population is minimized in an attempt to provide findings that can be generalized. In this fashion, epidemiologic necropsy can provide reliable estimates of the reservoir of undetected lesions/disorders in the general population.

Although some data exist on the prevalence of colorectal adenomas in older adults (50 years of age and older), information is lacking in younger adults. Therefore, this study examined the natural occurrence of colorectal adenomas in the younger adults with comparison to older adults utilizing the study design of epidemiologic necropsy.

METHODS

Study population

The study population comprised serial autopsy subjects undergoing necropsy examination from January 1, 1985 to December 31, 2004 of patients hospitalized at the Johns Hopkins Hospital. The study was approved by the Johns Hopkins University School of Medicine Institutional Review Board.

Study design

This investigation utilized the study design of epidemiologic necropsy to analyze the occurrence of colorectal adenomas in younger adults (age 20 to 49) with comparison to older adults (age 50 to 89). This methodology requires quantification of disease which was undetected or unsuspected during life (5). Therefore, all individuals with evidence or suspicion of colorectal adenomatous polyps before death as determined by review of premortum hospital records were excluded on the basis of the following criteria: (1) history of colorectal cancer or polyps, (2) polyps visualized on barium enema or endoscopy, (3) presence of a familial intestinal polyposis syndrome or hereditary nonpolyposis colorectal cancer, (4) stool with overt or occult blood, or (5) history of inflammatory bowel disease. Also excluded were colorectal cancers detected during the autopsy (to eliminate bias in the composition of necropsy data due to clinical selection), necropsies without examination of the abdomen, or subjects with previous

surgical resection of the colorectum. Moreover, autopsies were only included if the large intestine was inspected which is the standard procedure in our institution for all necropsies irrespective of cause of death.

Autopsies included in the study were performed in the standard fashion which includes opening and cleaning of the large bowel, inspection of the mucosa, counting and measuring polyps and microscopic evaluation of each lesion. The finding of an adenomatous polyp was confirmed by histopathologic review. Consequently, the number, anatomical location, and type of polyps were noted. Other histological types of polyps identified (hyperplastic, juvenile, inflammatory, etc.) were not included in this analysis. Also, data on age, sex, race, date of autopsy were recorded. The anatomical location of polyps in the colorectum was classified as right-sided (cecum, ascending colon, transverse colon, or splenic flexure) or left-sided (descending colon, sigmoid colon, or rectum). For analysis of polyp location, patients with adenomas in both the right and left colon (n= 29) and those in which the location was not recorded (n= 25) were excluded. Also, each patient was counted as one observation regardless of the number of polyps.

Data Analysis

Patients were categorized by sex, race and 10-year age groups from 20 to 89 years of age. Crude prevalences were adjusted for differences in demographics between the study group and the general population by direct standardization (6) in accordance with the study design of epidemiologic necropsy (5). The 2000 Maryland population was used as reference (7). No major differences existed between age distribution and composition of other demographic variables between the study and standard population. For each 10-year age group an overall age-sex- and race-group-standardized prevalence of adenomas was computed with 95% confidence limits. The adenoma prevalence and location was compared between younger adults (age 20 to 49) and older adults (50 to 89 years old), and in both age groups between men and women, and whites and blacks. The mean number and standard deviation of adenomas found on autopsy in those affected with adenomas was compared by age.

RESULTS

The results of 3558 serial autopsies performed between January 1, 1985 and December 31, 2004 were reviewed. The mean autopsy rate during this period was 24.8% and steadily declined from 34.6% in 1985 to 16.3% in 2004. Of these, 607 were excluded from analysis because of premortem suspicion or evidence of colorectal adenomatous polyps, colorectal cancer or inflammatory bowel disease, colorectal cancer found at autopsy, necropsies without examination of the abdomen, or subjects with previous surgical resection of the colorectum. In the younger adults 161 cases were excluded from analysis including 13 with premortem colorectal neoplasia (4 with adenomas, 8 with colorectal cancer and 1 with both lesions). In older adults 446 cases were excluded for analysis including 119 with premortem colorectal neoplasia (39 with adenomas, 77 with colorectal, and 3 with both).

The standardized rate of occurrence of adenomas by decade of age is shown in Table 1. In younger adults, the prevalence of adenomas increased steadily from 1.72 to 3.59 per hundred autopsies from the 3rd to 5th decade of age. This rate sharply increased after 50 years of age with prevalence of adenomas ranging from 10.1 to 12.06 per hundred autopsies in the 6th and 9th decade of life, respectively. The risk ratio (RR) of adenomas in older to younger adults was 3.76 (95% CI 3.73–3.79), $p < 0.001$.

In young adults, the prevalence of adenomas was greater in men than women (RR 1.09; 95% CI 1.07–1.11; $p < 0.001$) and in whites compared to blacks (RR 1.28; 95% CI 1.26–1.31;

$p < 0.001$) (Table 2). In older adults, the prevalence of adenomas was also greater in men than in women but greater in blacks rather than whites.

In both younger and older adults, the overall standardized prevalence of left-sided adenomas was higher than right-sided adenomas (Table 3). Compared with younger adults, older adults had increased prevalence of adenomas on both sides of the colorectum, but a relatively greater prevalence of right-sided adenomas. Consequently, the right/left ratio increased from 0.59 in younger adults to 0.81 in older adults. Analysis of men and women revealed a similar pattern in both groups as described overall. When the location of adenomas was compared in racial groups, whites had the same pattern to that described above. However, blacks had a higher standardized prevalence of right-sided adenomas than left-sided adenomas with right to left ratios greater than unity in both younger and older adults.

The number of synchronous adenomas present in those affected described by decade of age is shown in Table 4. In younger adults, the greatest mean number of adenomas was 1.1. In individuals under age 50, occurrence of 2 or more adenomas is greater than 2 standard deviations from the mean. In older adults, the mean number of adenomas ranged between 1.6 and 1.9. In this group, occurrence of 5 or more adenomas was 2 standard deviations from the mean in all decades except 60–69 in which 4 or more adenomas fulfilled that criterion.

The rate of advanced adenomas (size ≥ 1 cm, any villous histology, or dysplasia) found in the autopsy series was 35.5% and was not statistically significantly different between the younger and older adult autopsy groups.

The cause of death in the entire autopsy study group was cardiovascular 24.2%, malignant neoplasm 26.1%, and other 49.7%. These findings are similar to the most recent statistics for the general U.S. population: cardiovascular 27.3%, malignant neoplasm 22.9%, and other 49.8% (8).

DISCUSSION

Little information exists on the occurrence of colorectal adenomas in younger adults. The present study evaluated the large intestine of 1001 individuals undergoing necropsy between 20 and 49 years old for the presence of adenomas and represents, to our knowledge, the largest investigation (by several fold) of this kind. A low but increasing prevalence of colorectal adenomas (1.72% to 3.72%) was noted from the 3rd to 5th decade of life. Other data concerning the prevalence of adenomas in younger adults are scarce but comes from two sources- autopsy studies and colonoscopy screening for colorectal cancer. The largest autopsy series are those of Haghighi et al. (9) (411 Iranian necropsies between ages 20–49) and Restrepo et al. (10) (332 Columbian cases <44 of age). These investigators found the prevalence of colorectal adenomas to be 1.2% and 2.4%, respectively. Although, these results are similar to ours, these investigations did not utilize epidemiologic necropsy methodology (excluding cases with premortem suspicion of colorectal neoplasia), and the data was not standardized to the general population. Additional autopsy studies exist (11–20) with estimates of prevalence in young adults from 3.9% to 35.7%. These investigations studied far fewer subjects, lacked exclusion criteria as mentioned above, and did not standardize the data.

Two colorectal cancer screening studies utilizing colonoscopy have examined individuals between ages 40 to 49 for the presence of colorectal neoplasia. These investigations report a colorectal adenoma prevalence of 8.7% and 9.0% (21,22), a higher rate than in the present study. These results could have occurred from enrichment of the cohorts with affected individuals through selection bias and from lack of exclusion of those individuals with rectal bleeding (22) or a family history of colorectal cancer (21). Of note, when persons without family history of colorectal cancer are analyzed in one study, the prevalence of adenomas

decreases from 9.0% to 6.6% (22) highlighting the sensitivity of these results to the population studied.

The prevalence of colorectal adenomas found in this study might be influenced by the increasing application of general population colorectal cancer screening especially by colonoscopy. Premortem screening would lower the rate of colorectal neoplasia ultimately found at autopsy. Although, this factor might apply to the older adults (50 years of age or above), the younger adults did not meet screening guidelines and, consequently, would have been unlikely to have undergone screening tests.

Of interest, the present study found a greater than 3 fold increase in prevalence of colorectal adenomas in older adults, abruptly starting in the 6th decade. These data are similar to autopsy and colonoscopy studies which reveal an increase in prevalence of adenomas with age and a dramatic increase in colorectal cancer incidence occurring after age 50. Taken together these data support the rationale given for colorectal cancer screening guidelines recommending screening of the general population starting at age 50 years old.

Overall, younger adults had predominately left-sided polyps (right/left ratio 0.59) with 63% of adenomas found in the left colon from splenic flexure to rectum; older adults had 55% of adenomas left-sided. Remarkably, blacks in both age groups had predominately right-sided adenomas. In younger adult blacks the right/left ratio was 6.40 primarily due to a relative absence of left sided adenomas. In older blacks, the right/left ratio was 1.43. Of note, information on colorectal cancer screening uptake in this autopsy cohort was not available. Nevertheless, these data are consistent with the finding that younger black adults have more proximal colorectal cancer than younger white adults (23) and argue that screening and diagnostic evaluations of African Americans should include complete evaluation of the colorectum.

The present study found that the mean number of adenomas occurring in affected younger adults ranged from 1.0 to 1.1. Consequently, individuals under 50 years of age with 2 or more adenomas had polyp burdens greater than 2 standard deviations from the mean. In persons 50 years of age or older, 5 or more adenomas represented such a threshold. To our knowledge, this is the first study to quantitate the number of naturally occurring adenomas in any age group. Consequently, persons presenting with polyp numbers at or above these threshold values are individuals with polyp burden outside the normal expectation.

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REFERENCES

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ, et al. Cancer statistics. *CA Cancer J Clin* 2007;57:43–66. [PubMed: 17237035]
2. Smith RA, von Eschernbach AC, et al. American Cancer Society guidelines for the early detection of cancer: update of early detection guidelines for prostate, colorectal, and endometrial cancer. Also: update 2001- testing for lung cancer detection. *CA Cancer J Clin* 2001;51:38078.
3. Winawer SJ, Fletcher RH, Miller L, Godlee F, Stolar M, Mulrow CD, Woolf SH, Bond JH, Glick SN, Rosen L, Zapka JG, Olsen SJ, Giardiello FM, Ganiats TG, Sisk J, Antwerp R, Brown-Davis C, Marciniak D, Mayer RJ. Colorectal cancer screening and surveillance: clinical guidelines, evidence, and rationale. *Gastroenterology* 1997;112:594–642. [PubMed: 9024315]

4. Giardiello FM, Brensinger JD, Petersen GM. American Gastroenterology Association Technical Review on Hereditary colorectal cancer and genetic testing. *Gastroenterology* 2001;121:198–213. [PubMed: 11438509]
5. McFarlane MD, Feinstein AR, Wells CK, Chan CK. The epidemiologic necropsy. Unexpected detections, demographic selections and changing rates of lung cancer. *JAMA* 1987;258:331–8. [PubMed: 3599325]
6. Breslow, NE.; Day, NE. Statistical methods in cancer research. 82. IARC scientific publication; 1987. p. 52–61.
7. Census 2000 Data for the State of Maryland. <http://www.census.gov/census2000/states/md.html>
8. Minino AM, Heron MP, Smith BL. Deaths: Preliminary Data for 2004. *National Vital Statistics Reports* 2006;54(19):1–50.
9. Haghighi P, Nasr K, Mohallatee EA, Ghassemi H, Sadri S, Nabizadeh I, Sheikholeslami MH, Mostafavi N. Colorectal polyps and carcinoma in Southern Iran. *Cancer* 1977;39:274–278. [PubMed: 832242]
10. Restrepo C, Correa P, Duque E, Cuello C. Polyps in a low-risk cancer population in Colombia, South America. *Dis Colon Rectum* 1981;24:29–36. [PubMed: 7472099]
11. Jass JR, Young PJ, Robinson EM. Predictors of presence, multiplicity, size and dysplasia of colorectal adenomas. A necropsy study in New Zealand. *Gut* 1992;33:1508–1514. [PubMed: 1452076]
12. Williams AR, Balasooriya BAW, Day DW. Polyps and cancer of the large bowel: a necropsy study in Liverpool. *Gut* 1982;23:835–42. [PubMed: 7117903]
13. Johannsen LGK, Momsen O, Jacobsen NO. Polyps of the large intestine in Aarhus, Demark: An autopsy study. *Scand J Gastroenterol* 1989;24:799–806. [PubMed: 2799283]
14. Gerharz CD, Gabbert H, Krummel F. Age-dependent shift-to-the-right in the localization of colorectal adenomas. *Virchows Arch A* 1987;411:591–8.
15. Vatn MH, Stalsberg H. The prevalence of polyps of the large intestine in Oslo: An autopsy study. *Cancer* 1982;49:819–825. [PubMed: 7055790]
16. Eide TJ, Stalsberg H. Polyps of the large intestine in Northern Norway. *Cancer* 1978;42:2839–48. [PubMed: 728878]
17. Bombi JA. Polyps of the colon in Barcelona, Spain. *Cancer* 1988;61:1472–76. [PubMed: 3345499]
18. Paspatis GA, Papanikolaou N, Zois E, Michalodimitrakis. Prevalence of polyps and diverticulosis of the large bowel in the Cretan population: An autopsy study. *Int J Colorectal Dis* 2001;16:257–261. [PubMed: 11515686]
19. Rickert RR, Auerbach O, Garfinkel L, Hammond EC, Frasca JM. Adenomatous lesions of the large bowel: An autopsy survey. *Cancer* 1979;43:1847–57. [PubMed: 445371]
20. Clark JC, Collan Y, Eide TJ, Esteve J, Ewen S, Gibbs NM, Jensen OM, Koskela E, MacLennan R, Simpson JG, Stalsberg H, Zaridze DG. Prevalence of polyps in an autopsy series from areas with varying incidence of large-bowel cancer. *Int J Cancer* 1985;36:179–86. [PubMed: 4018911]
21. Imperiale TF, Wagner DR, Lin CY, Larkin G, Rogge JD, Ransohoff DF. Results of screening colonoscopy among persons 40 to 49 years of age. *N Engl J Med* 2002;346:1781–5. [PubMed: 12050337]
22. Regula J, Rupinski M, Kraszewska E, Polkwoski M, Pachlewski J, Orlowska J, Nowacki M, Butruk E. Colonoscopy in colorectal-cancer screening for detection of advanced neoplasia. *N Engl J Med* 2006;355:1863–72. [PubMed: 17079760]
23. Fairley TL, Cardinez CJ, Martin J, Alley L, Friedman C, Edwards B, Jamison P. Colorectal cancer in U.S. adults younger than 50 year of age, 1998–2001. *Cancer* 2006;107(5 suppl):1153–61. [PubMed: 16862554]

Table 1
Standardized rates of autopsies with colorectal adenomas per hundred autopsies by decade of age.

	Age (years)						
	20-29	30-39	40-49	50-59	60-69	70-79	80-89
Crude rates*	2/144	8/334	19/523	57/558	71/652	57/521	26/219
Adjusted rate per hundred†	1.72	2.76	3.59	10.10	10.50	10.08	12.06

* Crude rates= Number of autopsies with colorectal adenomas/number autopsies

† Crude prevalences were adjusted for differences in demographics between the study group and the general Maryland population

Table 2
Standardized rates of adenomas in younger and older adults by sex and race.

	Age 20–49			Age 50–89		
	Rate/hundred	Risk Ratio (95% CI)	P-value	Rate/hundred	Risk Ratio (95% CI)	P-value
Males	2.88	1.09 (1.07–1.11)	<0.001	10.68	1.05 (1.04–1.06)	<0.001
Females	2.65			10.18		
Whites	2.52	1.28 (1.26–1.31)	<0.001	9.91	0.73 (0.72–0.74)	<0.001
Blacks	1.97			13.61		

Table 3
Standardized rates of colorectal adenomas per hundred autopsies by age group according to site and ratio of right over left sided adenomas.

	Age 20-49			Ratio right/left	Age 50-89		
	Rate per hundred	Rates			Rate per hundred	Rates	Ratio right/left
Overall							
Right	1.00	23818/2374220		0.59		47918/1397428	0.81
Left	1.70	40285/2374220				59219/1397428	
Males							
Right	0.90	10428/1152927		0.45		26094/626804	0.97
Left	2.00	23028/1152927				27023/626804	
Females							
Right	1.10	13390/1221293		0.64		21874/770624	0.68
Left	1.42	17257/1221293				32196/770624	
Whites							
Right	1.59	17515/1546829		0.54		29283/1046632	0.65
Left	2.93	24173/1546829				45168/1046632	
Blacks							
Right	2.32	6303/704411		6.40		18634/300772	1.43
Left	0.36	2514/704411				13024/309772	

* Adjusted for general Maryland population