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Risk of Colorectal and Other Cancers in Patients With Serrated Polyposis

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Abstract

Patients with serrated polyposis develop multiple colorectal hyperplastic and/or serrated sessile adenomas/polyps. We investigated the risk of colorectal and other cancers by analyzing data from 64 patients with serrated polyposis (mean age at diagnosis, 54 y; 41% male; 92% white) listed in the Johns Hopkins Polyposis Registry. Medical, endoscopic, and histopathology reports were evaluated. Six patients (9.4%) had a history of colorectal cancer, diagnosed at a mean age of 56 y; 6 additional patients (9.4%) had at least 1 advanced colorectal adenoma. Extra-colonic cancers were found in 16% of the study population. The standard incidence ratio for colorectal cancer in patients with serrated polyposis was 18.72 (95% confidence interval, 6.87 – 40.74) and for extra-colonic cancer was 31.20 (95% confidence interval, 14.96 – 57.37), compared to the SEER population. Patients with serrated polyposis therefore have a high risk for colorectal cancer and

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require vigilant colorectal surveillance, starting at the time of diagnosis of serrated polyposis. The risk of extra-colonic cancer also appears to be increased, but this requires further evaluation.

Keywords

hyperplastic polyps; sessile polyps; premalignant; colon cancer

INTRODUCTION

Serrated polyposis (SP) is a disorder typically characterized by several dozen serrated polyps distributed throughout the colorectum. Also, these patients can have synchronous colorectal adenomas (1,2).

SP has been associated with an increased risk of colorectal cancer. Evidence for this concept comes from a limited collection of case reports providing variable estimates of colorectal cancer risk (3–8). The risk of extra-colonic malignancies in SP has not been well examined. This study reports colorectal and extra-colonic cancers in a cohort of SP patients.

METHODS

Study population

Patients with SP enrolled in the Johns Hopkins Registry between January 1, 2001 and October 1, 2012. These patients self-enrolled in the Registry without physician referral or were enrolled by a Hopkins physician who saw the patient. None were referred to the Registry because of a history of cancers or a family history of SP. Patients met the WHO criteria for SP with: I) at least 5 serrated polyps proximal to the sigmoid colon with 2 or more of these being >10mm; or II) any number of serrated polyps proximal to the sigmoid colon in an individual who has a first-degree relative with serrated polyposis; or III) >20 serrated polyps of any size but distributed throughout the colon (2).

Study design

Data were collected from medical records and histopathology reports. All cancers were confirmed by pathology report. Patients with advanced adenomas (an adenoma 1 cm or greater, with villous components, or with high-grade dysplasia) were identified. A risk assessment for colorectal adenocarcinoma and extra-colonic cancer risk was performed. The standardized incidence ratio (SIR) was estimated using the Indirect Method, with observed cancer incidence among patients with SP divided by the expected cancer incidence based on the SEER population rates (2000–2011) (9). SIR values were estimated by sex and type of cancer: colorectal cancer and extra-colonic cancer. SIR values derived from the comparison with SEER data were adjusted for age, but not sex.

RESULTS

The study population was 64 patients with SP from 62 pedigrees (Table 1). The mean age (SD) at diagnosis of SP was 53.6+11.5 yrs.

Patients with SP who developed colorectal and extra-colonic cancer are listed in Table 2. Six of 64 patients (9.4%) with SP developed colorectal cancer. The mean age of diagnosis of colorectal cancer was 56.0+13.0 (45–75). An additional 6 patients had advanced adenomas at a mean age of 57.17+10.8 (43–69). Sixteen percent of the study population developed an extra-colonic cancer (Table 2).

The SIR (95% CI) of colorectal cancer in patients with SP was 26.28 (7.16 – 67.29) for females, 11.72 (1.42 – 42.32) for males, and 18.72 (6.87 – 40.74) overall. The SIR (95% CI) for extra-colonic cancer in patients with SP was 39.42 (14.47 – 85.80) for females, 23.43 (6.38 – 59.99) for males, and 31.20 (14.96 – 57.37) overall.

DISCUSSION

Literature review reveals a large range, 7% to 70%, of risk of colorectal cancer in SP patients (1,3–8,10). In the 3 largest case series of patients with SP, a high percentage of patients (26% to 28.5%) were diagnosed with colorectal cancer (1,10,11). All published reports of SP found 122 of 308 patients (39.6%) diagnosed with CRC (12). Our study reports a high risk of colorectal cancer and advanced adenomas in SP. Overall SP patients had elevated SIR (19.01) of CRC with the risks greater for females than males. These high-risk estimates for CRC are consistent with the high rate of adenomas and sessile serrated adenomas/polyps found on initial colonoscopy evaluation (13). Also, Boparai et al. calculated a worrisome risk of colorectal cancer during surveillance of 7% at 5 years in those with intact colons (10).

In SP the increased risk of colorectal cancer appears associated with younger age of diagnosis. In our study, the average age of diagnosis of colorectal cancer was 56. Literature review of the three largest case series reveals a median age of colorectal cancer of 45, 56, and mean age of 63. All three studies reported patients diagnosed with CRC in the 4th decade of life (1,10,11).

Kalady et al., suggested 3 different phenotypes of serrated polyposis (11). These include patients with few large right-sided polyps, those with many small left sided polyps, and individuals with a combination of left- and right-sided polyps. Although differences in CRC risk could be associated with phenotype, the frequency of colorectal cancer noted by this investigator in these 3 types was similar (21–28%). The majority (77%) of patients in our cohort fulfill the third of the WHO criteria. Small numbers of observations made assessment of CRC risk by phenotype impossible.

Elevated risk of extra-colonic tumors is commonly noted in polyposis syndromes. Kalady et al. found that 28% of serrated polyposis patients had extra-colonic cancer (11). Also, 54% of patients had a family history of extra-colonic cancer. Jasperson et al. (14) found 24% of SP patients had extra-colonic cancer, although Hazewhinkel et al. (15) reported a relative risk of 0.69 (95% Cl 0.36–1.33) for extra-colonic cancers. In our study, 16% had extra-colonic cancer. Risk assessment showed an elevated risk for extra-colonic cancer in SP patients (SIR, 31.2) with the risks greater for females than males.

A caution raised when comparing a registry-based population to the general US population is detection bias meaning that surveillance of the population in the registry may lead to higher diagnosis of certain disorders compared to the general population. This concern cannot be discounted. Another limitation in interpretation of the results is that the small number of patients in the study causes large confidence intervals in the estimates of cancer risk.

This study, with other literature, argues for a high risk of colorectal cancer in patients with SP. These findings support at least initial annual colonoscopy surveillance in patients with intact colons and similar endoscopic evaluation in those with colectomy and retained colorectal segments with removal of all polyps at the time of examination. These recommendations are consistent with experts who promote close surveillance in patients treated endoscopically for SP (16). The NCCN guidelines recommend colonoscopy surveillance for serrated polyposis patients with intact colons every 1–3 years depending on the number of polyps found and cleared at colonoscopy (17). Young and Parry (18), recommend surgery when polyps cannot be controlled endoscopically, particularly if adenomatous features are present.

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Abbreviations

SP	serrated polyposis
CRC	colorectal cancer
RR	relative risk
NCCN	National Comprehensive Cancer Network

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Table 1

Characteristics of Study Patients

No. of patients	64
Sex – no. (%)	
Female	38 (59)
Male	26 (41)
Caucasian race: no. (%)	59 (92)
African American	5 (8)
No. of pedigrees	62
Serrated polyposis mean age at diagnosis- yr. Mean+SD (range)	53.6+11.2 (22–78)
No. (%) fulfilling WHO criteria for SPS	
I	17 (27)
II	0 (0)
III	47 (73)
Colorectal cancer mean age at diagnosis- yr. Mean+SD (range)	56.0+13.0 (45–78)

Table 2

Patients with serrated polyposis who developed cancer

Age at diagnosis of cancer	Sex	Race	Cancer type
30	male	White/Caucasian	Basal cell carcinoma
40	female	White/Caucasian	Breast
49	female	White/Caucasian	Breast
60	female	White/Caucasian	Breast
35	female	White/Caucasian	Cervix
45	female	White/Caucasian	Colorectal (sigmoid)
47	female	White/Caucasian	Colorectal (sigmoid)
47	male	White/Caucasian	Colorectal (sigmoid)
50	male	White/Caucasian	Colorectal (cecum)
69	female	White/Caucasian	Colorectal (sigmoid)
75	female	White/Caucasian	Colorectal (ascending)
24	female	White/Caucasian	Hodgkins Lymphoma
50	female	White/Caucasian	Ovarian
53	male	White/Caucasian	Prostate
56	male	African American	Prostate
53	male	African American	Ureter