Endoscopic control of polyp burden and expansion of surveillance intervals in serrated polyposis syndrome

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Abstract

Introduction: Serrated polyposis syndrome (SPS) increases colorectal cancer (CRC) risk. We describe the numbers of colonoscopies and polypectomies performed to achieve and maintain low polyp burdens, and the feasibility of expanding surveillance intervals in patients who achieve endoscopic control.

Methods: We retrospectively evaluated a prospectively collected database on 115 SPS patients undergoing surveillance at Indiana University Hospital between June 2005 and May 2018. The endoscopist provided surveillance interval recommendations based on polyp burden. Endoscopic control was considered successful if surveillance examinations exhibited fewer polyps and if no or only an occasional polyp ≥1 cm in size was present at follow-up. Initial control was designated the clearing phase and the maintenance phase was surveillance after control was established.

Results: In total, 87 patients (75.7%) achieved endoscopic control, with some others in the clearing phase at this writing. Achieving control required a mean of 2.84 colonoscopies (including the baseline) over 20.4 months and a mean total 27.9 polyp resections. After establishing control, 71 patients were recommended to receive ≥24-month follow-up. Of those, 60 patients (69.0% of patients with initial control) continued surveillance at our center. The mean interval between colonoscopies during maintenance was 19.3 months with 6.74 mean polypectomies per procedure on polyps primarily <1 cm. There were no incident cancers or colon surgeries during maintenance.

Conclusion: Most patients achieved control of polyp burden with 2 to 3 colonoscopies over 1 to 2 years. After reaching control, 60 patients returned at intervals up to 24 months with no incident cancers and no surgeries required. Expansion of surveillance intervals to 24 months is effective and safe for many SPS patients who reach control of polyp burden.

<u>Introduction</u>:

Serrated polyposis syndrome (SPS), previously referred to as hyperplastic polyposis syndrome, is associated with an increased risk of colorectal cancer (CRC)[1-3]. The World Health Organization (WHO) criteria include three subtypes of SPS (Table 1)[4]. Patients with SPS are often recommended to undergo annual surveillance colonoscopy[2]. However, most cancers in SPS are identified at the prevalence colonoscopy and the risk of cancer during surveillance has been recently described as low[5,6].

Polyp burden, a term that generally refers to both increasing number and size of polyps, is quite variable in SPS. Patients with low polyp burden may be effectively controlled after a single colonoscopy with polyp resections. In other cases, several colonoscopies are needed (or one or two lengthy colonoscopies), using many polyp resections, to bring the polyp burden to a level where short-term risk of cancer seems minimal. In our practice, we often extend the surveillance interval beyond 1 year in SPS patients once the number of polyps has been reduced

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substantially and all large polyps are resected[7]. In this report we describe our experience with achieving control of polyp burden and expansion of surveillance intervals in SPS patients.

Materials and Methods:

We retrospectively analyzed a prospectively collected database of 115 SPS patients who received treatment at Indiana University Hospital. The database included demographic information and the results of each colonoscopy. All patients were examined with Olympus (Olympus Corporation, Center Valley, Pa, United States) colonoscopes by DKR between June 2005 and May 2018. Colonoscopes in Olympus 180 and 190 series were universally high-definition instruments. Patients were usually referred by other colonoscopists outside the institution for polyp resection, though some were recognized as SPS patients during routine screening or surveillance colonoscopies. They were entered into the database as the diagnosis of SPS was recognized, almost invariably by the senior endoscopist (very few patients were referred with the diagnosis of SPS).

The endoscopist made surveillance interval recommendations based on polyp burden at the end of each colonoscopy. Endoscopic control was considered successful if subsequent examinations exhibited fewer polyps and if no or only an occasional polyp ≥1 cm was present at follow-up. No specified minimum number of polyps was required to reach a point considered to be control. Rather, control was considered achieved when the polyp burden based on number and size of lesions was substantially reduced from baseline. The mean number of polyps removed per

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procedure in the maintenance phase (see results) gives a reasonable sense of the residual polyp burden at the point of control. Patients with cancer or polyps that could not be endoscopically resected (eg, a lesion surrounding the appendiceal orifice), or who had extensive burdens and indicated a preference for surgery, were referred for extended right hemi-colectomy or subtotal colectomy as appropriate.

We considered endoscopic treatment to occur in 2 phases. The first phase was the clearing phase defined as treatment required to the lower polyp burden with intent of achieving endoscopic control. Thus, the clearing phase required at least 2 examinations, including at least one to adequately clear the colon, and another to confirm the polyp burden was effectively reduced. The second phase was the maintenance phase defined as procedures performed to maintain control by keeping the polyp burden low. No statistical analysis was performed, as the results are descriptive.

Throughout the study interval polyps <1 cm in size were removed almost entirely by cold snaring. Endoscopic mucosal resection (EMR) was performed throughout the study interval using a contrast agent (indigo carmine or methylene blue) in the submucosal injectate. Initially the submucosal injection fluid was usually saline and later hetastarch. EMR was performed using snare electrocautery, until about 2015, when we began using predominantly cold snare resection to perform EMR on serrated lesions [8]. Consistent attempts were made to resect normal margins at the polyp edges. Patients requiring multiple EMRs of lesions in the same vicinity often underwent submucosal injection of multiple lesions before snare resection of any of the lesions in order to reduce time for passing devices

through the colonoscope. Resection margins of cold snare and EMR sites were routinely inspected to identify residual polyp pits and resect them as needed. The registered nurse working in the procedure room was charged with counting the polyps removed, including numbers of polyps ≥10 mm and by colon location. Procedures were typically scheduled according to the amount of anticipated time for resections at 30, 45, 60, or 90 minutes.   In general the approach to reduction of polyp burden followed an approach we've previously described for control of polyp in familial adenomatous polyposis (FAP) [9] (reliance primarily on extensive cold snaring), though there were more large polyps requiring EMR than were needed in the FAP patients who were considered candidates for endoscopic control. If the work needed to achieve control was not completed in the time allotted time for the colonoscopy, then another procedure was scheduled within 3 to 6 months and for a procedure duration that reflected the endoscopist's assessment of the patient's cancer risk based on endoscopic survey of numbers and sizes of polyps not yet removed.   Once the polyp burden was under control, the intervals between examinations were expanded to 18 to 24 months and occasionally longer intervals.

Polyps of the same predicted histology and in the same segment of the colon were placed in the same formalin bottle for assessment by pathology. Histology was predicted endoscopically using criteria expressed in the Narrow Band Imaging (NBI) International Colorectal Endoscopic Classification (NICE). [10] Before 2013, no standardized histologic definition of sessile serrated polyp was used in the pathology department.   Beginning in 2013, the WHO criteria for sessile serrated polyp were used. [4]

Permission to review the de-identified database was granted by the Institutional Review Board at Indiana University on June 25, 2018.

Results:

The mean age of the 115 SPS patients at diagnosis was 64.2 years, and 73 (63.5%) were female.   The indications for the procedure during (or shortly after) which the diagnosis was made included screening (n=39), referral for resection of a large polyp (n=25), polyp surveillance (n=24), hematochezia (n=5), history of colorectal cancer (n=5), positive fecal blood test (n=4), and miscellaneous (n=13). There were 429 colonoscopies performed on 115 patients diagnosed with SPS.   Of those, 112 underwent more than 1 colonoscopy at our center. Four patients had cancer at the prevalence examination and each was operated. One additional patient elected surgery after discussion of a baseline colonoscopy that showed a very extensive polyp burden. Another 5 patients were referred for surgery because of polyps that could not be endoscopically resected. Four of these were because of a polyp in the appendiceal orifice that could not be fully exposed for endoscopic resection. One patient had a very complex cecal insertion and had a recurrence of a right colon serrated lesion that was very difficult to access endoscopically.   At the time of this writing, 19 patients diagnosed with SPS had not yet reached control and were still in the process of colonoscopic clearing.   The mean total surveillance period (time between first and last examination) was 2.1 years, or 25 months.

There were 75 patients that met WHO diagnostic criterion 1 only, 2 patients meeting criterion 2, 19 patients met criterion 3, and 19 patients met both criteria 1 and 3.

In total, 87 patients achieved endoscopic control (Table 2). The number of procedures per patient in those who achieved control ranged from 2 to 8 with a range of 1 to 135 polypectomies per procedure. Achieving initial control required a mean of 2.84 examinations (range 2-5) over 20.4 months with a mean total 27.9 (range 5-195) polyp resections (Table 3). There were 4 patients who had more than 100 polyps removed in the clearing phase and 20 who had ≥10 endoscopic mucosal resections (EMRs). Sessile serrated polyps with cytological dysplasia were found in 13 patients and ≥1 conventional adenoma in 80 of the patients who achieved control. The largest number of polyps removed in a single colonoscopy was 135 and the largest number of EMRs in a single colonoscopy was 32. Recommended follow up intervals within the clearing phase included 3, 4, 6, or 12 months. As expected, Type 3 (mean 46.6 polyp resections) and Type 1 and 3 (mean 67.0 resections) patients had higher mean numbers of polypectomies in the clearing phase. Type 1 patients had fewer mean polypectomies than other types, but had a high mean number of large polyps (≥1 cm) at 8.14 per patient. Patients who met both Types 1 and 3 criteria had the highest mean number of large polyps at 13.2.

After establishing control, 71 patients were recommended to return for maintenance examinations in ≥24 months due to low polyp burdens. Of the patients recommended to return in ≥24 months, 10 did not seek further treatment at our center. After achieving control, the mean interval between examinations was

19.3 months with 6.74 mean polypectomies performed per colonoscopy on polyps primarily <1 cm in size.   Of 61 patients who returned to our center for maintenance colonoscopies, 60 stayed in control. Of these, 43 returned at intervals that were actually ≥24 months, and 18 returned at shorter intervals, in some cases because of symptoms. One patient had an increase in polyp burden at follow-up and was recommended to return to shorter examination intervals. No patient developed cancer or required surgery during the cleaning or maintenance phase.

There were 98 patients who had conventional adenomas in addition to the serrated lesions present to meet SPS diagnosis.   At this writing, 80 patients with conventional adenomas had lowered their polyp burden to the point of control.

There were no perforations. Two patients had post procedure symptoms consistent with postpolypectomy coagulation syndrome (hospitalized for 2 and 3 days, respectively), and there were no delayed hemorrhages that required hospitalization, transfusion, or repeat colonoscopy.

Discussion

In this report we describe one of the largest single center experiences with endoscopic management of SPS.   Several multicenter studies from outside the United States include larger numbers of SPS patients [5,6]. Compared with these series our patient population is skewed toward patients with Type 1 SPS (at least 5 serrated lesions proximal to the sigmoid with at least 2 >1 cm in size). Thus, 85% of our patients met Type 1 criteria, compared with 55% and 59% in 2 large European multicenter studies [5,6].   Further, the number of large polyps resected per patient was higher than other series [5,6,11,12]. The number of large lesions and patients with

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Type 1 SPS almost certainly reflects referral bias because the senior author has often identified SPS in patients referred for resection of one or more large serrated lesions. Despite that, we did not encounter incident colorectal cancers during surveillance, indicating that endoscopic control of SPS is feasible is patients with substantial numbers of large lesions. Our data indicate that extensive use of EMR is both required (based on lesion size) and effective for control of polyp burdens in patients that meet Type 1 criteria.

Others have also recently identified a lower risk of CRC during surveillance of SPS than was identified in early studies. For example, in one study from 18 centers in Spain, 296 patients with SPS had an incidence of cancer of 1.9% over 5 years of surveillance [5]. We had no incident cancers during surveillance, but we also had fewer patients, shorter follow-up, and a single expert endoscopist. Overall, recent studies indicate that SPS patients without cancer at their baseline examination have a low incidence of cancer when their colons are aggressively cleared of polyps and they continue in surveillance. We found that substantial numbers of SPS patients could reach low polyp burdens that allowed expansion of their surveillance interval to two years, and this expansion occurred safely. Thus, although guidelines generally recommend annual surveillance in SPS, our results are consistent with others who report using intervals of 1 to 2 years in SPS patients, depending on the polyp burden [5,6,12]. Expanding the interval between colonoscopies to 2 years in selected patients will reduce costs and burdens of SPS surveillance to patients and society.

Our impression is that endoscopic control of SPS requires a commitment to colonoscopies that are often longer than standard procedures. Successful control of SPS requires a willingness to perform large numbers of polypectomies, including numbers of EMRs, in a single procedure. Success is facilitated by allowing more time on the schedule to complete colonoscopy during the clearing phase. Anecdotally, "cold EMR" has made clearing the colon easier and less expensive because large resection sites in the cecum and proximal colon do not generally need clip closure [13] after EMR to prevent delayed adverse events.

Limitations of this study include its retrospective nature and the imperfect follow-up. Nevertheless, a large number of patients did return for follow up and comprise a substantial population to establish the safety of surveillance in SPS. Second, the patient population is skewed toward SPS Type 1, but the population is informative with regard to expected work to achieve polyp control in an SPS population with a heavy polyp burden of large lesions.

In summary, we have demonstrated that the majority of SPS patients can realize control of their polyp burdens after a few colonoscopies, and subsequently maintain control after expansion of surveillance intervals to 24 months. Expansion of surveillance intervals should increase the acceptance, feasibility, and cost-effectiveness of surveillance colonoscopy in SPS.

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Table 1. World Health Organization criteria for SPS *

Type 1 – At least 5 serrated polyps** proximal to the sigmoid colon, with at least 2 > 10 mm in size
Type 2 – An individual with any number of serrated polyps proximal to the sigmoid colon who has a first degree relative of a patient with serrated polyposis syndrome
Type 3 – At least 20 serrated polyps of any size distributed throughout the colon
*from reference 4
** includes sessile serrated polyps/adenomas, hyperplastic polyps and traditional serrated adenomas

Table 2. Number and percentage of patients who were diagnosed with SPS, achieved control of their polyp burden, and maintained control of polyp burden per WHO diagnostic type.

	Total Patients	Type 1	Type 2	Type 3	Types 1 and 3*
Diagnosed	115	75 (65.2%)	2 (1.7%)	19 (16.5%)	19 (16.5%)
Achieved Control	87	59	1	13	14
Cancer at Baseline	4	2	0	1	1
Required Surgery for Polyp Removal	5	4	0	1	0
Still in Clearing Phase	19	10	1	4	4

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Table 3. Mean time to achieve endoscopic control, mean number of examinations, polyps removed, and large polyps per diagnostic type in the clearing phase.

	Patients who achieved control	Type 1	Type 2	Type 3	Types 1 and 3
Mean no. exams	2.84(0.87)*	2.95(0.89)	2.0(0.0)	2.50(0.87)	2.93(0.87)
Mean time (months) to control	20.4(19.5)	22.2(19.8)	12.0(0.0)	18.5(19.0)	16.0(19.0)
Mean no. polypectomies performed per patient to achieve control	27.9(35.8)	14.0(31.2)	7.0(0.0)	46.6(37.4)	67.0(32.1)
Mean no. polyps ≥1 cm resected to achieve control	6.39(7.20)	8.14±7.27	1.0(0.0)	2.08(7.61)	13.2(7.59)

*Mean (standard deviation)

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Table 4. Mean number of examinations obtained by patients, intervals between examinations, polypectomies performed per examination, and large polyps in patients who received maintenance examinations after obtaining control.

	All patients	Type 1	Type 2	Type 3	Types 1 and 3
Mean no. exams	2.7(0.95)*	2.69(0.78)	2.0(0.0)	2.8(0.99)	3.14(0.79)
Mean interval between exams (months)	19.3(13.5)	18.6(13.9)	25.0(0.0)	21.4(13.0)	19.9(14.8)
Mean no. polypectomies performed per exam	6.74(8.21)	6.13(7.92)	3.0(0.0)	9.57(8.18)	14.7(8.37)
Mean no. polyps ≥1 cm per exam	0.73(0.85)	0.76(0.84)	0.0(0.0)	0.3(0.37)	1.23(1.18)

- Mean (standard deviation)

Acronyms:

SPS: serrated polyposis syndrome

CRC: colorectal cancer

Cm: centimeters

WHO: The World Health Organization

PA: Pennsylvania

DKR: Douglas K. Rex

EMR: endoscopic mucosal resection

Mm: millimeters

FAP: familial adenomatous polyposis

U.S.: United States