

Impact of changing diagnostic criteria on the diagnosis of serrated polyposis syndrome



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ABSTRACT

Background and study aims The World Health Organization criteria for serrated polyposis syndrome (SPS) were established in 2010 and modified in 2019. Neither set of criteria have been validated against genetic markers or proven to be the optimal criteria for defining colorectal cancer risk in patients with serrated colorectal lesions. In this study, we sought to gain insight into how frequently the change in SPS criteria in 2019 impacted the diagnosis of SPS.

Patients and methods We reviewed 279 patients with SPS diagnosed between 2010 and 2019 using the 2010 criteria (n = 163) or since 2019 using the 2019 criteria (n = 116). We reviewed whether patients in each group met the diagnosis of SPS by the alternative criteria.

Results Of those diagnosed using 2010 criteria, 5.5% did not meet 2019 criteria. Of those diagnosed by 2019 criteria, 10.3% did not meet 2010 criteria.

Conclusions Most patients with SPS in our database met the diagnosis of SPS by both 2010 and 2019 criteria, with only 5% to 10% of patients in each cohort not meeting the alternative diagnostic criteria.

Introduction

Serrated polyposis syndrome (SPS) is characterized by increased numbers of colorectal serrated lesions, including sessile serrated lesions, hyperplastic polyps, and traditional serrated adenomas [1], and is associated with an increased risk of colorectal cancer [2]. However, no genetic basis for SPS has been identified, and thus, exact validation of a set of clinical criteria associated with an increased risk of colorectal cancer is challenging [3,4].

The World Health Organization (WHO) criteria [5, 6] are commonly used to identify SPS. In 2010, the WHO defined three types of SPS [5] (► **Table 1**). In 2019, the SPS criteria [6] were modified by the WHO (► **Table 1**).

In this study, we evaluated 279 patients from a single center diagnosed with SPS by the WHO criteria from either 2010 or

2019. Within this cohort, we evaluated how many patients met both sets of criteria and how many failed to meet one set of criteria.

Patients and methods

We prospectively maintained a database of all patients diagnosed with SPS. In general, the diagnosis of SPS was made in our center. Many patients were referred for endoscopic management of serrated lesions and were recognized to have SPS by the numbers of serrated lesions identified by one or more colonoscopies at our center, sometimes in combination with documented serrated lesions removed by referring physicians.

Permission to review the de-identified database was granted by the Institutional Review Board at Indiana University on May 6, 2022.

► **Table 1** World Health Organization diagnostic criteria for serrated polyposis syndrome in 2010 and 2019.

WHO serrated polyposis criteria	Type I	Type II	Type III
2010	≥ 5 serrated polyps proximal to the sigmoid colon with at least 2 of these > 10 mm in size	Any number of serrated polyps proximal to the sigmoid colon in a person with a first degree relative with SPS	> 20 serrated polyps of any size, distributed throughout the colon
2019	≥ 5 serrated polyps/lesions proximal to the rectum, all ≥ 5 mm in size, with at least 2 ≥ 10 mm in size	> 20 serrated polyps/lesions of any size distributed throughout the large bowel, with ≥ 5 proximal to the rectum	N/A

WHO, World Health Organization; N/A, not applicable.

To determine the eligibility of patients for the diagnosis of SPS, we utilized all colonoscopies in the database, beginning with the colonoscopy that made the diagnosis and previous procedures available to us, with the results recorded in the database. Patients diagnosed between 2010 and 2019 had their original diagnosis made using the 2010 WHO criteria [5]. This included 163 patients. Patients diagnosed after the publication of the 2019 revised WHO criteria (116 patients) had their primary diagnosis made using the 2019 criteria [4, 6].

We retrospectively reviewed 279 consecutive cases diagnosed from the interval date, 2010 until May 2022, and applied both the 2010 and 2019 criteria.

Statistics

We described continuous variables using means and standard deviations and categorical variables using counts and proportions. We compared the ages of both cohorts using student's t-test and compared the female gender proportion using Chi square test. We used the Jeffrey's binomial interval to calculate the confidence interval for the difference in proportion of patients included by switching to the 2019 diagnostic criteria. All statistical analyses were performed using IBM SPSS 27 software (IBM Corp, Armonk, New York, United States).

Results

Of the 279 patients who met the criteria either by 2010 or 2019, 184 of the 279 patients were female (65.9%), and the mean age at diagnosis was 64.0 ± 9.23 years. There were 163 patients diagnosed using the 2010 criteria in the initial period 2010-June 2019, and 116 diagnosed using the 2019 criteria. ► **Table 2** shows the number of patients diagnosed before 2019 who met the 2010 criteria for Type I, II, or III, as well as Type I plus Type III, and those diagnosed from 2019 who met the 2019 criteria for Type I, II, or both Type I plus Type II.

The mean age of the cohort diagnosed in 2010 to 2019 (64.2 ± 9.4) was similar to the cohort diagnosed from 2019 on (63.8 ± 9.0 ; $P=0.722$). The female gender proportion of the cohorts was also similar at 65.0% for the 2010–2019 cohort and 67.2% for the later cohort ($P=0.703$).

We identified nine patients diagnosed by the 2010 criteria (5.5%) who did not meet the 2019 criteria. In seven of these nine cases, the patient had adequate numbers of lesions above

► **Table 2** Number of patients in the cohort diagnosed with serrated polyposis syndrome using World Health Organization 2010 and 2019 criteria.

2010 Criteria	
Total	163
Type 1, n (%)	71 (43.5)
Type 2, n (%)	1 (0.61)
Type 3, n (%)	20 (12.3)
Type 1 and 3, n (%)	71 (43.5)
2019 Criteria	
Total	116
Type 1, n (%)	70 (60.3)
Type 2, n (%)	25 (21.6)
Type 1 and 2, n (%)	21 (18.1)

the sigmoid colon to meet the 2010 Type I criteria, but there was not a total of five lesions ≥ 5 mm. The eighth patient was diagnosed with Type II SPS in 2010 based on the presence of a serrated lesion plus a first-degree relative with SPS. This patient had 2 SSLs, including a 25-mm lesion in the cecum, but did not meet the Type I or Type II SPS by 2019 criteria. The ninth patient had Type III SPS according to 2010 criteria, but there was insufficient documentation of how many serrated lesions were proximal to the rectum to meet the diagnosis of Type II by 2019 criteria.

There were 12 patients diagnosed with SPS by the 2019 criteria (10.3%) who did not meet the 2010 criteria. One case had only a single serrated lesion ≥ 10 mm proximal to the sigmoid colon. The rest had insufficient numbers of serrated lesions proximal to the sigmoid colon to meet the 2010 criteria for Type I SPS, including no lesions in one case, only two in one case, only three in three cases, and only four in six cases.

Of 279 patients in our study, 267 fit the 2010 diagnostic criteria and 270 fit the 2019 diagnostic criteria. The comparison of the paired portions was not statistically significant ($P=0.531$).

Discussion

In this report, we describe the fraction of patients meeting the WHO criteria for SPS in 2010 or 2019 who did not meet the diagnosis of SPS when the alternative criteria were applied to their polyp findings. These findings suggest the change in WHO criteria has some influence on which patients are diagnosed with SPS, but most patients in the database met criteria for SPS by both 2010 and 2019 criteria. Since neither set of criteria are validated by precise correlation with the risk of colorectal cancer and there are no genetic markers to utilize in validating a set of clinical criteria, the impact of the change in criteria on colorectal cancer prevention is uncertain. Some data suggest that even patients with significant numbers of serrated lesions who do not meet the diagnosis of SPS have an increased risk of CRC [7]. However, our data give some sense of the impact of the change in WHO criteria on the diagnosis of SPS. The rationale for the change in diagnosis of SPS has been previously outlined [4, 6].

We found that the fraction of patients meeting the 2010 criteria who did not meet the 2019 criteria was numerically lower (5.5%) than the fraction of patients meeting the 2019 criteria who did not meet the 2010 criteria (10.3%). This numerical difference suggests that the 2019 criteria might be more inclusive in making a diagnosis of SPS. This is probably appropriate, given the evidence that patients with large numbers of SPS criteria which are insufficient to meet the diagnosis of SPS still have an increased risk of colorectal cancer [7], and that many SPS cancers are located in the distal colon [4, 6].

Strengths of this study include the prospective collection of data with polyp locations, sizes, and histologies recorded in the database. There was only one case diagnosed as not meeting the alternate criteria based on insufficient documentation of polyp size, location, or histology. Limitations include the data were collected at a single center and largely by a single endoscopist, a known high detector of both adenomas [8–11] and serrated lesions [10–12]. As we reported previously, we have not encountered a single interval cancer during surveillance of SPS patients [13], despite lengthening surveillance intervals in patients with lower polyp burdens, and likely also reflecting high detection rates for precancerous lesions. In addition, the endoscopist has a special interest in SPS [13, 14], so the sensitivity for SPS diagnosis is likely high. Thus, the database may include a relatively high fraction of patients who had just enough lesions to meet the criteria for SPS, either the 2010 or 2019 criteria. To the extent that any database includes largely patients with more severe SPS, patients might be more likely to meet both the 2010 and 2019 criteria. Further, a number of the patients were diagnosed after they were referred to the study endoscopist for resection of large serrated lesions [14], which could skew the database toward patients with Type 1 SPS by both the 2010 and 2019 criteria. Finally, we did not prospectively use both sets of criteria during both study periods. Thus, we do not know the numbers of patients encountered in clinical practice during the 2010 to 2019 interval who might have met the diagnosis for SPS using the 2019 criteria, which had not yet been published, and vice versa for the period from

publication of the 2019 criteria. Despite the limitations, the study still provides some insight into the impact of the change in criteria on the diagnosis of SPS.

Conclusions

In conclusion, we found that most patients diagnosed with SPS in a prospectively collected database of SPS at a single center met the diagnostic criteria for SPS using both the 2010 and 2019 criteria. The long-term impact of using strict criteria for the diagnosis of SPS, or the change in criteria for SPS in 2019, on the incidence of colorectal cancer in patients with multiple serrated lesions, remains unknown.

Competing interests

Dr. Rex is a consultant for Olympus Corporation, Boston Scientific, Aries Pharmaceutical, Braintree Laboratories, Lumendi, Ltd., Norgine, Endokey, GI Supply, Medtronic, and Acacia Pharmaceuticals; has received research support from: EndoAid, Olympus Corporation, Medivators, Erbe USA Inc, and Braintree Laboratories; and is a shareholder in Satisfai Health.

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