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ACG 2020 ABSTRACT SUBMISSION DEADLINE EXTENDED 2 WEEKS!

NEW!! DEADLINE: JUNE 15, 2020
11:59pm Eastern

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Gastrointestinal Manifestations of COVID-19

Latest Data on Symptoms, Stool Testing, and Clinical Outcomes

MONDAY, MAY 18, 2020 Webinar

8:00 to 9:00 pm Eastern Daylight Time

Presenters

- Brennan M. R. Spiegel, MD, MSHS, FACG
- Paul Y. Kwo, MD, FACG
- Millie D. Long, MD, MPH, FACG
- Jordan E. Axelrad, MD, MPH

Moderators

- Mark B. Pochapin, MD, FACG
- David A. Greenwald, MD, FACG

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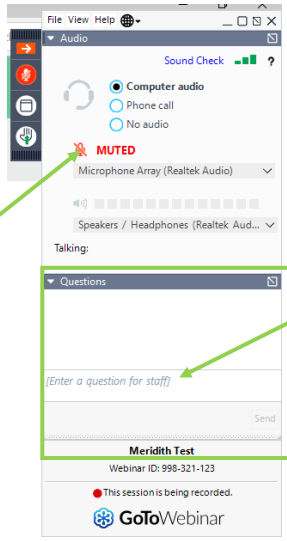
Participating in the Webinar



All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

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How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR

ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2020 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2021 for this activity.

ACG will submit MOC points on the first of each month. Please allow 3-5 business days for your MOC credit to appear on your ABIM account.

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MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement.
THESE ANSWERS WILL BE REVIEWED.

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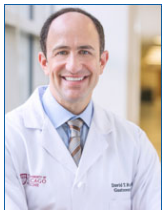

Week 9: Positioning of Old and New Therapies in IBD
David T. Rubin, MD, FACG
May 21, 2020 at Noon EDT

Week 10: Colorectal Cancer Screening in a Post Covid World
Renee L. Williams, MD, MHPE, FACG
May 28, 2020 at Noon EDT

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Disclosures:

Moderator:

Brooks D. Cash, MD, FACG

Consultant: Allergan, QOL Medical, Salix, Takeda
Speakers Bureau: Allergan, QOL Medical, Salix, Takeda

Speaker:

Carol A. Burke, MD, FACG

Consultant: Aries, Ferring, Freenome
Research Grant: Cancer Prevention Pharmaceuticals, Janssen

Off Label Use:

None

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Serrated Polyps and Serrated Polyposis Syndrome: Cancer Risk and Appropriate Surveillance

Carol A. Burke, MD, FACG

Department of Gastroenterology, Hepatology and Nutrition

Cleveland Clinic, Cleveland Ohio

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Objectives

- Understand the nomenclature of serrated polyps and diagnostic criteria for serrated polyposis syndrome
- Identify endoscopic features of serrated lesions
- Recognize CRC risk and formulate strategies to manage patients with serrated polyps and serrated polyposis syndrome

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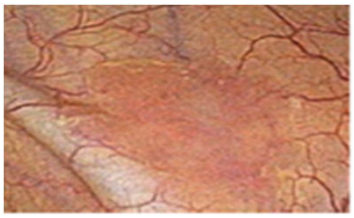
Precursors to Colorectal Cancer

75%

Adenoma

25%

Sessile Serrated Lesion



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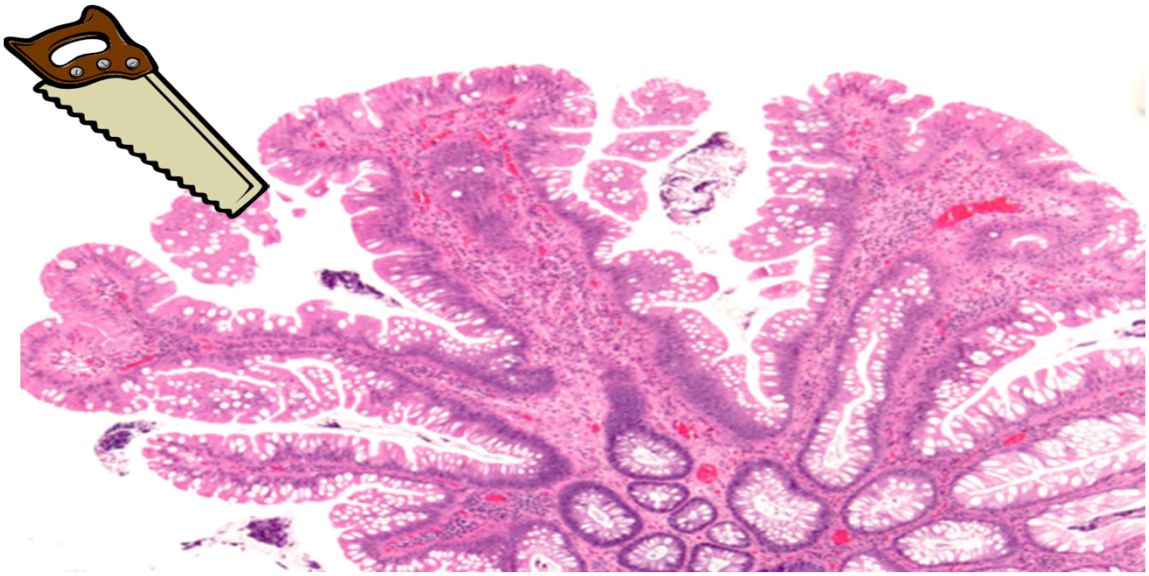
Classification of Serrated Polyps



Snover D, et al. WHO classification of tumours. 4th ed. Berlin: Springer-Verlag. 2010

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Nomenclature of Serrated Polyps

- Hyperplastic Polyp (HP)
- Sessile Serrated Lesion (SSL)
  - Formerly: sessile serrated adenoma / sessile serrated polyp
- Traditional Serrated Adenoma (TSA)

Snover D, et al. WHO 2010

17

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What Pathology Criteria Distinguish SSL from HP?

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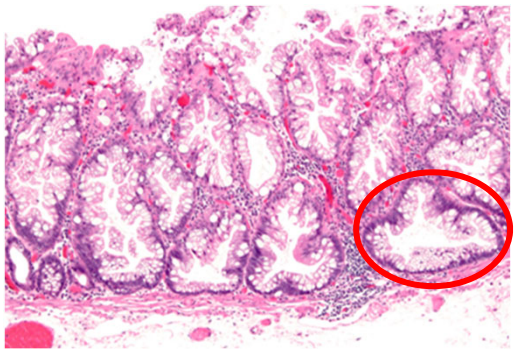
Histology of Serrated Lesions



Snover D, et al. WHO classification of tumours. 4th ed. Berlin: Springer-Verlag. 2010

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How Does a Pathologist Diagnose SSL?

- WHO criteria (2010)[1]
  - 2-3, contiguous abnormal crypts
- Consensus criteria (2012)[2]
  - ≥ 1 unequivocal abnormal crypt
- WHO criteria (2019)
  - > 1 unequivocal abnormal crypt

[1] Bosman, WHO Classification of Tumours of the Digestive System 2010
[2] Rex D, Am J Gastroenterol 2012; 107:1315
[3] World Health Organisation. Classification of Tumours of the Digestive Tract. Lyon: IARC Press, 2019.

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What is SSL prevalence in average risk patients?

A. < 1%

B. 1-2%

C. 4-7%

D. 15%

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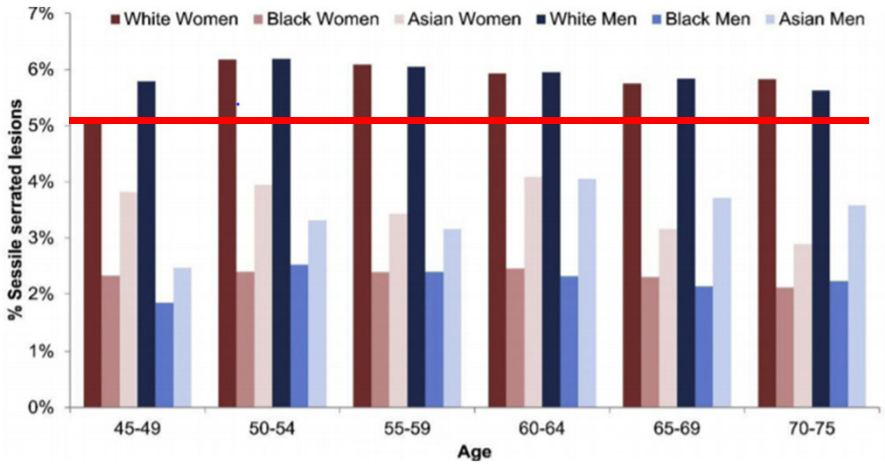
Prevalence of SSL

US screening colonoscopy data, 2012–2016 (1.6 million procedures)



Crockett S, et al. Gastroenterology2019;156:254–272

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Detection Rate of SSL

56 endoscopists	Overall (N=16.089)	Men (N=7749)	Women (N=8339)
ADR	32.3%	36.9%	26%
SSLDR	4.6%	4.6%	4.6%
Screening colonoscopies; single center, 2015-2017			

Sarvepalli S, et al. JAMA Surg 2019 Jul 1;154(7):627-635

ADR	CSSDR (SSL, TSA, HP ≥ 10 mm) Median (IQR)
< 15%	1.3% (0.9-3.1)
15-25%	3.5% (2.5-4.8)
25-<35%	6.3% (3.0-7.2)
≥ 35%	10.0% (8.5-13.1)
77 endoscopists, 28 centers;2009-2014	

Correlation Coefficient Between ADR and SSL P= .69

Anderson J, et al GIE 2017;85:1188-94

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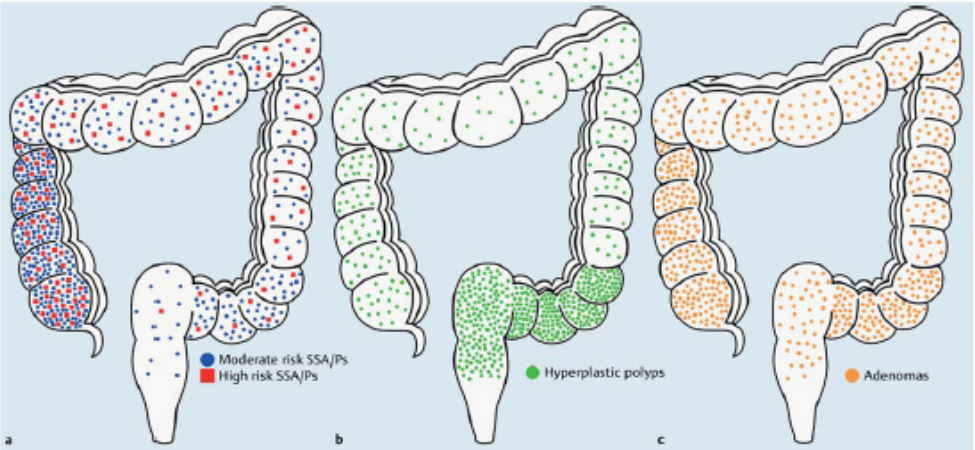
Prevalence and Location of Serrated Lesions

- 3364 patients, 2011-2015, Single center
- 25 endoscopists, ADR 38.5% (22.5%–53.9%)
- SSL detection rate: 7.3% (2.5% -13.6%); 2 dilated crypts and/or hyper-serrations in crypt base



IJspeert JE. Endoscopy.2016;48:740-6

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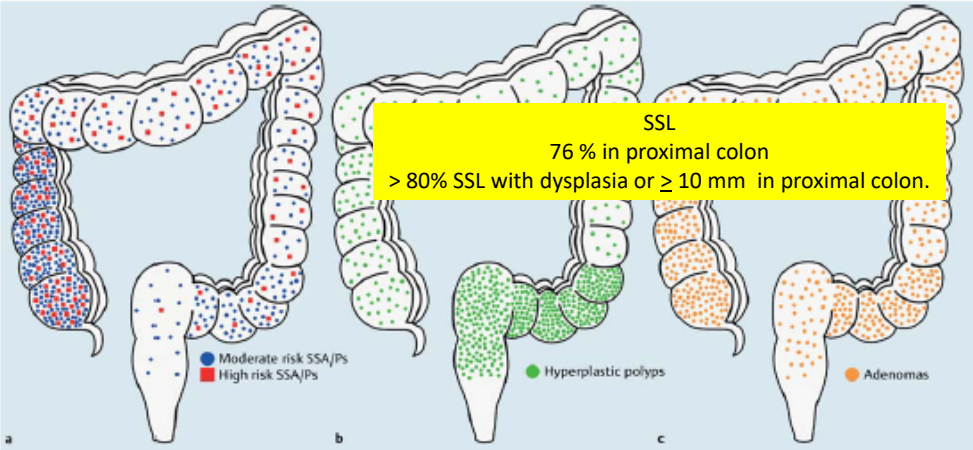

IJspeert JE. Endoscopy.2016;48:740-6

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Factors Associated with SSL Detection Associated of SSL with Synchronous Advanced Neoplasia

Factor	Detection of SSL (95% CI)
Age, yrs	1.01 (1.00-1.03)
Male gender	1.04 (0.81-1.34)
Colonoscopy Indication	
Symptoms	Reference
FIT +	1.08 (0.75-1.54)
Family History CRC	1.52 (1.05-2.22)
Surveillance	1.73 (1.20-2.49)
SSPDR ≥ 7.3% vs < 7.3%	2.65 (2.00-3.50)

SSL Feature	Risk of Synchronous Advanced Neoplasia (95% CI)
≥ 1 SSL	1.71 (1.25-2.34)
Proximal	1.69 (1.20-2.39)
≥ 10 mm	2.78 (1.56-4.96)
≥ 10 mm/with dysplasia	2.65 (1.56-4.67)

IJspeert JE. Endoscopy.2016;48:740-6

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Incident CRC Risk Based on Histology

- Case control Danish population study 1977–2009
- 2045 CRC cases and 8105 CRC-free controls
- Identified first polyp with biopsy excision during initial colonoscopy

CRC case-control study in 272,342 patients with colonoscopy (1977-2009)	Adjusted OR (95% CI)	Estimated 10 yr Risk
No polyps	reference	reference
HP only	1.30 (0.96-1.77)	1.2%
Adenomas only	2.50 (2.24-2.80)	2.3%
SSL Overall	2.75 (1.99-3.80)	2.6%
SSL w/synchronous Adenoma	2.66 (1.70-4.16)	2.5%
SSL w/o synchronous Adenoma	3.40 (2.35-4.91)	3.2%
SSL w/Dysplasia	4.76 (2.59-8.73)	4.4%
TSA Overall	4.84 (2.36-9.93)	4.5%
TSA w/o synchronous SSL or adenoma	1.79 (0.49–6.59)	NE

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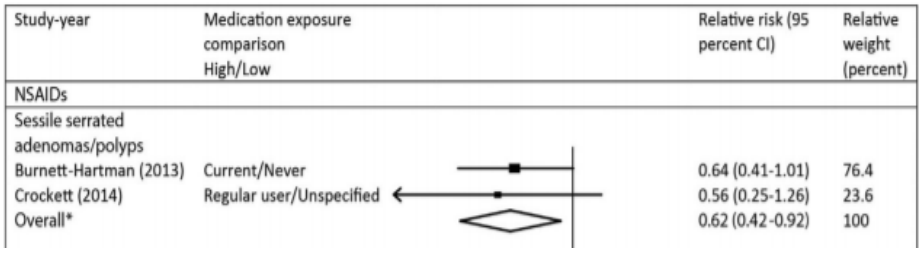
Factors associated with SSL

- Smoking (OR 3.4, 1.90-6.07) and ETOH (OR 1.85, 1.03-3.32)
- Post-hoc analysis aspirin polyp chemoprevention trial on serrated polyps
  - Proximal SPs: 81 mg RR, 0.56 (95% CI, 0.34-0.91); 325 mg RR, 0.58 (95% CI, 0.36-0.95)
- Inverse association between NSAIDs



Baille, Gastroenterology 2017;152:92-104

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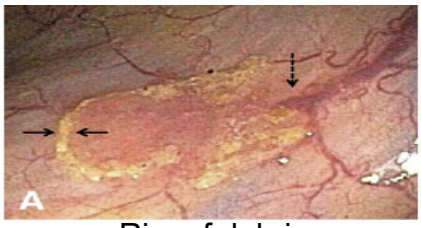
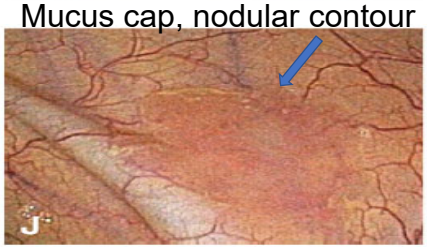
Endoscopic Features of SSL



Rim of debris

Mucus cap, nodular contour

Superficial telangiectasia



Obscuring blood vessels

Tadepalli U, et al. GIE 2011;74:1360-8

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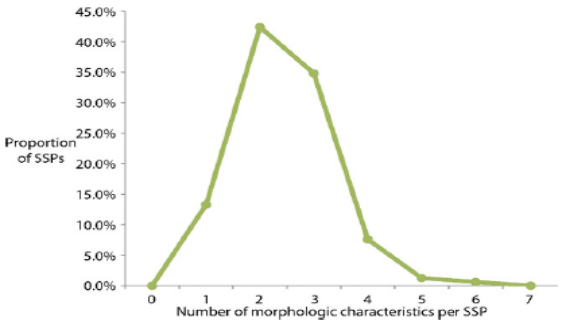
Prevalence of Endoscopic Features of SSL

Feature	Prevalence
Mucous Cap	64%
Rim debris/bubbles	52%
Abnormal fold contour	37%
Obscuring blood vessels	32%
Nodular Surface	30%



Tadepalli U, et al. GIE 2011;74:1360-8

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NBI NICE Classification

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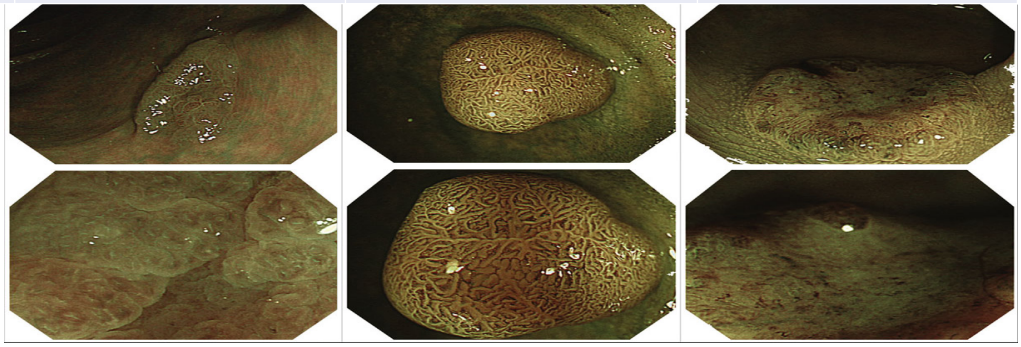
	Type 1	Type 2	Type 3
Color	Same or Lighter	Brown	Brown or Dark Brown, or patchy white area
Vessels	None or lacy vessels coursing across lesion	Brown vessels surrounding white structures	Areas of disrupted or missing vessels
Surface	Dark or white spots of uniform size or homogenous absence of pattern	Oval, tubular or branched white structures surrounded by brown vessels	Amorphous or absent surface pattern
Histology	Serrated	Adenoma (includes SM-s)	Deep SM Invasion



Hayashi N, GIE 2013;78

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Limitations of NICE

- Does not distinguish SSL from HP
- Need ability to distinguish lesions < 10 mm
  - Adenoma vs HP vs SSLs
- High level discrimination may facilitate resect and discard

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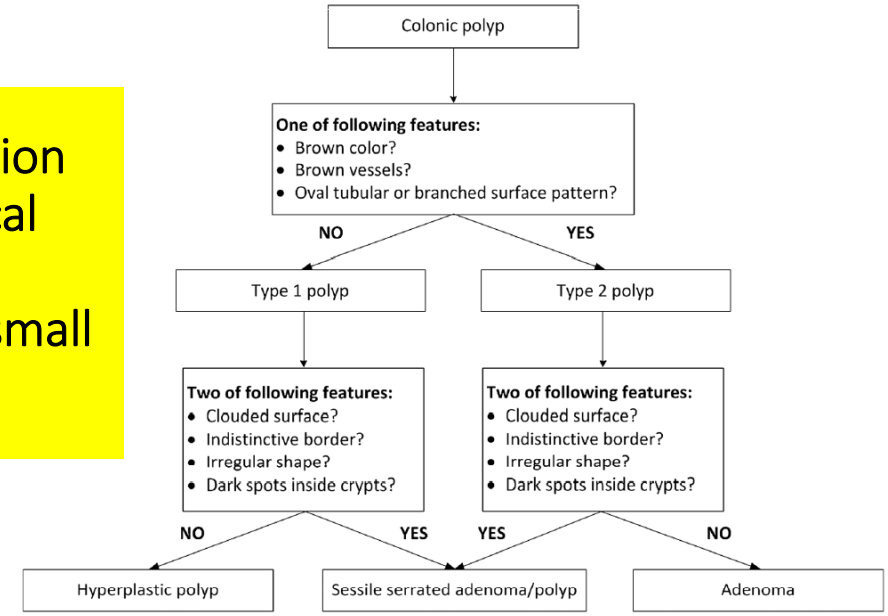
WASP Classification System for Optical Diagnosis of diminutive and small polyps



IJspeert JEG. Gut 2016;65:963-970

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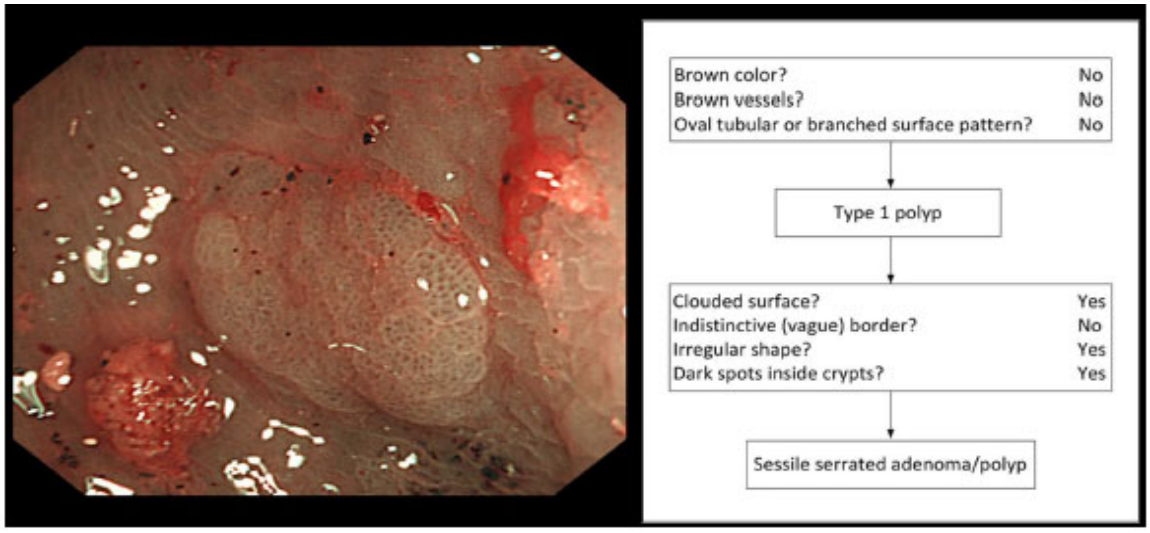

IJspeert JEG. Gut 2016;65:963-970

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Impact of WASP training

Table 1 First validation phase: comparison of the overall pooled diagnostic accuracy of optical diagnosis before and after training

	Accuracy (95% CI) before training	Accuracy (95% CI) after training	Improvement (95% CI)	p Value
Overall analysis	0.63 (0.54 to 0.71)	0.79 (0.72 to 0.86)	0.16 (0.09 to 0.22)	<0.001
With high confidence	0.73 (0.64 to 0.82)	0.87 (0.80 to 0.95)	0.14 (0.04 to 0.24)	<0.01
Diminutive lesions	0.61 (0.55 to 0.66)	0.77 (0.72 to 0.81)	0.16 (0.08 to 0.24)	<0.001
With high confidence	0.71 (0.64 to 0.78)	0.86 (0.81 to 0.91)	0.15 (0.03 to 0.27)	0.02
Small lesions	0.67 (0.60 to 0.75)	0.83 (0.77 to 0.89)	0.16 (0.06 to 0.26)	<0.01
With high confidence	0.77 (0.68 to 0.85)	0.90 (0.84 to 0.95)	0.13 (0.02 to 0.24)	0.02

Table 3 Second validation phase: pooled overall and dichotomised diagnostic accuracy of optical diagnosis

	Accuracy all lesions (95% CI)	Accuracy diminutive lesions (95% CI)	Accuracy small lesions (95% CI)
Overall analysis	0.76 (0.72 to 0.80)	0.74 (0.69 to 0.79)	0.81 (0.75 to 0.88)
With high confidence	0.84 (0.81 to 0.88)	0.83 (0.79 to 0.88)	0.86 (0.80 to 0.93)
SSA/P versus non-SSA/P	0.87 (0.84 to 0.90)	0.86 (0.82 to 0.90)	0.88 (0.83 to 0.94)
With high confidence	0.91 (0.88 to 0.94)	0.91 (0.87 to 0.94)	0.91 (0.85 to 0.96)
AD versus non-AD	0.83 (0.80 to 0.87)	0.81 (0.77 to 0.85)	0.89 (0.84 to 0.94)
With high confidence	0.90 (0.87 to 0.93)	0.88 (0.84 to 0.92)	0.93 (0.89 to 0.98)
Neoplastic lesions versus HP	0.82 (0.79 to 0.86)	0.81 (0.77 to 0.85)	0.85 (0.80 to 0.92)
With high confidence	0.89 (0.85 to 0.92)	0.88 (0.84 to 0.92)	0.90 (0.84 to 0.95)

IJspeert JEG. Gut 2016;65:963-970

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Effectiveness of Polyp Resection

- Prospective 2 center study
- Snare resection blended coagulation
- Polyps 5-20mm
- Attestation of complete polyp removal
- Biopsies from the resection margin
  - 2 from opposing sides of 5–9 mm polyps
  - 4 quadrant from 10–20 mm polyps

Incomplete Resection
Adenoma: 7%
SSL: 31%

Pohl H, et al. Care study. Gastroenterology 2013:144;74

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Endoscopic Resection of SSLs

- Hampered by flat morphology
- Inconspicuous surface features
- Indistinct borders

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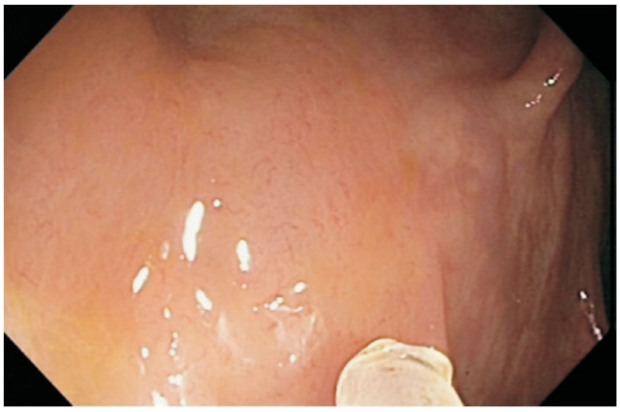
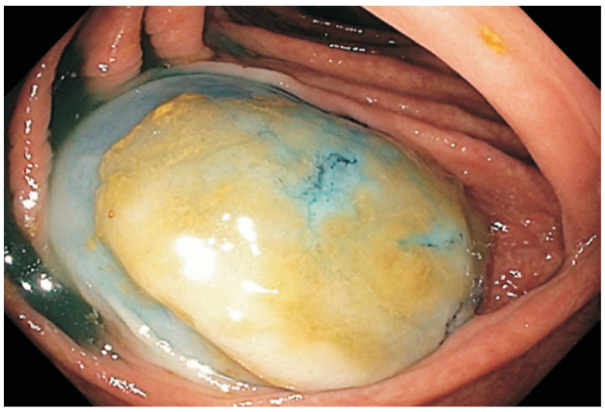
Benefit of Submucosal Contrast Agent





Ma M, et al. Gut Liver 2017;11:747-

Saline/hydroxyethyl starch with methylene blue or indigo carmine
Commercial submucosal lifting agents

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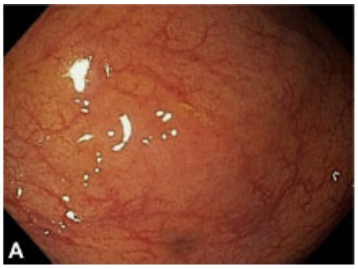
Impact of Acetic Acid Spray



2% Acetic Acid

Papoutchi G, et al
https://doi.org/10.1016/j.vgie.2017.11.011

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Serrated Polyp Surveillance Recommendations

Lesion	US MSTF 2012	BSG	ESGE*
< 10 mm, distal HPs < 10 mm HP*	10 yrs	None*	None*
SSL < 10 mm	5 yrs	None	None
SSL ≥ 10 mm, or SSL w/dysplasia, or TSA	3 yrs		
Piecemeal resection ≥ 20 mm (>10mm*)	2-6 months		

Excludes patients with SPS

Lieberman D, et al. Gastro 2012;143:844
East JE, et al. Gut 2017;66:1181-1196
Hasson C, et al. Endoscopy. 2013;(10):842-851

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USMSTF Recommendations for Surveillance in Individuals with Serrated Polyps

Baseline Colonoscopy Finding	Interval for Colonoscopy	Strength of Recommendation	Quality of Evidence
≤ 20, HPs < 10 mm in rectosigmoid ≤ 20, HPs < 10 mm above sigmoid	10 yrs 10 yrs	Strong Weak	Moderate Very Low
1 to 2 SSPs < 10 mm	5 -10 yrs	Weak	Very low
3 to 4 SSPs < 10 mm, HP ≥ 10 mm*	3 - 5 yrs	Weak	Very low
5 to 10 SSPs, SSP ≥ 10 mm or w/dysplasia, TSA	3 yrs	Weak	Very low
Piecemeal resection of SSP ≥ 20 mm	6 mos	Strong	Moderate

Gupta et al. Gastroenterol 2020;158:1131-1153

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Serrated Polyposis Syndrome

- Under-recognized
- Predisposition Syndrome
- Basis uncertain
  - Environmental
  - Familial
  - Hereditary: *RNF43* mutation

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Do you have patients with SPS?

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Serrated Polyposis Syndrome

- **WHO Criteria 2010**
  1. ≥ 5 SPs proximal to sigmoid & ≥ 2 are > 10 mm; or
  2. > 1 SP proximal to sigmoid with Family Hx of SPS; or
  3. > 20 SPs throughout colon

- **WHO Criteria 2019**
  1. ≥ 5 SPs proximal to rectum, all ≥ 5mm, with ≥ 2, ≥ 10 mm or
  2. > 20 SPs throughout colon with at least 5 proximal to rectum

Rosty C, Brosens LA, Dekker E, Nagtegaal ID. Serrated Polyposis. In: WHO Classification of tumours of the digestive system, 5th Edition. Lyon: International Agency for Research on Cancer, Forthcoming 2019

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Serrated Polyposis Syndrome

- **WHO Criteria 2010**

1. ≥ 5 SPs proximal to si… 2 are > 10 m…
2. > … Fa…
3. > 2… …out colon

…rectum, all …n ≥ 2, ≥ 10 mm or > 20 SPs throughout colon with at least 5 proximal to rectum

CUMULATIVE DIAGNOSIS
Includes any serrated polyp

Rosty C, Brosens LA, Dekker E, Nagtegaal ID. Serrated Polyposis. In: WHO Classification of tumours of the digestive system, 5th Edition. Lyon: International Agency for Research on Cancer, Forthcoming 2019

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Which polyps are present in SPS patients?

1. Hyperplastic polyps
2. Sessile Serrated Lesions
3. Traditional Serrated Adenomas
4. Conventional Adenomas

80% will have conventional adenomas!

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SPS Frequently Undiagnosed

- 529 patients referred for removal polyp ≥ 20 mm
- 4% (20) met the WHO criteria
  - 9 at index examination
  - 11 during surveillance
- Only 1 (5%) suspected by referring MD
- 50% (10) diagnosed by endoscopist
- Failure to detect attributed to lack of systematic application of WHO criteria

Vemulapalli KC, GIE 2012;75:1206-1210

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Detection Rate of SPS

	UK	Spain	Netherlands	Poland
Cohort	G-FOBT	FIT	Colonoscopy	Colonoscopy
Number Patients	205,949	6091	1426	12,361
Diagnosed SPS 1st exam	0.03	0.5	0	0.1
Diagnosed during FU	-	0.3	0.4	-
Diagnosed overall		0.8	0.4	

IJspeert JEG, et al. Gut 2017;**66**:1225-1232.

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Most Common Polyposis Syndrome
1 in 127 to 1 in 242 patients
Undergoing colonoscopy

IJspeert JEG, et al. Gut 2017;**66**:1225-1232.

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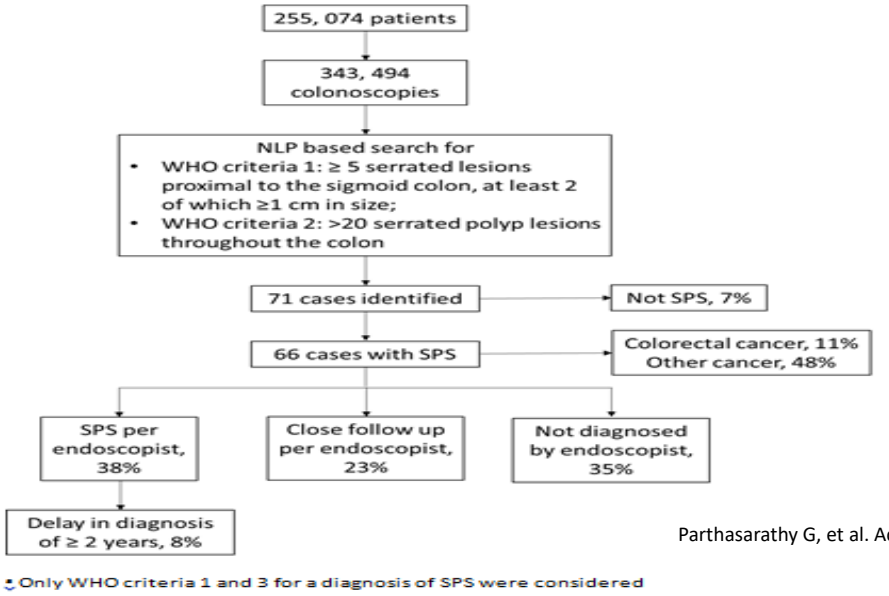
Enhancing Diagnosis of SPS by NLP



Parthasarathy G, et al. Accepted GIE 2020

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CRC in SPS

- Reported in up to 70% of SPS patients
- Nearly all occurs before or at SPS diagnosis
- Mean age: 50-60 years
  - 50% in recto-sigmoid colon
- Risks for CRC
  - Fulfilling WHO 1 and 3 (OR 1.60, 1.04 - 2.51)
  - SP with dysplasia (OR 2.07, 1.28 - 3.33)
  - Advanced adenoma (OR 2.30, 1.47 - 3.67)
    - 80% of SPS patients have coexistent adenomas

IJspeert JEG, et al. Gut 2017;66:278-284

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Extra-colonic Cancer Risk

- None known
- No additional surveillance indicated outside colon

- *Except when SPS coexists with other genetic syndrome

BSG: East JE, et al. Gut 2017;66:1181-1196

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CRC Risk in FDR of SPS patients

- Boparai: (RR 5.4, 3.7 to 7.8)
  - Gut 2010 Sep;59(9):1222-5
- Win: (SIR 5.16, 3.7-7.3)
  - Am J Gastroenterol 2012;107(5):770-778

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CRC in SPS vs Multiple Serrated Polyps

53 SPS pts & 145 pts w/ ≥ 10 polyps with ≥ 50% serrated
Compared CRC risk in patients and their FDRs

	SPS Patient	MSP Patient	SPS FDR	MSP FDR
Prevalent CRC	22.6%	28.3%	12.2%	10.4%
Cumulative CRC	2.7%	4.1%		

Egoavil C, Juarez M, Gastro 2017:153;06-112

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Lymphoma and SPS

Lymphoma Prevalence

	US Population (SEER)	Serrated Polyposis Syndrome		
	Prevalence	Prevalence	95% Confidence Interval	P-value
Overall	0.34%	9.80%	(4.80%, 17.29%)	<0.0001
Male	0.37%	10.87%	(3.62%, 23.57%)	<0.0001
Female	0.31%	8.93%	(2.96%, 19.62%)	<0.0001

N =102 patients with SPS
Hx lymphoma=10; preceded SPS dx by 21 yrs

SPS Prevalence

	HL N= 101	No HL N=1426	P value
Advanced Neoplasia	25%	12%	< .001
Advanced Serrated Polyp	12%	4%	< .001
	6%	0%	< .001

Rigter LS, et al. Cancer 2018;0:1-10.

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SPS Prevalence

	HL N= 101	No HL N=1426	P value
Advanced	25%	12%	< .001
		4%	< .001
	6%	0%	< .001

Rigter LS, et al. Cancer 2018;0:1-10.

Consider colonoscopy in HL survivors treated with abdominal radiotherapy and/or procarbazine

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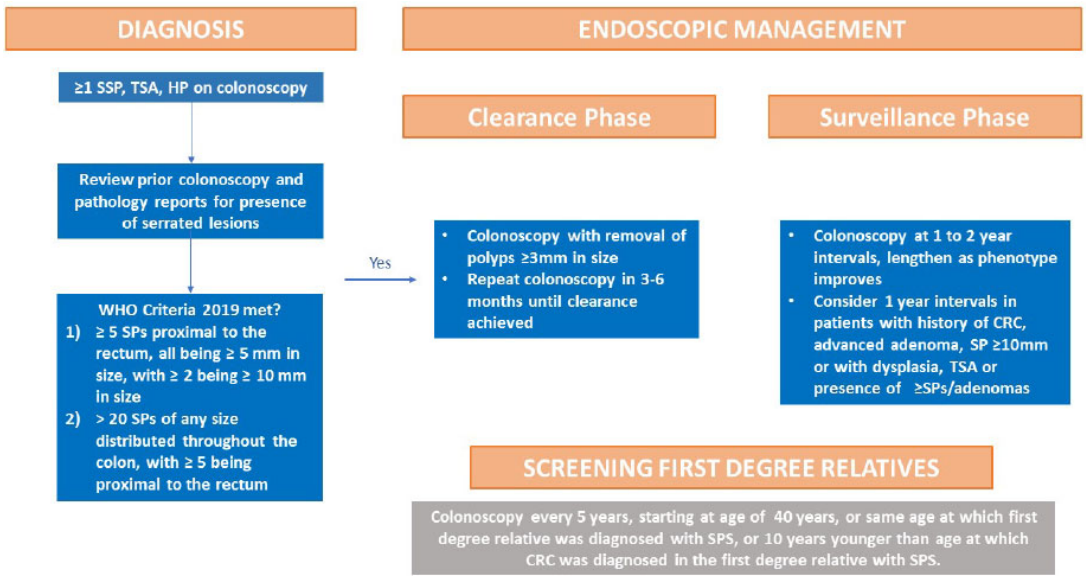

Mankaney G, Rouphael C, Burke CA. Clin Gastroenterol Hepatol. 2020;18(4):777-779

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Surveillance Recommendations in SPS

USMSTF	• ESGE and BSG • Every 1-2 years	NCCN
Every 1 year		Every 1-3 years

ESGE: Kaminski MF, et al. Endoscopy 2014:46:435-449
MSTF: Lieberman DA, et al. Gastroenterology 2012;143:844-857
BSG: East JE, et al. Gut 2017;66:1181-1196
NCCN: Genetic/Familial High Risk Assessment-Colorectal. NCCN.org;V3 2018

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CRC Incidence After Clearing Colonoscopy

- 3.1% at 3 years, 6.4% at 5 years[1]
  - 152 patients, surveillance interval 1-3 years
- 1.4% at median follow-up of 3.2 years [2]
  - 434 patients, median surveillance interval 1.2 years
- 1.3% at 5 years[3]
  - 271 SPS patients, individualized interval 1 vs 2-years
- 0% at median follow up of 3.1 years[4]
  - 41 patients, median surveillance interval of 1 year

[1]Rodriguez-Alcade D, et al. Endoscopy 2019;51:142
[2]IJspeert JEG, et al. Gut 2017;66:278-284
[3] Bleijenberg AGC, et al. Gut 2019;0:1–9. doi:10.1136/gutjnl-2018-318134
[4]Hazewinkel Y, et al. Gastroenterology 2014;147:88-95

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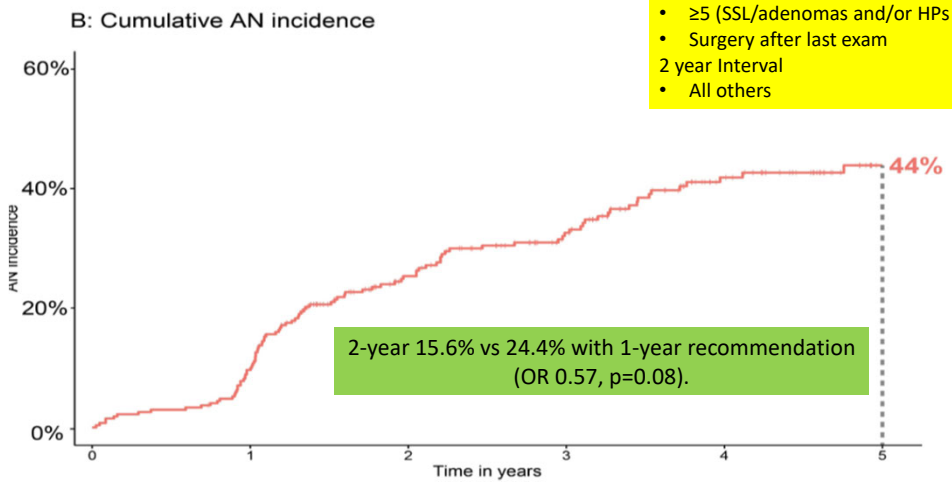
Incidence of Metachronous Advanced Neoplasia

1 year Interval
- ≥ 1 advanced SPs
- ≥5 (SSL/adenomas and/or HPs ≥5 mm
- Surgery after last exam

2 year Interval
- All others



2-year 15.6% vs 24.4% with 1-year recommendation (OR 0.57, p=0.08).

Bleijenberg AGC, et al. Gut 2019;0:1–9. doi:10.1136/gutjnl-2018-318134

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Colonoscopy Surveillance in FDRs

✓ Begin colonoscopy every 5 years at earliest of:

- Age 40
- Same age as youngest diagnosis of SPS
- 10 years younger than earliest CRC complicating SPS

NCCN: Genetic/Familial High Risk Assessment-Colorectal. NCCN.org;V1 2018

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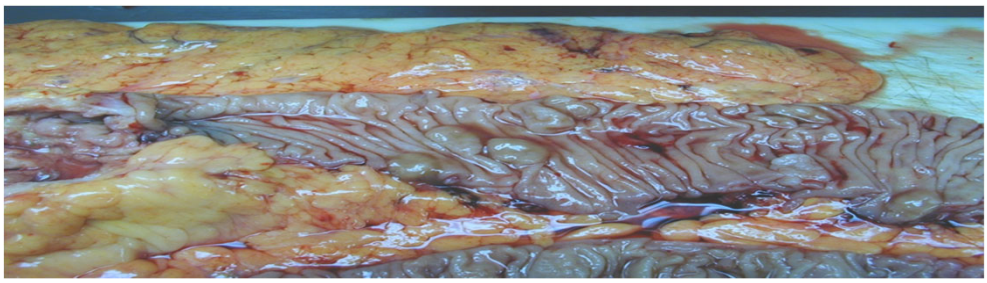
Surgery in SPS

- Treatment for CRC

- When endoscopically unmanageable
  - Remove segments with all lesions not amenable to endoscopic resection



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Conclusions

- Variety of serrated colorectal lesions exist
- SSLs and SPS underdiagnosed and CRC risk factor
- Characteristic endoscopic features of SSPs established
- Patients with SPS and their FDR are high risk group, surveillance warranted

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