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ACG 2020 ABSTRACT SUBMISSION DEADLINE
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NEW!! DEADLINE: JUNE 15, 2020
11:59pm Eastern
**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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- **CHAPEL HILL** | September 12, 2020
- **HOUSTON** | September 26, 2020

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

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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
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

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
Precursors to Colorectal Cancer

75% Adenoma

25% Sessile Serrated Lesion

Classification of Serrated Polyps

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

What Pathology Criteria Distinguish SSL from HP?
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
What is SSL prevalence in average risk patients?

A. < 1%
B. 1-2%
C. 4-7%
D. 15%

Prevalence of SSL

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

Detection Rate of SSL

**56 endoscopists**

<table>
<thead>
<tr>
<th></th>
<th>Overall (N=16,089)</th>
<th>Men (N=7749)</th>
<th>Women (N=8339)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR</td>
<td>32.3%</td>
<td>36.9%</td>
<td>26%</td>
</tr>
<tr>
<td>SSLDR</td>
<td>4.6%</td>
<td>4.6%</td>
<td>4.6%</td>
</tr>
</tbody>
</table>

Screening colonoscopies; single center, 2015-2017

<table>
<thead>
<tr>
<th>ADR</th>
<th>CSSDR (SSL, TSA, HP &gt; 10 mm) Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15%</td>
<td>1.3% (0.9-3.1)</td>
</tr>
<tr>
<td>15-25%</td>
<td>3.5% (2.5-4.8)</td>
</tr>
<tr>
<td>25-&lt;35%</td>
<td>6.3% (3.0-7.2)</td>
</tr>
<tr>
<td>≥ 35%</td>
<td>10.0% (8.5-13.1)</td>
</tr>
</tbody>
</table>

77 endoscopists, 28 centers; 2009-2014

Correlation Coefficient Between ADR and SSL: P= .69


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

Uspeert JE. Endoscopy, 2016;48:740-6
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

SSL 76 % in proximal colon > 80% SSL with dysplasia or > 10 mm in proximal colon.

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

<table>
<thead>
<tr>
<th>Factor</th>
<th>Detection of SSL (95% CI)</th>
<th>SSL Feature</th>
<th>Risk of Synchronous Advanced Neoplasia (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>1.01 (1.00-1.03)</td>
<td>&gt; 1 SSL</td>
<td>1.71 (1.25-2.34)</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.04 (0.81-1.34)</td>
<td>Proximal</td>
<td>1.69 (1.20-2.39)</td>
</tr>
<tr>
<td>Colonoscopy Indication</td>
<td></td>
<td>&gt; 10 mm</td>
<td>2.78 (1.56-4.96)</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Reference</td>
<td>&gt; 10 mm/with dysplasia</td>
<td>2.65 (1.56-4.67)</td>
</tr>
<tr>
<td>FIT +</td>
<td>1.08 (0.75-1.54)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family History CRC</td>
<td>1.52 (1.05-2.22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surveillance</td>
<td>1.73 (1.20-2.49)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSPDR ≥ 7.3% vs &lt; 7.3%</td>
<td>2.65 (2.00-3.50)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

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
**Endoscopic Features of SSL**

- Rim of debris
- Mucus cap, nodular contour
- Superficial telangiectasia
- Obscuring blood vessels

**Prevalence of Endoscopic Features of SSL**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucous Cap</td>
<td>64%</td>
</tr>
<tr>
<td>Rim debris/bubbles</td>
<td>52%</td>
</tr>
<tr>
<td>Abnormal fold contour</td>
<td>37%</td>
</tr>
<tr>
<td>Obscuring blood vessels</td>
<td>32%</td>
</tr>
<tr>
<td>Nodular Surface</td>
<td>30%</td>
</tr>
</tbody>
</table>

### NBI NICE Classification

<table>
<thead>
<tr>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Color</strong></td>
<td>Same or Lighter</td>
<td>Brown</td>
</tr>
<tr>
<td><strong>Vessels</strong></td>
<td>None or lacy vessels coursing across lesion</td>
<td>Brown vessels surrounding white structures</td>
</tr>
<tr>
<td><strong>Surface</strong></td>
<td>Dark or white spots of uniform size or homogenous absence of pattern</td>
<td>Oval, tubular or branched white structures surrounded by brown vessels</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>Serrated</td>
<td>Adenoma (includes SM-s)</td>
</tr>
</tbody>
</table>

---

### 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
WASP Classification System for Optical Diagnosis of diminutive and small polyps
**Impact of WASP training**

![Table 1](image1)

![Table 2](image2)

**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%

![Image](image3)
Endoscopic Resection of SSLs

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

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
Impact of Acetic Acid Spray

2% Acetic Acid

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

Serrated Polyp Surveillance Recommendations

<table>
<thead>
<tr>
<th>Lesion</th>
<th>US MSTF 2012</th>
<th>BSG</th>
<th>ESGE*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10 mm, distal HPs</td>
<td>10 yrs</td>
<td>None*</td>
<td>None*</td>
</tr>
<tr>
<td>&lt; 10 mm HP*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSL &lt; 10 mm</td>
<td>5 yrs</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>SSL &gt; 10 mm, or SSL w/dysplasia, or TSA</td>
<td>3 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piecemeal resection &gt; 20 mm (&gt;10mm*)</td>
<td>2-6 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Excludes patients with SPS

### USMSTF Recommendations for Surveillance in Individuals with Serrated Polyps

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

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

### Serrated Polyposis Syndrome

- Under-recognized
- Predisposition Syndrome
- Basis uncertain
  - Environmental
  - Familial
  - Hereditary: *RNF43* mutation
Do you have patients with SPS?

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

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 > 5 mm, with > 2, > 10 mm or
  2. > 20 SPs throughout colon with at least 5 proximal to rectum


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!
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

Detection Rate of SPS

<table>
<thead>
<tr>
<th></th>
<th>UK</th>
<th>Spain</th>
<th>Netherlands</th>
<th>Poland</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort</td>
<td>G-FOBT</td>
<td>FIT</td>
<td>Colonoscopy</td>
<td>Colonoscopy</td>
</tr>
<tr>
<td>Number Patients</td>
<td>205,949</td>
<td>6091</td>
<td>1426</td>
<td>12,361</td>
</tr>
<tr>
<td>Diagnosed SPS 1st exam</td>
<td>0.03</td>
<td>0.5</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>Diagnosed during FU</td>
<td>-</td>
<td>0.3</td>
<td>0.4</td>
<td>-</td>
</tr>
<tr>
<td>Diagnosed overall</td>
<td></td>
<td>0.8</td>
<td>0.4</td>
<td></td>
</tr>
</tbody>
</table>

Detection Rate of SPS

<table>
<thead>
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<td>FIT</td>
<td>Colonoscopy</td>
</tr>
<tr>
<td>Number Patients</td>
<td>205,949</td>
<td>6,091</td>
<td>1,426</td>
</tr>
<tr>
<td>Diagnosed SPS 1st exam</td>
<td>0.03</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>Diagnosed during FU</td>
<td>0.3</td>
<td>0.4</td>
<td>-</td>
</tr>
<tr>
<td>Diagnosed overall</td>
<td>0.8</td>
<td>0.4</td>
<td>-</td>
</tr>
</tbody>
</table>

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


Enhancing Diagnosis of SPS by NLP

255,674 patients
343,494 colonoscopies

NLP based search for
- WHO criteria 1: ≥5 serrated lesions proximal to the sigmoid colon, at least 2 of which ≥3 cm in size;
- WHO criteria 2: >20 serrated polyp lesions throughout the colon

71 cases identified

66 cases with SPS
- SPS per endoscopist, 38%
- Close follow up per endoscopist, 23%
- Not diagnosed by endoscopist, 35%

Colorectal cancer, 11%
Other cancer, 48%

Not SPS, 7%

Delay in diagnosis of ≥2 years, 8%

Parthasarathy G, et al. Accepted GIE 2020

Only WHO criteria 1 and 3 for a diagnosis of SPS were considered
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

Extra-colonic Cancer Risk

- None known
- No additional surveillance indicated outside colon
- *Except when SPS coexists with other genetic syndrome

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

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

<table>
<thead>
<tr>
<th></th>
<th>SPS Patient</th>
<th>MSP Patient</th>
<th>SPS FDR</th>
<th>MSP FDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalent CRC</td>
<td>22.6%</td>
<td>28.3%</td>
<td>12.2%</td>
<td>10.4%</td>
</tr>
<tr>
<td>Cumulative CRC</td>
<td>2.7%</td>
<td>4.1%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

**Lymphoma Prevalence**

<table>
<thead>
<tr>
<th>US Population (SEER)</th>
<th>Serrated Polyposis Syndrome</th>
<th>Prevalence</th>
<th>Prevalence</th>
<th>95% Confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.34%</td>
<td>9.80%</td>
<td>(4.80%, 17.29%)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.37%</td>
<td>10.87%</td>
<td>(3.62%, 23.57%)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.31%</td>
<td>8.93%</td>
<td>(2.96%, 19.62%)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

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

**SPS Prevalence**

<table>
<thead>
<tr>
<th></th>
<th>HL N=101</th>
<th>No HL N=1426</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced Neoplasia</td>
<td>25%</td>
<td>12%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Advanced Serrated Polyp</td>
<td>12%</td>
<td>4%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>6%</td>
<td>0%</td>
<td>&lt; .001</td>
<td></td>
</tr>
</tbody>
</table>


Consider colonoscopy in HL survivors treated with abdominal radiotherapy and/or procarbazine.
Surveillance Recommendations in SPS

**USMSTF**
Every 1 year

- ESGE and BSG
- Every 1-2 years

**NCCN**
Every 1-3 years

NCCN: Genetic/Familial High Risk Assessment-Colorectal. NCCN.org;V3 2018
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

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).

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

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Surgery in SPS

• Treatment for CRC

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