Serrated polyp detection rates and factors associated with detection

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WEO Colorectal Cancer Screening Committee  
Right-Sided Lesions and Interval Cancers  
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**Serrated polyps**: Epithelial lesions of the colorectum that demonstrate a “saw-toothed” or serrated appearance on histologic section due to infolding of crypt epithelium.

Normal colon  
Hyperplastic polyp  
Sessile serrated polyp

Huang et al. AJG 2010; 42(1), Snover. Hum Pathol 2010
Background: WHO taxonomy (2010)

Serrated lesions of the colorectum

- Hyperplastic polyp (HP)
  - Microvesicular type (MVHP)
  - Goblet cell rich type (GCHP)
  - Mucin poor type (MPHP)

- Sessile serrated polyp (SSP)
  - SSP with cytologic dysplasia

- Traditional serrated adenoma (TSA)
  - TSA with conventional dysplasia

AKA:
- Sessile serrated adenoma (SSA)
- Sessile serrated adenoma or polyp (SSA/P)
- Sessile serrated lesion (SSL)

Note: 5th edition WHO guidelines will be published in early 2019

Snover et al. WHO Classification of tumors. 4th Ed. 2010
The cancer preventive benefit of colonoscopy is dependent on the detection and removal of all precancerous polyps including both conventional adenomas and a subset of serrated polyps (SSPs and TSAs).

Premalignant serrated polyps are receiving more attention with respect to colonoscopy quality, but there is no agreed upon target for serrated polyp detection.

Different metrics used in literature: PSPDR, SSPDR, CSSPDR.

Most studies on this topic are single center.
Endoscopic features

Endoscopic features of SSPs
• Proximally located (75%)
• Flat (45%) or sessile (Paris Is, Ila, IIb)
• Pale color (almost all)
• Indistinct borders (70%)
• Cloud-like surface (60%)
• Mucus cap (60%)
• Rim of debris (50%)
• Obscure underlying vasculature (30%)

Because of subtle features, SSPs are subject to substantial underdetection

Hazewinkel et al. GIE 2013; Tadepalli et al. GIE 2011; Ijspeert et al. Endoscopy 2016
Detection of SSPs

Non-colonoscopy CRC Screening tests

- FOBT and FIT: Poor/nil
- CT Colonography: Poor
- Flexible sigmoidoscopy: Poor
- MT Stool DNA: Mediocre (42% of SSPs ≥1cm)

Colonoscopy

- Colonoscopy is the best screening test to detect SSPs
- BUT: underdetection of SSPs is a major problem

Crockett JAMA 2017; Chang et al. CGH 2017; Imperiale et al. NEJM 2014; Ijspeert et al AJG 2016; Kahi et al. CGH 2015
Prevalence and Variable Detection of Proximal Colon Serrated Polyps During Screening Colonoscopy

CHARLES J. KAHL, DAVID G. HEWETT, DUSTIN LEE NORTON, GEORGE J. ECKERT, and DOUGLAS K. REX

Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University School of Medicine; Richard L. Roudebush VA Medical Center; Indiana University School of Medicine; and Division of Biostatistics, Indiana University School of Medicine, Indianapolis, Indiana

Variation in the Detection of Serrated Polyps in an Average Risk Colorectal Cancer Screening Cohort

Jeremy T. Hetzel, BS, MPH, Christopher S. Huang, MD, Jennifer A. Coukos, BS, Kelsey Omstead, BS, Sandra R. Cerda, MD, Shi Yang, MD, Michael J. O’Brien, MD, MPH and Francis A. Farraye, MD, MSc
### Table 1. Screening Colonoscopies and Detection Rates

<table>
<thead>
<tr>
<th>Endoscopist</th>
<th>Number of colonoscopies</th>
<th>Patient age*</th>
<th>Male</th>
<th>≥1 Adenoma</th>
<th>≥1 Serrated polyp</th>
<th>Adenoma detection rate per colonoscopy*</th>
<th>Proximal serrated polyp detection rate per colonoscopy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3189</td>
<td>59.8 ± 8.0</td>
<td>52%</td>
<td>47%</td>
<td>18%</td>
<td>1.06 ± 1.79</td>
<td>0.26 ± 0.68</td>
</tr>
<tr>
<td>2</td>
<td>154</td>
<td>57.8 ± 8.0</td>
<td>45%</td>
<td>31%</td>
<td>10%</td>
<td>0.76 ± 1.59</td>
<td>0.14 ± 0.46</td>
</tr>
<tr>
<td>3</td>
<td>532</td>
<td>57.4 ± 7.3</td>
<td>45%</td>
<td>33%</td>
<td>6%</td>
<td>0.73 ± 1.57</td>
<td>0.08 ± 0.35</td>
</tr>
<tr>
<td>4</td>
<td>109</td>
<td>58.2 ± 7.0</td>
<td>46%</td>
<td>39%</td>
<td>11%</td>
<td>0.86 ± 1.46</td>
<td>0.18 ± 0.55</td>
</tr>
<tr>
<td>5</td>
<td>331</td>
<td>57.4 ± 6.9</td>
<td>48%</td>
<td>40%</td>
<td>13%</td>
<td>0.77 ± 1.36</td>
<td>0.18 ± 0.53</td>
</tr>
<tr>
<td>6</td>
<td>124</td>
<td>58.4 ± 6.9</td>
<td>44%</td>
<td>33%</td>
<td>8%</td>
<td>0.77 ± 1.66</td>
<td>0.11 ± 0.41</td>
</tr>
<tr>
<td>7</td>
<td>528</td>
<td>58.9 ± 7.7</td>
<td>41%</td>
<td>31%</td>
<td>11%</td>
<td>0.69 ± 1.47</td>
<td>0.16 ± 0.48</td>
</tr>
<tr>
<td>8</td>
<td>56</td>
<td>59.2 ± 7.6</td>
<td>50%</td>
<td>46%</td>
<td>13%</td>
<td>1.20 ± 1.86</td>
<td>0.14 ± 0.40</td>
</tr>
<tr>
<td>9</td>
<td>348</td>
<td>57.7 ± 7.5</td>
<td>37%</td>
<td>36%</td>
<td>12%</td>
<td>0.74 ± 1.48</td>
<td>0.17 ± 0.52</td>
</tr>
<tr>
<td>10</td>
<td>359</td>
<td>57.7 ± 7.3</td>
<td>53%</td>
<td>25%</td>
<td>3%</td>
<td>0.45 ± 1.05</td>
<td>0.04 ± 0.20</td>
</tr>
<tr>
<td>11</td>
<td>90</td>
<td>57.7 ± 6.7</td>
<td>52%</td>
<td>17%</td>
<td>1%</td>
<td>0.22 ± 0.56</td>
<td>0.01 ± 0.11</td>
</tr>
<tr>
<td>12</td>
<td>83</td>
<td>59.1 ± 8.3</td>
<td>52%</td>
<td>27%</td>
<td>2%</td>
<td>0.46 ± 0.98</td>
<td>0.02 ± 0.15</td>
</tr>
<tr>
<td>13</td>
<td>327</td>
<td>58.1 ± 7.8</td>
<td>60%</td>
<td>29%</td>
<td>11%</td>
<td>0.50 ± 0.95</td>
<td>0.15 ± 0.49</td>
</tr>
<tr>
<td>14</td>
<td>297</td>
<td>59.5 ± 8.2</td>
<td>50%</td>
<td>21%</td>
<td>4%</td>
<td>0.38 ± 1.07</td>
<td>0.06 ± 0.37</td>
</tr>
<tr>
<td>15</td>
<td>154</td>
<td>57.8 ± 8.0</td>
<td>45%</td>
<td>31%</td>
<td>10%</td>
<td>0.76 ± 1.59</td>
<td>0.14 ± 0.46</td>
</tr>
<tr>
<td>Combined</td>
<td>6681</td>
<td>58.9 ± 7.8</td>
<td>49%</td>
<td>38%</td>
<td>13%</td>
<td>0.84 ± 1.60</td>
<td>0.19 ± 0.57</td>
</tr>
</tbody>
</table>

*Mean ± SD.
### Table 3. Polyp detection prevalence per 100 colonoscopies by endoscopist (95% confidence intervals)

<table>
<thead>
<tr>
<th>Endoscopist (colonoscopies)</th>
<th>Adenoma (n=1,595*)</th>
<th>HP (n=844*)</th>
<th>SSA (n=46*)</th>
<th>DSP (n=15*)</th>
<th>Cancer (n=13*)</th>
<th>Other (n=593*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (488)</td>
<td>24.6 (20.2, 29.0)</td>
<td>10.5 (7.6, 13.3)</td>
<td>0.6 (0.0, 1.3)</td>
<td>0.2 (0.0, 0.6)</td>
<td>0.2 (0.0, 0.6)</td>
<td>10.9 (7.9, 13.8)</td>
</tr>
<tr>
<td>B (649)</td>
<td>23.9 (20.1, 27.6)</td>
<td>12.3 (9.6, 15.0)</td>
<td>0.9 (0.2, 1.7)</td>
<td>—</td>
<td>0.3 (0.0, 0.7)</td>
<td>7.1 (5.0, 9.1)</td>
</tr>
<tr>
<td>C (276)</td>
<td><strong>33.0 (26.2, 39.7)</strong></td>
<td><strong>22.8 (17.2, 28.5)</strong></td>
<td><strong>2.2 (0.4, 3.9)</strong></td>
<td>—</td>
<td>—</td>
<td><strong>17.4 (12.5, 22.3)</strong></td>
</tr>
<tr>
<td>D (273)</td>
<td>23.8 (18.0, 29.6)</td>
<td>12.1 (8.0, 16.2)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>11.4 (7.4, 15.4)</td>
</tr>
<tr>
<td>E (1,209)</td>
<td>23.7 (20.9, 26.4)</td>
<td>12.9 (10.9, 14.9)</td>
<td>1.0 (0.4, 1.6)</td>
<td>0.3 (0.0, 0.7)</td>
<td>0.4 (0.1, 0.8)</td>
<td>7.9 (6.3, 9.4)</td>
</tr>
<tr>
<td>F (679)</td>
<td>16.2 (13.2, 19.2)</td>
<td>8.8 (6.6, 11.1)</td>
<td>0.3 (0.0, 0.7)</td>
<td>0.1 (0.0, 0.4)</td>
<td>0.1 (0.0, 0.4)</td>
<td>6.0 (4.2, 7.9)</td>
</tr>
<tr>
<td>G (378)</td>
<td>13.5 (9.8, 17.2)</td>
<td>9.5 (6.4, 12.6)</td>
<td>0.3 (0.0, 0.8)</td>
<td>—</td>
<td>—</td>
<td>4.8 (2.6, 7.0)</td>
</tr>
<tr>
<td>H (534)</td>
<td>30.1 (25.5, 34.8)</td>
<td>14.0 (10.9, 17.2)</td>
<td>0.4 (0.0, 0.9)</td>
<td>0.2 (0.0, 0.6)</td>
<td>—</td>
<td>10.3 (7.6, 13.0)</td>
</tr>
<tr>
<td>I (1,463)</td>
<td>19.8 (17.5, 22.1)</td>
<td>7.7 (6.2, 9.1)</td>
<td>0.7 (0.3, 1.1)</td>
<td>0.3 (0.0, 0.5)</td>
<td>0.1 (0.0, 0.2)</td>
<td>5.3 (4.1, 6.4)</td>
</tr>
<tr>
<td>J (538)</td>
<td>18.6 (14.9, 22.2)</td>
<td>11.0 (8.2, 13.8)</td>
<td>—</td>
<td>0.4 (0.0, 0.9)</td>
<td>0.2 (0.0, 0.6)</td>
<td>6.3 (4.2, 8.4)</td>
</tr>
<tr>
<td>K (296)</td>
<td>17.6 (12.8, 22.3)</td>
<td>13.5 (9.3, 17.7)</td>
<td>—</td>
<td>—</td>
<td>0.7 (0.0, 1.6)</td>
<td>8.8 (5.4, 12.2)</td>
</tr>
<tr>
<td>L (225)</td>
<td>20.9 (14.9, 26.9)</td>
<td>9.8 (5.7, 13.9)</td>
<td>0.9 (0.0, 2.1)</td>
<td>0.4 (0.0, 1.3)</td>
<td>—</td>
<td>4.9 (2.0, 7.8)</td>
</tr>
<tr>
<td>M (184)</td>
<td>36.4 (27.7, 45.1)</td>
<td>31.0 (22.9, 39.0)</td>
<td>1.1 (0.0, 2.6)</td>
<td>0.5 (0.0, 1.6)</td>
<td>—</td>
<td>21.2 (14.5, 27.8)</td>
</tr>
</tbody>
</table>

$P$ value: $<0.001$ $<0.001$ 0.020 0.823 0.391 $<0.001$

Cancer, adenocarcinoma; DSP, dysplastic serrated polyp; HP, hyperplastic polyp; SSA, sessile serrated adenoma.

*Number of patients with at least one lesion; dashes indicate categories with no observations.

* $P$ values from Pearson’s χ²-test.
Cleveland Clinic cross-sectional study

- n = 2,167 patients, 65 endoscopists
  - SSP DR; 1.8%
  - Poor correlation between ADR and SSP DR (r = 0.35)
  - No correlation between SSP DR and endoscopist specialty, but majority were gastroenterologists or colorectal surgeon endoscopists
• Dutch study, 2011-2015
• n = 3,364 patients undergoing colonoscopy at center with high detection and experienced pathology
• Median ADR: 38.5%
• Median SSP DR: 7.3% (range 2.5-13.6)
• Patient factors associated with SSP detection:
  – Age: weak risk factor; M = F
  – FH CRC: OR 1.5
  – Surveillance vs. diagnostic: OR 1.7
New Hampshire colonoscopy registry cross-sectional study, 2009-2014
• n = 45,996 colonoscopies, 77 endoscopists, 28 facilities
• Proposed targets based on comparison with ADR thresholds:
  – CSSPDR = 7%
  – PSPDR = 11%
• Of note, 25% of endoscopists with ADR ≥ 25% did not meet CSSP DR benchmark
SSP detection by center

- Post-hoc analysis of PreSEPT trial (n=7215, 32 endoscopy centers)
- Proportion of colonoscopies with $\geq 1$ proximal serrated lesion = 2.8%
- Range between centers: 0 – 10%
- 4 centers reported no detection of proximal serrated polyps at all
Cross-sectional study of colonoscopy data

- 4 sites (UNC, UPMC, KP Washington, Central Illinois)
- 104,618 colonoscopies performed by 201 endoscopists between 2013-2015
- Colonoscopy and pathology data extracted by natural language processing
- Serrated polyp detection rate (SPDR) measured as proportion of colonoscopies with pathology that was “serrated” (high fidelity for SSPs)
Overall mean endoscopist SPDR = 5.1% (range 0 - 18%)

Variation by site (range 4.4 – 10.6%)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean ± SD</th>
<th>Median (IQR)</th>
<th>Min, Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Serrated polyp detection rate (%)</td>
<td>5.1 ± 3.8</td>
<td>4.1 (2.4, 7.0)</td>
<td>0, 18.8</td>
</tr>
<tr>
<td>Proximal SPDR (%)</td>
<td>3.9 ± 3.3</td>
<td>3.3 (1.6, 5.2)</td>
<td>0, 15.2</td>
</tr>
<tr>
<td>Rectosigmoid SPDR (%)</td>
<td>0.8 ± 0.9</td>
<td>0.6 (0, 1.2)</td>
<td>0, 3.9</td>
</tr>
<tr>
<td>Distal SPDR (non-rectosigmoid) (%)</td>
<td>0.4 ± 0.6</td>
<td>0.2 (0, 0.7)</td>
<td>0, 3.9</td>
</tr>
<tr>
<td>Large serrated polyp (≥1cm) (%)</td>
<td>1.0 ± 1.3</td>
<td>0.8 (0, 1.5)</td>
<td>0, 11.3</td>
</tr>
<tr>
<td>Traditional serrated adenoma (%)</td>
<td>0.2 ± 0.3</td>
<td>0 (0, 0.2)</td>
<td>0, 3.1</td>
</tr>
</tbody>
</table>
SPDR modestly correlated to ADR and other quality metrics
**Provider factors**

- Gastroenterologists > non-gastroenterologists
- Endoscopists with lower average bowel preps had lower serrated polyp detection

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Serrated polyp detection*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Endoscopist sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td>Female</td>
<td>1.10 (0.84, 1.44)</td>
</tr>
<tr>
<td>Primary specialty</td>
<td></td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>1.89 (1.33, 2.70)</td>
</tr>
<tr>
<td>Other</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td>Bowel preparation adequacy rate</td>
<td></td>
</tr>
<tr>
<td>&lt;0.85</td>
<td>0.60 (0.38, 0.97)</td>
</tr>
<tr>
<td>≥0.85</td>
<td>1.00 (Ref)</td>
</tr>
<tr>
<td>Cecal intubation rate</td>
<td></td>
</tr>
<tr>
<td>&lt;0.95</td>
<td>0.96 (0.75, 1.22)</td>
</tr>
<tr>
<td>≥0.95</td>
<td>1.00 (Ref)</td>
</tr>
</tbody>
</table>

*adjusted ORs obtained via logistic regression model adjusting for patient age, sex, colonoscopy indication, and site. SEs clustered at the physician level.
Provider factors

- Gastroenterologists > non-gastroenterologists
- Endoscopists with lower average bowel preps had lower serrated polyp detection
- Fewer years in practice and higher procedure volumes associated with higher SSP detection (importance of education/training and repetition)

Crockett et al. Endoscopy 2018
Pathology interpretation

Variation in Pathologist Classification of Colorectal Adenomas and Serrated Polyps

Rebecca A. Gourovitch, MS1, Sherri Roso, PhD1, Seth D. Crockett, MD, MPH2, Michele Morris, BA3, David S. Carroll, PhD4, Julia B. Greer, MD, MPH5, Reetesh K. Pali, MD6, Robert E. Schoen, MD, MPH4 and Ateev Mehrotra, MD, MPH6

- 85,526 colonoscopies with pathology specimens
- 48 reading pathologists
- Wide variation in classification rate of serrated polyps which affects endoscopists’ detection rates
Discussion

Strengths
• Large sample
• Multiple centers, different practice settings, geographically diverse

Limitations
• NLP is imperfect
• HP not included in SPDR measure. Thus, large or proximal HPs not captured
• Some of variation could be attributable to pathologist readings
• No data on withdrawal time, use of NBI or high definition endoscopy equipment
Colonoscopy is a game of hide and seek
Colonoscopy is a game of hide and seek
Improving endoscopic detection

**Patient factors**
- History of serrated polyps
- Family history of CRC
- Smokers

**Procedural factors**
- Bowel preparation
  - Poor prep = worse SSP detection
  - Split prep is important for cleansing right colon
- Withdrawal time
  - Optimal SSP detection occurs in providers with withdrawal times ≥ 9 min
  - Careful inspection in proximal colon in particular

Clark et al. CGH 2016; de Wijkerslooth et al. GIE 2013; Butterly et al. AJG 2014; Anderson et al. GIE 2014; Ijspeert et al. Endoscopy 2016
Improving endoscopic detection

Tools to improve detection

• NBI: No clear benefit
• Chromoendoscopy: Possible benefit, but questions about practicality**
• Wide angle endoscopy: No clear benefit
• Cap or cuff assisted colonoscopy: Probable benefit
• Retroflexion or 2nd anterograde inspection in right colon: Probable benefit

Quality improvement:

• In order to optimize SSP detection in colonoscopy screening programs, it must be measured
• For endoscopists with suboptimal detection:
  – Training in recognition of flat and subtle lesions
  – Assiduous inspection of the right colon
  – Use of mucosal exposure device

*Dulwani et al. CONSCOP trial, DDW 2018; *Repici et al. MB MMX trial, DDW 2018
If SSPs are so bad, why don’t we find dysplastic SSPs more often?

4 reasons:

1. **Underdection**: Like SSPs, SSPDs are missed.
2. **Window is short**: development of dysplasia corresponds to hMLH1 loss and development of MSI and rapid growth
SSPD “length time bias”

If SSPs are so bad, why don’t we find dysplastic SSPs more often?

4 reasons:

1. **Underdection**: Like SSPs, SSPDs are missed.

2. **Window is short**: development of dysplasia corresponds to hMLH1 loss and development of MSI and rapid growth

3. **Misdiagnosis**: due to pathologic misclassification, many SSPDs may be called “mixed polyps” or simply conventional adenomas. SSPs totally replaced by cytologic dysplasia can be difficult for pathologists to interpret.

4. **Incomplete resection**: due to subtle margins, some endoscopists may only resect the polypoid/dysplastic area (which is read as conventional adenoma) and leave the adjacent SSP portion behind.
Dysplastic SSP images

Burgess et al. GIE 2014; Burgess et al. Gut, 2016
<table>
<thead>
<tr>
<th>Metric</th>
<th>Definition</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADR</td>
<td>Proportion of colos with ≥ 1 adenoma</td>
<td>• Intuitive, easy to calculate • Correlated with interval cancer and cancer mortality • Difficult to game</td>
<td>• Does not capture serrated polyps • No credit for &gt;1 adenoma</td>
</tr>
<tr>
<td>AADR</td>
<td>Proportion of colos with ≥ 1 advanced adenoma</td>
<td>• Analogous to ADR • Measures what is important • Most directly linked to CRC prevention</td>
<td>• Rare, less reliable for low volume endoscopists • Can be partially gamed (size)</td>
</tr>
<tr>
<td>ADR + serrated</td>
<td>Proportion of colos with either adenoma or SSP or TSA</td>
<td>• Measures what’s important • Builds on existing quality framework • Credit for colos with only SSPs</td>
<td>• Changes in SSP DR dwarfed by ADR- difficult to separate or target for QI</td>
</tr>
<tr>
<td>PSP DR</td>
<td>Proportion of colos with ≥ 1 proximal serrated polyp</td>
<td>• Not dependent on pathologist • Correlates with SSPDR • Less volume dependent</td>
<td>• Location is subjective • Not as important as SSPDR • Can be gamed</td>
</tr>
<tr>
<td>SSP DR</td>
<td>Proportion of colos with ≥ 1 sessile serrated polyp</td>
<td>• Analogous to ADR • Measures what is important • Difficult to game</td>
<td>• Uncommon; less reliable for low volume endoscopists • Dependent on pathologist</td>
</tr>
<tr>
<td>CSSP DR</td>
<td>Proportion of colos with ≥ 1 large HP, SSP, or TSA</td>
<td>• Measures what’s important • Captures TSA and proximal HP detection</td>
<td>• Confusing, cumbersome • Somewhat dependent on pathologist (SSP) readings</td>
</tr>
</tbody>
</table>
Questions?
END