Sessile Serrated Polyps
What Do We Need to Know?

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• None
Goals

To Understand:

• The challenges in identifying serrated polyps
• The role of serrated polyps in interval colon cancers and how to minimize these interval cancers
• The importance of looking for Serrated Polyposis Syndrome and how to manage this syndrome
WHO Classification of Serrated Lesions

- Hyperplastic Polyp
  - Microvesicular Hyperplastic Polyps (MVHP)
  - Goblet Cell Rich Hyperplastic Polyps (GCHP)
  - Mucin Poor Hyperplastic Polyps (MPHP)
- Sessile Serrated Adenoma/Polyp (SSA/P)
  - No Dysplasia
  - With Dysplasia
- Traditional Serrated Adenoma

Clinical Features of Serrated Lesions

Prevalence of Serrated Lesions

- 27%-51% of all colorectal polyps are serrated
- Of All Serrated Lesions:
  - 83-96% are Hyperplastic
  - 3-11% are SSA/P
  - 1-7% are TSA
Hyperplastic Polyps

• Straight crypts
  – Extend symmetrically from the surface of the polyp to the muscularis mucosae
  – Crypts are wider at the polyp surface and narrower at the base
• Nuclei are small, round, regular, and basal
• Mitoses are confined to basal half of crypts
• Serrated at luminal surface

Microvesicular Hyperplastic Polyp (MVHP)

- Straight Crypts
- Small droplet mucin in cytoplasm of most cells
- Scattered goblet cells are common
- Common in rectum
- 10-15% in transverse and right colon
- Luminal surface and crypts show a serrated contour

Goblet Cell Hyperplastic Polyp (GCHP)

- Straight Crypts
- Near exclusive presence of goblet cells
- Mucin not present
- 90% in the left colon
- Proliferative zone is less than MVHP
- Few or no luminal serrations vs MVHP

Mucin Poor Hyperplastic Polyp (MPHP)

- Straight Crypts
- Mucin deplete
- Nuclei are very hyperchromatic
- Luminal serration pattern similar to MVHP
- Rare

Sessile Serrated Adenoma/Polyp

- Crypts at basal portion appear dilated “boot” or “L” or “anchor” shaped
- Irregular distribution of crypts
- Excessive serrated pattern
  - termed “hyperserrated”
- Disorganized crypt growth pattern
- Goblet and mucinous cells throughout
- Excessive mucin in lumen of crypts creates a mucus cap
- Various degrees of nuclear atypia
- Mitoses can occur anywhere in crypt

Minimum Criteria to Establish SSA/P

AGA

• The presence of at least one unequivocal architecturally distorted, dilated, and/or horizontally branched crypt

Pathology Challenges

- There is poor interobserver agreement between pathologists in the differentiation of HP vs SSA/P
  - Even Amongst Expert Pathologist
  - Contributes to a high variability in serrated polyp detection rates

Hyperplastic Polyps Get Reclassified on Re-Review

- Canadian study: previously reported hyperplastic polyps were re-reviewed by two GI pathologists
  - 17% of proximal HPs and 20% of HPs greater than 5 mm were reclassified as SSA/P
  - Proximal location (OR 4.7) and Size > 5 mm (OR 4.2) were independent predictors of reclassification


- Some advocate treating all right sided lesion HPs larger than 1 cm in size the same as SSA/P with respect to surveillance recommendations

Tumor Biology

Colorectal Cancer

~70% Adenomatous Pathway
Chromosomal Instability (CIN)
Microsatellite Stable (MSS)
Slow Progression

~20-30% Serrated Pathway
BRAF Mutation
CpG Island Methylation (CIMP)*
Microsatellite Instability (MSI) or MSS
Possible Rapid Progression

* Methylation of CpG islands is a way to reduce gene expression
  • More Methylation = Less Expression or Silencing
  • If methylation occurs in a tumor suppressor gene, then silencing of the gene can lead to carcinogenesis
Interval Colon Cancers

• Up to 5% of patients with colonoscopy in the past 5 years develop an interval CRC
• Studies show that interval colon cancers have a higher prevalence of
  – Proximal Location
  – CpG Island Methylation (CIMP)
  – Microsatellite Instability from silencing of DNA Mismatch Repair
    - Characteristics of Serrated Polyps
SSA/P & Interval Colon Cancers

- Missed SSA
- Rapid SSA Progression
- Incompletely Resected SSA
- Appropriate Surveillance Intervals

Optimize Endoscopic Detection
Improve Polypectomy Technique
Begins with recognition of endoscopic features of sessile serrated adenomas/polyps
Endoscopic Features of SSA/P

- Sessile or flat morphology > 90%
- Indistinct borders 73%
- Pale color 75%
- Mucus caping 64%-100%
- Rim of debris or bubbles 52%
- Resemblance to prominent folds 37%
- Interruption of the underlying mucosal vascular pattern in 32%

Optimizing Endoscopic Detection

• Withdrawal Time (WT)
  – New Hampshire Colonoscopy Registry: serrated polyp detection increased with each minute of withdrawal time above 6 min with a maximum benefit at 9 min

• High Definition Colonoscopy: Marginal Benefit
  – Dutch screening cohort, use of HD scopes vs Standard-Definition scopes provided a marginal incremental yield in polyp detection rate of 3.8% (95% CI 1% to 6.7%)

• Narrow Band Imaging: No clear Benefit
  – Four meta-analyses on NBI vs White Light with more than 3000 patients failed to show improved serrated lesion detection
Optimizing Endoscopic Detection

• Chromoendoscopy
  – Consistently improves detection rates
  – German Based Study reported an increase in serrated lesion detection rate from 29.5% to 46.2%
• Proximal Colon Retroflexion
  – Modest increase in detection, although similar gain is achieved with repeated examination in forward view
• Bowel Preparation
  – US registry based study serrated polyp detection rates were similar in optimal vs fair bowel preparation
  – Thicker mucus cap on serrated lesions with lower prep quality may assist in detection

British Society of Gastroenterology Position Statement on Serrated Polyps in the Colon and Rectum. 
Optimize Endoscopic Detection of SSA/P

Serrated Detection Rate (SDR)

- Guidelines recommend thresholds for adenoma detection rates (ADR) by individual endoscopists
- No serrated detection rate guideline as of current
- There is a strong correlation between ADR and serrated detection rates
- Similar to ADR, serrated detection rates vary by endoscopist
- SDR Benchmarks proposed: 7-11%

SSA/P & Interval Colon Cancers

- Missed SSA
- Incompletely Resected SSA
- Rapid SSA Progression
- Interval Cancer

- Optimize Endoscopic Detection
- Improve Polypectomy Technique
- Appropriate Surveillance Intervals
SSA/P are more likely to be Incompletely Resected

• CARE Study (Complete Adenoma Resection Study)
  – Prospective study
  – Adults 40 - 85 yoa, with at least one non-pedunculated polyp 5-20 mm in size
  – Primary outcome was to measure the incomplete resection rate of polyps
  – All polyps were removed using hot snare with intention of en bloc resection
  – After polyp removal was macroscopically considered complete, forcep biopsies were obtained from the polyp resection margin
    • 2 biopsies from opposing sides of margin for 5-9 mm polyps
    • 4 biopsies for 10-20 mm polyps from 4 quadrants
  – One expert GI pathologist reviewed all research specimens

CARE Study

• The overall incomplete resection for all neoplastic polyps was 10.1% (95% CI: 6.9%-13.3%)
• Larger polyps were more likely to be incompletely resected vs small neoplastic polyps 17.3% vs 6.8% (P=0.03)
• SSA/P were more likely to be incompletely resected vs other neoplastic polyps 31% vs 7.2% (P<0.001)
• Size and SSA/P status showed the strongest association with incomplete resection

Take Home
SSA/P are more likely to be incompletely resected as compared to other polyps
What are the Challenges We Face in Removing Serrated Lesions?
Challenges of Removing Serrated Lesions

- Endoscopic resection of both conventional adenomas and serrated lesions may prove challenging due to:
  - Size
  - Shape
  - Location

- Removal of Serrated Lesions poses one additional challenge:
  - Identification of the Border of the Lesion
Optimizing Endoscopic Resection

- Chromoendoscopy
- Submucosal Injection of fluid with contrast
  - Methylene Blue
  - Indigo Carmine
    - Superior to normal saline in terms of delineation of the lesion margin

Removal of Serrated Lesions

Smaller than 1 cm
• +/- electrocautery
• Cold snare better than piecemeal resection with forceps
• Include a narrow margin of normal mucosa if cold snaring

Larger than 1 cm
• Not associated with increased risk of complications
• Piecemeal resection with APC of residual tissue is ok
  – Repeat colonoscopy in 3-6 months to check for completeness of excision
Serrated Polyposis Syndrome (SPS)
Serrated Polyposis Syndrome (SPS)

• Formerly Hyperplastic Polyposis Syndrome
• Characterized by multiple serrated polyps
  – Typically SSA/P and Hyperplastic Polyps

• ~ 1/200
  Prevalence of SPS in the colorectal cancer screening population

• 7%
  CRC cumulative risk of at 5 years

WHO Criteria for SPS

1) At least 5 serrated polyps proximal to the sigmoid colon with 2 or more being larger than 10 mm
2) Any number of serrated polyps proximal to the sigmoid colon in an individual who has a 1st degree relative with SPS
3) Over 20 serrated polyps of any size distributed throughout the colon

Risk of CRC in Family Members of Patients with SPS

- First Degree relatives of patients with SPS have a $5X$ greater risk of CRC than general population.
- Screening colonoscopy in first degree relatives of patients with SPS should begin at
  - Age 40
  or
  - Beginning at an age 10 years younger than the age at diagnosis of the youngest affected relative
    whichever is sooner
- Colonoscopy is then recommended at 5 year intervals if normal or more frequently if polyps are found.
Genetics Referral for SPS Patients

- Multiple polyps
- Higher risk of CRC
- Evidence of Familial Clustering
- Increased risk of CRC in first degree relatives

All patients with SPS should be referred to clinical genetics
  - To ensure that an alternative diagnosis is not missed
  - Identification of relatives who should have surveillance
  - Facilitate research into SPS

Endoscopic Management of SPS

• The goal of long-term endoscopic management of polyps with annual colonoscopy is to:
  – Clear the proximal colon of all serrated lesions
    or
  – all serrated lesions more than 5 mm in size if multiple diminutive polyps present

• Surveillance interval and management strategy should be altered if colonoscopies reveal progressive control or loss of control of polyp burden

• Endoscopic control is feasible in ~90% of patients
Surgery in SPS

• Recommended when:
  – CRC is diagnosed
  OR
  – When the size and or number of polyps makes endoscopic control not feasible
• Extended right hemicolecctomy and subtotal colectomy are the most common
• Annual endoscopic surveillance of any residual colon and rectum
Prevention of Interval Colon Cancers

- Missed SSA
- Rapid SSA Progression
- Incompletely Resected SSA
- Interval Cancer
- Appropriate Surveillance Intervals

- Optimize Endoscopic Detection
- Improve Polypectomy Technique

SSA
# Post Polypectomy Surveillance Guidelines

<table>
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<th>Condition</th>
<th>USMTF (1)</th>
<th>ESGE (2)</th>
<th>BSG (3)</th>
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<td>Serrated Polyposis Syndrome</td>
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Manage as High Risk Adenomas

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Take Home

- Increase detection of SSA/P by performing high quality colonoscopy, recognizing features of serrated polyps and communicating with your pathologist
- Improve complete resection of SSA/P by delineating borders, submucosal injection with contrast
- Look for serrated polyposis syndrome, refer to genetics specialist, control polyp burden endoscopically – you likely will be able to
- Follow appropriate surveillance intervals
- Decreasing interval colon cancer from SSA/P requires increased detection, improved resection, and appropriate surveillance