BC CANCER
Provincial Health Services Authority

Polyp classification from the microscope

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3 January 2018

OUTLINE

Serrated lesions:
- Updates on terminology
- Updates on sessile serrated polyposis

HGD / intramucosal carcinoma / carcinoma in situ:
- Clarify the terminology
- Discuss diagnostic fears of pathologists

The subtle polyp:
- Are some polyps really only hidden from the pathologist?
- Do additional levels help?

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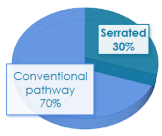
WHY CARE ABOUT SERRATED POLYPS?

SPORADIC CRC



FIT not useful

At best moderate agreement between expert GI pathologist

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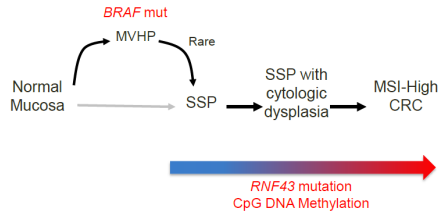
SIMPLIFIED VIEW OF SERRATED PATHWAY



Important points

- SSPs probably develop from MVHPs: MVHPs aren't completely innocuous but transformation to SSP is likely a rare event (occurs more commonly in the right colon)
- Serrated pathway is characterized by hypermethylation of CpG islands (CIMP-high) and BRAF mutations

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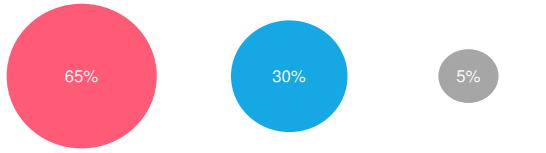
TYPES OF SERRATED POLYPS

UNTIL JULY 2019



Hyperplastic polyp (HP)
Microvesicular (MVHP)
Goblet cell rich (GCHP)

Sessile Serrated adenoma/polyp (SSA/P)

Traditional Serrated Adenoma (TSA)

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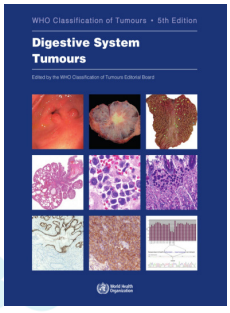
WHO 5TH ED.

RECOMMENDED TERMINOLOGY



- Sessile serrated lesion (SSL)
- Sessile serrated lesion with dysplasia (SSLD)
- ~~Cytological dysplasia~~

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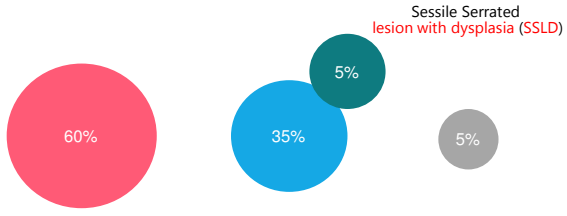
Types of serrated polyps – WHO 5th Ed.



Hyperplastic polyp (HP)
Microvesicular (MVHP)
Goblet cell rich (GCHP)

Sessile Serrated lesion (SSL)

Traditional Serrated Adenoma (TSA)

<1% Serrated adenoma - unclassified

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SSL: DIAGNOSTIC AGREEMENT

Histologic agreement among 7 GI pathologists on 109 serrated polyps

Only moderate interobserver agreement.

Polyp	Overall Kappa	Individual Kappa	95% CI	Interpretation
All polyps	0.5		0.47-0.52	Moderate
HP		0.52	0.48-0.57	Moderate
SSL		0.56	0.51-0.60	Moderate
SSLD		0.8	0.75-0.84	Excellent

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SESSILE SERRATED POLYPS WITH DYSPLASIA

Prevalence

About 5% of SSPs in one large study harbor dysplasia
(Arch Pathol Lab Med. 2015 Mar;139(3):388-93.)

No point to separate into high- and low-grade.

Must see dysplasia in same fragment as SSL in order to be certain this represents true dysplasia rather than a separate conventional adenoma

MLH1 IHC may be helpful if separate fragments contain SSL and dysplasia (MLH1 loss suggests SSLD)

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SSL: RISK OF CRC

- Danish CRC study: 2,060 CRC cases, 8,237 controls
- Determined what polyps at index colonoscopy increase risk of CRC
- Reviewed all serrated polyps (4 GI pathologists)

Polyp type	Cases %	Controls %	Adjusted OR
No polyp	56.5	74.2	1.00 (reference)
SSL	2.9	1.4	2.75
SSLD	1.0	0.3	4.76
Conventional adenoma	37	21	2.51
Hyperplastic polyp	2.7	2.9	1.30

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Erichsen, R, et al. Gastroenterology. 2016 Apr;150(4):895-902

SSL: RISK OF SUBSEQUENT SSL

- New Hampshire Colonoscopy registry: 3198 patients with no adenomas at index and 2 colonoscopies >12 months apart
- Determined what serrated polyps at index colonoscopy increase risk of subsequent large serrated polyps

Polyp type at index	Total, n	Adjusted OR (95% CI)
No serrated polyp	2396	1.00 (reference)
SSL (or TSA)	**104**	**9.70 (3.63-25.92)**
SSL ≥ 10 mm	**65**	**14.34 (5.03-40.86)**
SP < 10 mm	452	1.14 (0.38-3.45)
HP	698	1.85 (0.79-4.36)

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Anderson JC. Gastroenterology. 2017. PMID: 28927878.

WHAT ABOUT PTS WITH BOTH SSL AND TA?

- New Hampshire Colonoscopy registry: 5,433 patients with 2 colonoscopies >12 months apart
- Determined what polyps at index colonoscopy increased risk of subsequent high risk adenomas (large, villous or HGD)

Polyp type at index	Total, n	Adjusted OR (95% CI)
No adenoma or serrated polyp	2396	1.00 (reference)
High risk adenoma (HRA)	817	3.86 (2.77-5.39)
HRA + SP ≥ 10 mm	18	5.61 (1.72-18.28)
HRA + SSP or TSA	28	16.04 (6.95-37.00)
HRP + HP	186	3.51 (2.17-5.68)

Anderson JC. Gastroenterology. 2017. PMID: 28927878

SSL: TAKE HOME POINTS

- SSLs increase the risk of metachronous serrated polyps, independent of size of index SSL
- SSLs increase the risk of subsequent CRC
- SSLs+ high-risk adenomas markedly increase the risk of metachronous high-risk adenomas independent of SSL size
- SSLs can develop dysplasia with different morphologies
  - Minimal deviation dysplasia is very difficult to recognize
- SSL with "high-grade dysplasia" often harbor invasive CRC

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SERRATED POLYPOSIS SYNDROME

Criterion 1 (25% pts)	**At least 5 serrated lesions proximal to the rectum all ≥ 5 mm, with at least 2 ≥ 10 mm**
Criterion 2 (45% pts)	More than 20 serrated polyps of any size but distributed throughout the large bowel, with at least 5 proximal to the rectum

WHO 4th edition: ~~Criterion B omitted~~

At least 1 serrated polyp in a 1st degree relative

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'INTRAMUCOSAL CARCINOMA' VS 'HGD'

Preferred Term	Depth of Involvement	Finding	Usual Management
LGD	Mucosa (epithelium)	Low-grade dysplasia	Polypectomy/local excision* (No risk of mets)
HGD		High-grade dysplasia	
		Carcinoma in situ	
	Mucosa (lamina propria)	Intramucosal carcinoma	
Invasive carcinoma	Submucosa	Invasive carcinoma (submucosal invasion)	Polypectomy/local excision or resection** (Met risk depends on histology)

** Depends on endoscopic resectability*
***Depends on endoscopic resectability and presence of high-risk features for lymph node metastases*

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CAUSES FOR ABSENCE OF EPITHELIAL POLYP

- Sampling by endoscopist
  - Non-lesion (prominent mucosal fold/tag)
  - Lymphoid or mesenchymal lesion
  - Mucosa overlying submucosal lesion
- Lesion sampled but not sectioned (superficial or on opposite aspect of specimen)
- Subtle lesion histologically
- Error or artefact: In endoscopy suite, grossing, embedding/processing

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OFTEN THESE GET SIGNED OUT DESCRIPTIVE

Diagnosis:
- Submitted as "Colonic polyp":
  - Prominent lymphoid aggregate
  - No epithelial lesion identified
- Prominent mucosal fold; negative for dysplasia.

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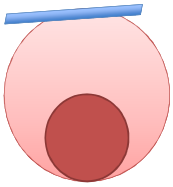
FACTORS THAT AFFECT DETECTION OF SUBMITTED POLYPS

- Size of lesion relative to polyp
- Sectioning protocol used by laboratory
  - YLMV (Your lab may vary)
- Orientation of lesion within tissue fragment relative to microtome blade



HOW OFTEN DO DEEPER LEVELS DETECT A POLYP?

- Among cases submitted as 'polyp' in which 3 original sections obtained
- In **4-30%**, lesions detected on further sections (most studies 20-25%), usually adenomas
- Rotation of 180 degrees and re-embedding detects lesions in 30% of cases (adenoma in 20% and HPs in 10%)

SUMMARY

- Deeper levels often detect lesions when initial sections are non-diagnostic (~20-25%)
- Size of lesion/tissue, sectioning protocol and orientation influence detection
- **Adenomas** are the lesions most frequently detected → may influence surveillance intervals (0 vs 1 and 2 vs 3 adenomas)

THANK YOU