

Lesioni serrate: criticità della diagnostica istologica

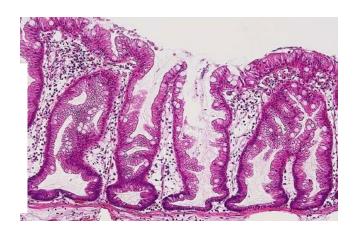
Paola Cassoni Università di Torino, Città della Salute e della Scienza

Lesioni serrate: dove eravamo rimasti?

Guidelines



British Society of Gastroenterology position statement on serrated polyps in the colon and rectum GUT, 2017



Statement 13

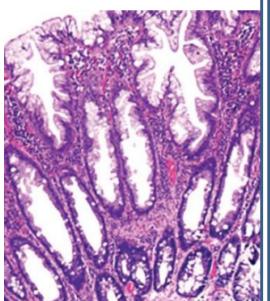
We recommend that clinicians involved in the care of patients with serrated polyps, especially endoscopists and pathologists, acquire the knowledge and skills to recognise and differentiate the various types of SLs (strong recommendation, moderate quality evidence, 100% agreement).

For the pathologist, endoscopist, gastroenterologist, and colorectal surgeon who were practicing before the year 2000, the emergence of the 'serrated pathway' of colorectal neoplasia has been a fairly momentous development that has stirred up significant emotions in many (disbelief, anger, mistrust, and fear, among likely many others). These emotions have been so strong because a bedrock dogma in medicine, that hyperplastic polyps (HPPs) of the colon are innocuous, has been shaken.

Kenneth P Batts

Modem Pathology (2015) 28, S80-S87

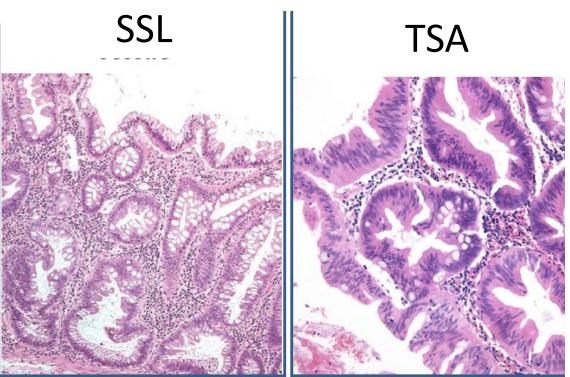
HP





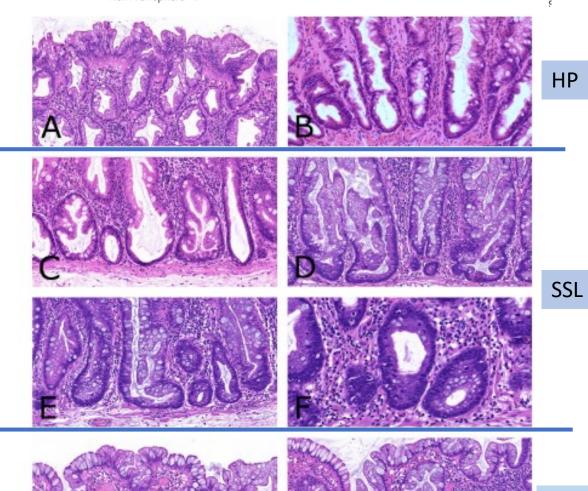
1° step: which entity?

So similar, so difficult to differentiate



Microvesicular hyperplastic polyp and sessile serrated lesion of the large intestine: a biological continuum or separate entities?

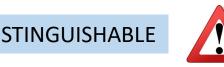
Adrian C Bateman , Adam L Booth , Raul S Gonzalez , Raul S Gonzalez Neil A Shepherd © 4



1° step: which entity?

Figure 1 Comparison of the morphological features of HPs and SSLs. (A, B) Typical features of microvesicular HPs. (A) Sharp serration within crypts. (B) Nuclear enlargement, hyperchromasia and stratification at the crypt base—similar (although less marked) to that seen in SSLs. (C-F) Typical features of SSLs. (C) Crypt dilatation—this can be a subjective assessment. This feature may be associated with the presence of little lamina propria between the dilated glands. (D). A branched crypt (on the left of the image). (E) A laterally spreading crypt—this is diagnostic of an SSL according to the latest WHO classification. (F) Nuclear changes at the crypt base—these changes are more marked than those seen in HPs and have been termed 'dysmaturation'. (G, H) Examples of foci within SSLs showing features that—alone—would be indistinguishable from microvesicular HPs. This situation commonly occurs within small biopsies from larger lesions, or with superficial or tangential cutting. The point here is that without seeing obvious crypt architectural distortion and/or the nuclear changes at the crypt bases, it may not be possible to make a diagnosis of SSL based on the histological features of the received material alone. HPs, hyperplastic polyps; SSL, sessile serrated lesion.

J Clin Pathol, march 2023



INDISTINGUISHABLE



REVIEW ARTICLE



2nd step: what about dysplasia?

An update on the morphology and molecular pathology of serrated colorectal polyps and associated carcinomas

Rish K. Pai 101 · Mark Bettington 2,3,4 · Amitabh Srivastava · Christophe Rosty 102,3,6

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Table 2 Morphologic patterns of dysplasia in sessile serrated polyps

Patterns	Architectural changes	Cytologic features	MLH1 loss	Frequency
Dysplasia not otherwise specified	Easily identifiable and varied in appearance: crypt elongation, crowding, complex branching, change in serration	Obvious atypia with amphophilic or eosinophilic cytoplasm, hyperchromatic nuclei with pseudostratification, frequent mitotic figures and loss of polarity	Frequent (>80%)	79%
Minimal deviation	Subtle changes with crypt crowding, change in crypt branching pattern and often reduced serration	Cells with hypermucinous cytoplasm or slightly eosinophilic with gastric phenotype, basally located nuclei showing mild hyperchromasia and mitotic figures not restricted to the lower part of the crypts.	Required for the diagnosis	19%
Serrated dysplasia	Closely packed small glands with reduced serration and cribriforming	Cuboidal cells with eosinophilic cytoplasm, frequent mitotic figures, marked nuclear atypia with vesicular nuclei and prominent nucleoli	Rare	12%
Adenomatous dysplasia	Absence of crypt serration, same appearance as conventional adenomas; dysplastic component on the upper part of the lesion	Cells with amphophilic or basophilic cytoplasm, elongated hyperchromatic nuclei and variable amount of goblet cell differentiation resembling cells from conventional adenomas	Rare	8%

^aFrequency of each pattern from Liu et al. [28] Multiple patterns can be present in a single lesion.

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Fig. 3 Sessile serrated polyp with dysplasia. a-b Endoscopic appearance of sessile serrated polyps with dysplasia demonstrating an area of protuberant growth in a part of an otherwise slightly elevated lesion (a) or as a more diffusely protuberant polyp (b). c-h Different morphologic appearance of dysplasia in sessile serrated polyp including adenomatous (c), dysplasia not otherwise specified (d-e), minimal deviation dysplasia (f-g), and serrated dysplasia (h)

2nd step: what about dysplasia?

Adenomatous Dysplasia

NOS Dysplasia

NOS Dysplasia

Minimal deviation Dysplasia



Minimal deviation Dysplasia



Serrated Dysplasia

Call me by my name

Histopathology



Histopathology 2022, 80, 1019-1025. DOI: 10.1111/his.14618

REVIEW

Head to head: should we adopt the term 'sessile serrated lesion'?

Iris D Nagtegaal¹ & Dale C Snover²

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Yes: SSL should be introduced as a unifying term (Iris Nagtegaal)

WHAT IS A PROPER NAME?

'The beginning of wisdom is to call things by their proper names' is a well-known quotation by Confucius. It can be considered to be the guideline for our

No: we should use SSA as the term for this entity (Dale Snover)

SO WHAT IS AN ADENOMA?

As the argument against the use of the term SSA has been the absence of cytological dysplasia, with the implication that the term adenoma is inappropriate for any lesion which is not dysplastic, we should perhaps explore the meaning of adenoma with particular regard to the need for dysplasia as a defining feature.

4° edition, 2010



5° edition, 2019

Serrated Colorectal Lesions Classificati	on (2010 WHO 4th Edition)	Serrated Colorectal Lesions Classification (2019 WHO 5th Edition)		
Histological type	Histological sub-type	Histological type	Histological subtype	
Hyperplastic polyp (HP)	Microvescicular type (MVHP)Goblet-cell rich type (GCHP)Mucin-poor type (MPHP)	Hyperplastic polyp (HP)	 Microvescicular type (MVHP) Goblet-cell rich type (GCHP) 	
Sessile serrated adenoma/polyp (SSA/P)	SSA/P with dysplasiaSSA/P without dysplasia	Sessile serrated lesion (SSL)	SSLSSL with dysplasia (SSLD)	
		Traditional serrated adenoma (TSA)		
Traditional serrated adenoma (TSA)		Serrated adenoma, unclassified		

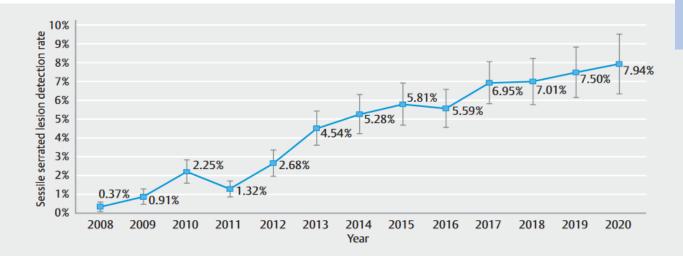
Sessile serrated lesion detection rates continue to increase: 2008–2020





Authors

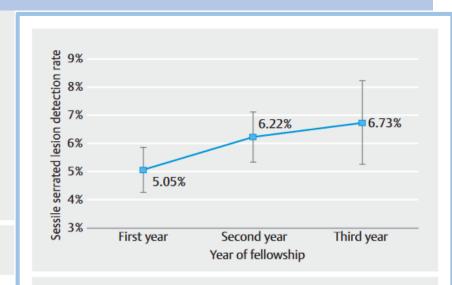
Nicholas Edwardson¹, Prajakta Adsul^{2,3}, Zorisadday Gonzalez², V. Shane Pankratz^{2,3}, Gulshan Parasher^{2,4}, Kevin English⁵, Shiraz Mishra^{3,6}



▶ Fig. 2 Adjusted sessile serrated lesion detection rate by year with 95% confidence intervals. Each marker represents the model-adjusted, division-level sessile serrated lesion detection rate including its 95% confidence interval.

Vengono detectati di più endoscopicamente?

Vengono diagnosticati di più istologicamente?



▶ Fig. 4 Adjusted sessile serrated lesion detection rate by fellowship year with 95% confidence interval. Each marker represents the model-adjusted, division-level sessile serrated lesion detection rate among fellows only including its 95% confidence interval.

Could the sessile serrated lesion detection rate become an ESGE quality parameter?





Authors

Cesare Hassan^{1,2}, Alessandro Repici^{1,2}, Tommy Rizkala¹, Michal F. Kaminski³

"Edwardson et al showed a 20-fold increase in SSL detection rate in the last 10 years, indicating that this indicator is susceptible to improvement and somewhat reflective of the overall quality improvement in the

setting of colonoscopy"

Vengono detectati di più endoscopicamente?

Vengono diagnosticati di più istologicamente?

BUT:

- ✓ Pathology is still an issue
- ✓ SSL should include HP or not in the overall count?
- ✓ USA



4° edition, 2010



5° edition, 2019

Serrated Colorectal Lesions Classificati	on (2010 WHO 4th Edition)	Serrated Colorectal Lesions Classification (2019 WHO 5th Edition)		
Histological type	Histological sub-type	Histological type	Histological subtype	
Hyperplastic polyp (HP)	Vengono detectati di più endoscopicamente ? Vengono diagnosticati di più istologicamente ?		 Microvescicular type (MVHP) Goblet-cell rich type (GCHP) 	
Sessile serrated adenoma/polyp (SSA/P)		Sessile serrated lesion (SSL)		
		Traditional serrated adenoma (TS	A)	
Traditional serrated adenoma (TSA)		Serrated adenoma, unclassified		

The **2019 WHO classification** now requires only **a single 'characteristic' crypt** to be present in order to make a diagnosis of an SSL. Within the 2010 WHO classification, **two or three such crypts** were needed.

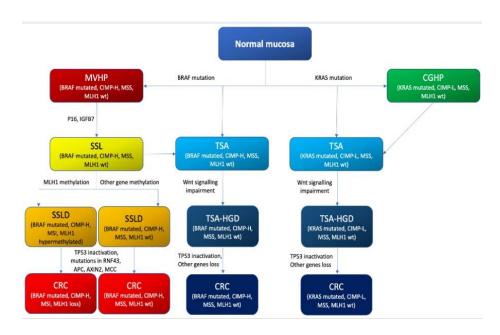
Now, while features such as goblet cells at the crypt bases and mild basal crypt dilatation are not sufficient for a diagnosis of SSL, the presence of at least one 'unequivocally distorted crypt' is enough for this purpose.

Bateman AC, et al. J Clin Pathol 2023

Review

Microvesicular hyperplastic polyp and sessile serrated lesion of the large intestine: a biological continuum or separate entities?

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A practical approach to the diagnosis of microvesicular HPs and SSLs

Despite the fact that location alone is not a key determinant of lesion type, some pathologists are very reluctant to make a diagnosis of microvesicular HP within the right colon and may have a lower threshold for making a diagnosis of SSL in lesions derived from this area

Studies have shown poor consistency in the histopathological differentiation between microvesicular HPs and SSLs, with under-recognition of the latter in studies where histopathological review has been performed. Reviews of the morphological features of lesions initially diagnosed as microvesicular HPs have revealed reclassification as SSLs in up to 30% of cases.



Site & Dimension impact in reclassification

Bateman AC, et al. J Clin Pathol 2023

Review

Microvesicular hyperplastic polyp and sessile serrated lesion of the large intestine: a biological continuum or separate entities?

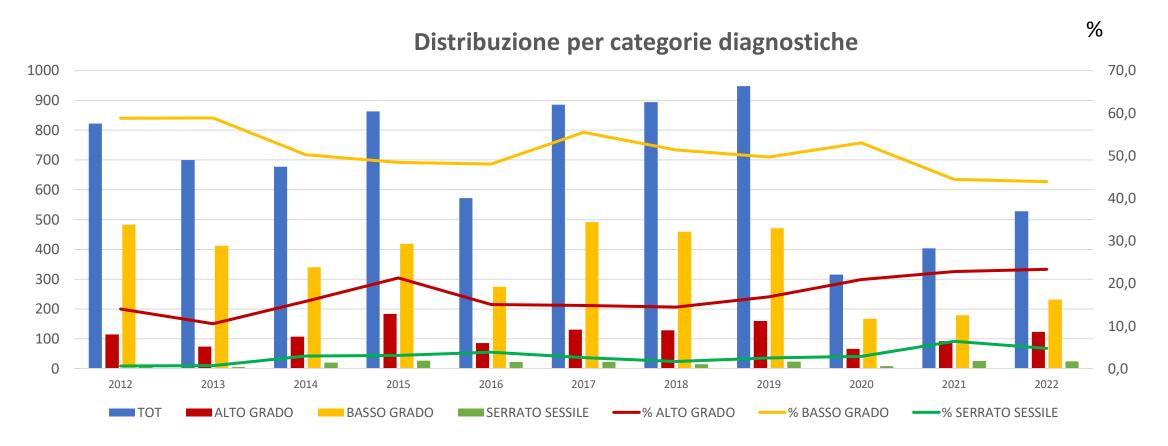
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In a routine diagnostic setting, we believe that it is reasonable to **take the location** and **size of lesions** into account when assessing serrated polyps.

When doubt occurs in the differential diagnosis between microvesicular HP and SSL, a <u>lower threshold</u> for a diagnosis of SSL may be appropriate for <u>right-sided lesions</u> and <u>larger lesions</u>, or if technical difficulties exist, for example, <u>suboptimal specimen</u> <u>orientation</u> or with small biopsies taken from larger lesions

What's appening in real life? Over year changes

Colonscopie di screening, singolo centro, Torino



Which entities are switched into SSL?

Both HP and TA/TVA LG: impact on Follow up???

Serrated polyp detection and risk of interval post-colonoscopy 🗲 🦒 🚇 📵 colorectal cancer: a population-based study



David E F W M van Toledo*, Joep E G IJspeert*, Patrick M M Bossuyt, Arne G C Bleijenberg, Monique E van Leerdam, Manon van der Vlugt, Iris Lansdorp-Voqelaar, Manon CW Spaander, Evelien Dekker

Added value of this study

We showed that serrated polyp detection is strongly related to interval post-colonoscopy colorectal cancer incidence, an effect that is independent of the ADR. Patients examined by endoscopists in the lowest quintile (in terms of serrated polyp detection) had a tripled risk for future interval postcolonoscopy colorectal cancer compared with those examined by an endoscopist in the highest quintile. Each percentage point increase in proximal serrated polyp detection rate (PSPDR) resulted in a 7% lower risk of interval postcolonoscopy colorectal cancer. The highest protective effect was found in endoscopists with an ADR and a PSPDR above the overall median.

Implications of all the available evidence

At present, the ADR is the only evidence-based polyp detection parameter. Based on our results, monitoring of serrated polyp detection could be a valuable addition to optimise colonoscopy quality and reduce interval postcolonoscopy colorectal cancer incidence.

Take Home Message

- 1) PSPDR indicatore di qualità endoscopica;
- 2) SSL continueranno ad aumentare per allargamento criteri WHO;
- 3) SSL asportate interrompono la cancerogenesi serrata dx;
- 4) Il FU segue le indicazioni delle linee guida



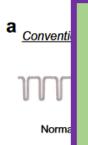


REVIEW

Sessile serrated lesions with dysplasia: is it possible to nip them in the bud?



OUT of our confort zone



Serrated



To be continued....

b BRAF mutation



Microvesicular hyperplastic polyp



SSL/SSLD

(Epi-1 signature)

Proliferation Stemness Oncogenic signature KRAS mutation



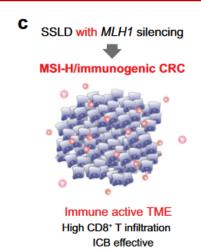
Goblet cell hyperplastic polyp



TSA

(Epi-2 signature)

Lysosome secretion Angiogenesis



MSS/mesenchymal CRC

Immunosuppressive TME
High stroma reaction

ICB resistant

The new classification proposed by Liu

Adenomatous dysplasia Serrated dysplasia Minimal deviation dysplasia Dysplasia not otherwise specified

10 World Health Organization