GISCOR gruppo italiano screening colorettale

### Detection Rate delle lesioni serrate: abbiamo bisogno di un nuovo indicatore?

Franco Radaelli UOC Gastroenterologia Ospedale Valduce, Como

CONVEGNO NAZIONALE GISCOR 2023 Hotel Astoria Palace. Palermo









## Serrated pathway: 20-30% sporadic cancers 30-40% iCRC have features suggesting serrated pathways (MSI, CIMP+)

# Factors associated to SSLs detection:



- Mucosal inspection (WT)
- Endoscopist's skill (high polyp detectors)

Meester RGS et al. Prevalence and Clinical Features of Sessile Serrated Polyps: A Systematic Review. Gastroenterology 2020; 159: 105-118

Right colon inspection (double inspection, retroflexion) Enhanced endoscopy (mucosal exposure device, chromoendoscopy) (?)

## SSLs detection:

Interoperator variability

	# Endoscopisti	ADR, range (delta)	SSL-DR, <u>range</u> (delta)
Hetzel, 2010 Boston, 1 academic center	13	13% - 36% (3)	1.1% – 7.9% (7)
Kahi, 2011 Indiana, 1 academic center	15	17% - 47% (3)	1% – 18% (18)
De Wijkerslooth, 2013 Amsterdan, Rotterdam, 2 academic centers	5	24% - 40% (2.5)	6% - 22% (4)
		Hetzel JT, Am J Gastr Kahi CJ, Clin Gastroen	oenterol 2010: 105: 256 terol Hepatol 2011; 9: 42

De Wijkerslooth, Gastrointest Endosc 2013; 77: 617-623

#### FIT-program 2022 - Valduce: Quality indicators 2022

	CIR (unadjusted)	ADR	ADV ADR	SSL DR	ADV ADR	SSL DR
1	98.2%	62.1%	10.3%	1.7%	10.3%	1.7%
2	100.0%	53.8%	7.7%	7.7%	7.7%	7.7%
3	100.0%	63.6%	18.2%	3.0%	18.2%	3.0%
4	100.0%	53.3%	26.7%	0.0%	26.7%	0.0%
5	96.0%	48.0%	24.0%	0.0%	24.0%	0.0%
6	100.0%	52.4%	14.3%	9.5%	14.3%	9.5%
7	100.0%	37.5%	8.3%	0.0%	8.3%	0.0%
8	100.0%	45.8%	12.5%	4.1%	12.5%	4.1%
9	100.0%	69.1%	14.3%	7.1%	14.3%	7.1%
10	93.1%	48.3%	17.2%	0.0%	17.2%	0.0%

Range 37-69% (X 1.5) Mean: 55.4% Range 0-9.5% (X 9) Mean: 3.6%

## CADe and serrated lesions: Metanalysis of RCTs

Patel et al, Digestive Disease Week, Chicago 2023

#### **SSLs** detection rate

12 RCTs		With Al	Without Al	RR
9,237 pts - With AI – 4595	All	5%	4%	1.15 (0.99-1.39)
Mean age: 59y, Males 54%	Screen/surv.	6%	5%	1.15 (0.92-1.45)
Mean age: 58y, Males 52%				

Thieme

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





Authors Cesare Hassan<sup>1,2</sup>, Alessandro Repici<sup>1,2</sup>, Tommy Rizkala<sup>1</sup>, Michal F. Kaminski<sup>3</sup>

# Criteria for the ideal KPM:

- Clinically relevant (associated with relevant outcomes)
- Measureable (easy to measure)
- Potentially amendable over time (CQI)
- Transparent (no susceptible of corruption)
- Comparable (benchmarking)
- Comprehensive

- 1. Does SSL-DR meet these criteria?
- 2. Does SSL-DR better discriminate low- *versus* high-quality colonoscopists than ADR ?
- 3. Is FIT-based screening program the right field for implementation of this new KPM?

## Sessile lesions and iCRC risk – FIT based screening programs

#### van Toledo DEF et al. Lancet Gastroenterol Hepatol 2022; 7: 747–54

Dutch screening program (FIT cut-off: 47 µg Hb/g faeces) 277.555 screening patients 55-77 yr (2014-2020) 441 endoscopists, 305 i-CRCs.

100 J 504 ---- PSPDR 2.0-40 1.5A djusted HR PSDPR (%) 30 1.0 20 0.5 10 0 Q1 Q2 Q3 Q4 0-2015 2016 2017 2018 Overall 2014 2019 2020 HR PSPDR 0.95 0.74 0.42 1 Year of colonoscopy 95% CI reference 0.70 - 1.290.53 - 1.030.28-0.64 0.21 - 0.550.8%-7.5% 7.6%-10.4% 10.5-12.9% 13.0-16.9% 17.0-29.1%

PSPDR = DR of proximal serrated polyp (SSLs+HPs proximal to the descending colon)

Every + 1% PSPDR = - 7% i-CRC risk

Q5

0.34

Median ADR: 66.3% (IQR 61.4-69.9) Median PSP-DR: 11.9 % (IQR 8.3-15.8)

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Median ADR: 66.3% (IQR 61.4-69.9) Median PSP-DR: 11.9 % (IQR 8.3-15.8) Median SSL-DR: 9.0 % (IQR 0.5-29.6)

From a clinical perspective, considering ease-of-use and expected effectiveness, the PSPDR appears to be the best proxy for the detection of clinically relevant serrated polyps in daily practice, overcoming the pathologists high interobserver variability in SSL diagnosis

	Median (range)	HR (95% CI)*
ADR	66·3% (43·0% - 83·2%)	0.94 (0.93 - 0.96)
SSLDR	9.0% (0.5% - 29.6%)	0.91 (0.87 - 0.94)

### Sessile lesions and iCRC risk – FIT based screening programs *Barbiellini Amidei C et al. Palermo, GISCOR 2023; DDW 2023 (GIE 2023: 65 AB 469)*

FIT cut-off: 20 µg Hb/g faeces 49,626 colonoscopies(2012-2017), f-up until 12/2021 311.287 person-years f-up 257 i-CRC median ADR 48.0% (IQR 43.7-55.0) median SSPDR 1.62% (IQR 0.75-3.60)

Table 1. Sessile serrated polyp detection rate with the risk and 95% confidence interval of developing an incident post-colonoscopy colorectal cancer over the follow-up.

Variable	PCCRC	Person- years	Incidence rate per 100,000 person-years	Hazard Ratio*	95% Confidence Interval
Sessile serrated polyp detection rate group					
0-1%	99	97,750	101.28 (83.17 - 123.33)	Ref.	-
1-2%	73	84,267	86.63 (68.87 - 108.97)	0.84	0.62 - 1.13
2-3.5%	31	50,479	61.41 (43.19 - 87.32)	0.60	0.40 - 0.89
3.5-5%	31	44,187	70.16 (49.34 - 99.76)	0.67	0.45 - 1.01
5-15.6%	23	34,604	66.47 (44.17 - 100.02)	0.60	0.38 - 0.96
Sessile serrated polyp detection continuous rate (1% increase)	257	311,287	82.56 (73.06 - 93.30)	0.90	0.84 - 0.97

ADR continuous rate (1% increase)	257	311,287	82.56 (73.06 - 93.30)	0.96	0.94 - 0.97
SSPDR continuous rate	257	211 207	92 EE (72 OE 02 20)	0.90	0.83 0.07
(1% increase)	257	511,267	82.50 (75.00 - 95.50)	0.90	0.83 - 0.97

Every + 1% ADR = - 4% i-CRC risk Every + 1% SSP-DR = - 10% i-CRC risk

\*Adjusted for sex, age group, year of endoscopy and follow-up recommendation.

Abbreviations: PCCRC: Post-colonoscopy colorectal cancer.

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- Comparable (benchmarking) (?)

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## Endoscopist SSPDR, ADR and risk of iCRC

#### van Toledo DEF et al. Lancet Gastroenterol Hepatol 2022; 7: 747–54



*Figure* 3: Risk of interval post-colonoscopy colorectal cancer for endoscopists with a high PSPDR and a high ADR compared with endoscopists with a high PSPDR and a low ADR, low PSPDR and high ADR, or low PSPDR and low ADR

#### 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.

### Sessile lesions and iCRC risk – FIT based screening programs Barbiellini Amidei C et al. Palermo, GISCOR 2023; DDW 2023 (GIE 2023: 65 AB 469)

Variable	PCCRC	Person- years	Incidence rate per 100,000 person-years	Hazard Ratio	95% Confidence Interval
ADR continuous rate (1% increase)	257	311,287	82.56 (73.06 - 93.30)	0.96	0.94 - 0.97
SSPDR continuous rate (1% increase)	257	311,287	82.56 (73.06 - 93.30)	0.90	0.83 - 0.97
ADR and SSPDR combinations					
High ADR - High SSPDR	46	78,032	58.95 (44.16 - 78.70)	Ref.	-
High ADR - Low SSPDR	53	78,225	67.75 (51.76 - 88.69)	1.15	0.83 - 1.60
Low ADR - High SSPDR	57	69,941	81.50 (62.86 - 105.65)	1.41	1.04 - 1.91
Low ADR - Low SSPDR	101	85,089	118.70 (97.67 - 144.26)	2.10	1.54 - 2.85

Abbreviations: PCCRC: Post-colonoscopy colorectal cancer; ADR: Adenoma detection rate; SSPDR: Sessile serrated polyp detection rate

Nonostante l'high-SSPDR conferisca un rischio leggermente inferiore negli endoscopisti con low-ADR, l'ADR sembra più fortemente associato al rischio di PCCRC, e rappresenta pertanto un parametro più robusto per monitorare la performance degli endoscopisti



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## Limits to SSL-DR as KPM (in FIT-based screening setting)

- Low-prevalence lesions
- Need for accurate pathology interpretation
- FIT has low-sensitivity for serrated polyps
- It is still uncertain whether SSL-DR really complementary to ADR to differenziate high vs. low performers
- The benchmark for the SSL detection rate is unclear (and what we should measure should be better standardized)
- Surveillance protocols for SSLs are poorly defined

## SSLs-DR: abbiamo bisogno di un nuovo indicatore?

- 1. Probabilmente SI, almeno nella pratica clinica (a livello del centro e del singolo endoscopista)
- 2. Probabilmente NO, nei programmi di screening organizzati con FIT

GISCOR gruppo italiano screening colorettale

## Lesioni serrate: criticità della diagnostica istologica

**CONVEGNO** 

**NAZIONALE** 

Hotel Astoria Palace, Palermo

**GISCoR 2023** 

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



### So similar, so difficult to differentiate



Review

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

Adrian C Bateman  $^{\odot}$  ,  $^1$  Adam L Booth  $^{\odot}$  ,  $^2$  Raul S Gonzalez  $^{\odot}$  ,  $^3$  Neil A Shepherd  $^{\odot}$   $^4$ 



## 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



Check for updates

#### **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 <sup>[b]</sup> · Mark Bettington<sup>2,3,4</sup> · Amitabh Srivastava<sup>5</sup> · Christophe Rosty <sup>[b]2,3,6</sup>

Received: 28 February 2019 / Revised: 28 March 2019 / Accepted: 29 March 2019 / Published online: 25 April 2019 © United States & Canadian Academy of Pathology 2019

1398

#### R. K. Pai et al.

#### Table 2 Morphologic patterns of dysplasia in sessile serrated polyps

Patterns	Architectural changes	Cytologic features	MLH1 loss	Frequency <sup>a</sup>
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%

<sup>a</sup>Frequency of each pattern from Liu et al. [28] Multiple patterns can be present in a single lesion.

R. K. Pai et al.



## 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 Nagtegaal<sup>1</sup> & Dale C Snover<sup>2</sup>

<sup>1</sup>Department of Pathology, Radboud University Medical Centre, Nijmegen, The Netherlands, and <sup>2</sup>Department of Laboratory Medicine and Pathology, University of Minnesota Medical School, Minneapolis, Minnesota, USA



## 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 Classif	ication (2019 WHO 5th Edition)
Histological type	Histological sub-type	Histological type	Histological subtype
Hyperplastic polyp (HP)	<ul> <li>Microvescicular type (MVHP)</li> <li>Goblet-cell rich type (GCHP)</li> <li>Mucin-poor type (MPHP)</li> </ul>	Hyperplastic polyp (HP)	<ul> <li>Microvescicular type (MVHP)</li> <li>Goblet-cell rich type (GCHP)</li> </ul>
Sessile serrated adenoma/polyp (SSA/P)	<ul> <li>SSA/P with dysplasia</li> <li>SSA/P without dysplasia</li> </ul>	Sessile serrated lesion (SSL)	<ul> <li>SSL</li> <li>SSL with dysplasia (SSLD)</li> </ul>
		Traditional serrated adenoma (TSA)	
Traditional serrated adenoma (TSA)		Serrated adenoma, unclassified	

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

#### ©••••=

#### Authors

Nicholas Edwardson<sup>1</sup>, Prajakta Adsul<sup>2,3</sup>, Zorisadday Gonzalez<sup>2</sup>, V. Shane Pankratz<sup>2,3</sup>, Gulshan Parasher<sup>2,4</sup>, Kevin English<sup>5</sup>, Shiraz Mishra<sup>3,6</sup>



▶ 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<sup>1,2</sup>, Alessandro Repici<sup>1,2</sup>, Tommy Rizkala<sup>1</sup>, Michal F. Kaminski<sup>3</sup>

"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





5° edition, 2019

## 4° edition, 2010



The **2019 WHO classification** now requires only <u>a single 'characteristic'</u> 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.





#### 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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Adrian C Bateman (0, 1) Adam L Booth (0, 2) Raul S Gonzalez (0, 3) Neil A Shepherd (0, 4)
```

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???

#### 

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-Vogelaar, Manon C W 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) II 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

