Optical diagnosis of sessile serrated polyps; bottleneck for the optical diagnosis paradigm?

J.L.A. Vleugels, J.E.G. IJspeert, Y. Hazewinkel, M. van der Vlugt, P. Fockens, L. Koens, E. Dekker
CHAPTER 8

ABSTRACT

Background
Optical diagnosis of diminutive (1-5mm) polyps could result in a more cost-effective colonoscopy practice. Previous optical diagnosis studies did not incorporate the differentiation of sessile serrated polyps (SSPs). This study aimed to evaluate the impact of optical diagnosis of diminutive SSPs on the overall performance of endoscopic polyp differentiation in daily colonoscopy practice.

Methods
Endoscopy data were prospectively collected between 2011 and 2014 in a colonoscopy center. Each endoscopist reported a real-time optical diagnosis (SSP, adenoma or hyperplastic polyp) for all lesions in a structured colonoscopy reporting system, using narrow band imaging at their discretion. Study outcomes were accuracy of optical diagnosis, surveillance interval agreement and negative predictive value (NPV) for diminutive recto-sigmoid neoplastic histology based on the optical diagnosis of diminutive polyps compared to histopathology.

Results
Of 2,853 removed diminutive polyps, 202 (7.1%) were histologically proven SSPs. Optical diagnosis of diminutive SSPs was accurate in 24.4%. Diminutive SSPs determined 6.9% of post-polypectomy surveillance assignments. Inaccurate optical diagnosis of diminutive SSPs led to lower surveillance interval agreement (78.1% vs. 53.3%, p<0.01) and pooled NPV per polyp (84.3% vs 50.0%; p<0.01) in patients with diminutive SSPs when compared to patients without diminutive SSPs. Accurate endoscopic identification of diminutive SSPs improved from 0% in 2011 to 47% in 2014 (p=0.02).

Conclusion
Endoscopic characterization of diminutive SSPs is difficult, impairing overall performance of optical diagnosis in patients with diminutive SSPs. Future optical diagnosis studies should use validated trainings and classification algorithms that include differentiation of SSPs.
INTRODUCTION

Colorectal cancer (CRC) is among the most common cancers worldwide and gradually develops from adenomatous or serrated polyps. By detecting and removing high-risk polyps or early cancers, colonoscopy has been shown to reduce mortality and morbidity from CRC. Approximately 90% of the lesions detected during screening colonoscopy are smaller than 10mm. These lesions rarely contain CRC (0.03 – 0.07%) or advanced histological features such as villous histology or high-grade dysplasia (1.7 – 6.6%), which is especially true for diminutive (1-5mm) polyps. As a result, routine histological analysis of these polyps is mainly used to guide surveillance interval recommendations. Colonoscopies could become more time-efficient and cost-effective if endoscopists would be able to accurately predict the histology of diminutive polyps during endoscopy, as this would obviate the need of histopathological evaluation.

This practice of optical diagnosis has two practical implications. Firstly, diminutive polyps in the colorectum are resected and discarded without the need for histopathological analysis. The endoscopic diagnosis as determined during the exam will be used to guide subsequent surveillance intervals. Furthermore, obvious non-neoplastic lesions in the recto-sigmoid, i.e. diminutive hyperplastic polyps (HPs), are left in situ to reduce unnecessary polypectomies and diminish associated risks and costs.

In order to implement such a policy, the diagnostic accuracy of optical diagnosis should be amply sufficient. Expert endoscopists have shown excellent accuracies in optical polyp differentiation, using either the NBI International Colorectal Endoscopic (NICE) or the Kudo classification. On the contrary, optical diagnosis studies in the non-academic setting have shown suboptimal results. The vast majority of these studies investigated the ability to differentiate between HPs and adenomatous polyps. However, premalignant sessile serrated polyps (SSPs) were usually not taken into account or erroneously considered as innocuous lesions. Nowadays, SSPs are thought to be precursor lesions for 15% of CRC. Although the reported prevalence of SSPs varies widely between studies, several recent studies have reported a SSP prevalence of 7.3-8.1%, which is higher than assumed earlier. Hence, excluding SSPs in optical diagnosis studies might have a substantial influence on the feasibility of implementing this strategy in daily practice. This study aimed to determine the accuracy of endoscopic polyp differentiation of diminutive SSPs in an ambulatory outpatient colonoscopy center.

METHODS

This study has a cross sectional design, using prospectively collected data from a single outpatient colonoscopy center. In our ambulatory endoscopy center most colonoscopies were performed for symptoms and surveillance for earlier detected polyps. No endoscopies were performed in patients...
with previously diagnosed inflammatory bowel disease, Lynch syndrome or polyposis syndrome. Data from colonoscopies between January 2011 and December 2014 were included in this study. The local Institutional Review Board declared that this study did not require formal approval as no additional interventions were performed and patient data had been collected during standard care.

**Endoscopists and endoscopy technology**

All colonoscopy procedures were performed by gastroenterologists or senior gastroenterology residents of the Academic Medical Centre in Amsterdam, the Netherlands. Endoscopists were instructed to resect all detected lesions, independent of the predicted polyp histology. All endoscopists were aware of the most common optical classification systems of diminutive polyps (NICE classification and Kudo-classification) but did not receive any formal training in optical diagnosis before the start of this study.

All procedures were performed using high definition colonoscopes (HDTV Olympus 180 EXERA; Olympus, Tokyo, Japan) and processors (CV-180 EXERA II processor; Olympus, Tokyo, Japan) with NBI available. All endoscopy suites were equipped with high-definition LCD screens (OEV262H high definition LCD monitor; Olympus, Tokyo, Japan).

**Colonoscopy data collection**

Reports of all colonoscopies were generated using the EndoALPHA reporting system (Endobase Olympus, Winter & Ibe GmbH, Hamburg, Germany). This endoscopy reporting system has been described in an earlier publication. In short, this automated and structured colonoscopy reporting system has been developed to generate complete data-sets for the evaluation of current key colonoscopy quality indicators such as cecal intubation rate and adenoma detection rate. For each colonoscopy, the quality of bowel cleansing was rated per colonic segment according to the validated Boston Bowel Preparation Scale. The maximum insertion depth and the outcome of the colonoscopy exam was reported using a synoptic reporting system.

For each lesion, the perceived endoscopic size was reported by the endoscopist. Routinely, a real-time optical diagnosis was reported for all polyps choosing between adenoma, SSP, HP, carcinoma or ‘other’. Selection of any of those options was obligatory. NBI for optical lesion differentiation was used at the discretion of the endoscopist. Confidence levels for histology prediction were not recorded. All lesions were collected in separate jars, enabling per polyp histopathological assessment. All lesions were removed by hot or cold polypectomy, endoscopic mucosal resection or biopsy forceps at the discretion of the endoscopist.

**Histopathology data collection**

All resected lesions were assessed by dedicated gastrointestinal pathologists, based on hematoxylin and eosin staining. In agreement with the 2010 World Health Organization classification system, SSPs...
were defined as serrated polyps with at least two irregular, dilated crypts, including dilatation of the base of the crypts that often have a boot, L- or inverted T-shape. Adenomas were reported, including the presence of histological features of low- or high-grade dysplasia and/or the presence of a villous component. SSPs were reported with the presence or absence of cytological dysplasia. Non-neoplastic histology was defined as normal mucosa, inflammatory, juvenile and hyperplastic histopathology outcomes.

Earlier reports demonstrated that the interobserver agreement for histological differentiation between HPs and SSPs is highly variable among pathologists. To strengthen the accuracy of the HP and SSP diagnosis made by the dedicated gastrointestinal pathologists, a centralized revision of a random sample of 10% of all diminutive HPs and SSPs was performed by an independent expert gastrointestinal pathologist (LK). During the revision of this random sample, the pathologist was blinded to the diagnosis made by the other pathologist, the endoscopic diagnosis of the lesion and patient characteristics.

Study outcomes and statistical analysis

Overall accuracy of optical diagnosis

The accuracy of optical diagnosis of diminutive polyps was based on the optical diagnosis reported by the endoscopists compared with the histopathological diagnosis of the pathologist. For an evaluation of different endoscopist experience, endoscopists were divided in senior gastroenterology fellows and consultant gastroenterologists. Patients were considered eligible for optical diagnosis when at least one diminutive lesion was detected. Patients were excluded when diagnosed with synchronous CRC, newly detected inflammatory bowel disease or polyposis syndrome during the endoscopy. Furthermore, patients in which a piecemeal polypectomy was performed and for which a subsequent scar assessment was needed were excluded. Finally, patients with incomplete colonoscopies due to poor bowel preparation (defined as Boston Bowel Preparation Scale <6) and/or incomplete cecal intubation were also excluded from this analysis.

Surveillance interval agreement

The agreement in the assignment of post-polypectomy surveillance intervals based on optical diagnosis of diminutive polyps was evaluated based on the 2012 USMSTF colorectal cancer surveillance guideline. This is the only international guideline that advises surveillance for SSPs of any size. The predicted surveillance interval, based on optical diagnosis, was determined by using the predicted histology of diminutive polyps combined with the histopathology outcome of polyps sized >5mm. For instance, a 9-mm histological proven tubular adenoma and 2 diminutive polyps endoscopically characterized as adenomas would result in a 3-year surveillance interval prediction. To determine agreement, the predicted surveillance interval was compared with the actual surveillance interval based on histopathology result of all 3 polyps. The predicted surveillance intervals were assigned by the study investigator (JV), and reviewed by two other authors (JIJ, YH) in a blinded and independent
fashion. To resemble previous studies in which optical diagnosis for diminutive SSPs was precluded, we compared surveillance interval agreement for patients with colonoscopies in which diminutive SSPs were detected to patients in whom only diminutive adenomas and/or hyperplastic polyps were detected. If diminutive lesions were lost for histopathology or if no endoscopic prediction was available, patients were excluded.

**Pooled negative predictive values**

The negative predictive value for diminutive neoplastic histology in the recto-sigmoid was calculated by creating 2x2 contingency tables. Neoplastic histology was evaluated by considering both adenomas and SSPs as neoplastic lesions. Negative predictive values were calculated with histology outcome as reference standard. Pooled NPVs per polyp were compared for patients with or without at least one diminutive SSP. All diminutive recto-sigmoid polyps for which a histopathological outcome was predicted were included for this analysis. Polyps were excluded from the analysis if endoscopic predictions or histopathology results were not available.

**Statistical analysis**

For normally distributed or continuous variables, mean and standard deviation (SD) were reported. Medians with an interquartile range were reported for non-normally distributed variables and percentages for categorical variables. Comparisons were made using Chi-square statistics or unpaired t-tests were appropriate. A Cohen’s kappa coefficient was calculated to evaluate the agreement in histopathological diagnosis between the first outcome and expert histology review. The kappa statistic was interpreted according to the recommendations of Landis and Koch. For all comparisons, P values of <0.05 were considered to be statistically significant. All statistical analyses were performed using SPSS statistics version 23 (SPSS, Chicago, Illinois, USA).

**Table 1** | Patient characteristics

<table>
<thead>
<tr>
<th>N = 3,271</th>
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<tr>
<td>Age (years)</td>
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<tr>
<td>Sex (female)</td>
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<tr>
<td>Colonoscopy indication</td>
</tr>
<tr>
<td>Symptoms</td>
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<tr>
<td>Surveillance for familial risk</td>
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<tr>
<td>Screening after positive FIT</td>
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<tr>
<td>Adenoma surveillance</td>
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<tr>
<td>Patients diagnosed with CRC</td>
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<tr>
<td>Patients with at least 1 diminutive polyp</td>
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<td>Patients with at least 1 diminutive SSP</td>
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<td>Total diminutive polyps removed</td>
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RESULTS

Twenty-five gastroenterologists and eleven senior gastroenterology residents performed 3,271 colonoscopies between January 2011 and December 2014. The majority of procedures was performed because of symptoms (Table 1). In 1,337 patients included in our study, 2,853 diminutive lesions were removed (Figure 1). None of the diminutive lesions contained CRC, 65.6% (CI: 63.9 – 67.3) were adenomatous, 7.1% (CI: 6.2 – 8.0) were SSPs and 27.2% (CI: 25.6 – 28.8) were non-neoplastic. At least one diminutive SSP was detected in 156 colonoscopies (4.8%, CI: 4.1 – 5.5). A total of 993 (34.8%, CI: 33.1 – 36.6) diminutive lesions that were removed, were located in the recto-sigmoid.

Figure 1 | Flowchart of included colonoscopies for surveillance interval agreement and negative predictive value calculation

Overall performance of optical diagnosis of diminutive lesions

For 2,785 of 2,853 (97.6%) diminutive lesions, both optical diagnosis and histopathology outcome were available. Optical diagnosis was accurate in 71.9% (CI: 71.6 - 72.2) of diminutive lesions. Adenomas were identified correctly in 80.0% (CI: 78.2 – 81.8) of cases, while optical diagnosis of diminutive SSPs was accurate in only 24.4% (CI: 18.5 – 30.3) and non-neoplastic lesions in 64.9% (CI: 61.5 – 68.3). Diminutive SSPs were incorrectly diagnosed as adenomas and HPs in 34.8% (CI: 28.2 – 41.4) and 41.3% (CI: 34.5 – 48.1), respectively (Figure 2). Overall, the accuracy of optical diagnosis of diminutive polyps did not differ between gastroenterologists and senior gastroenterology residents (71.4% vs. 73.8%, p=0.24).
CHAPTER 8

Table 2 | Performance of surveillance interval agreement in patients with or without diminutive SSPs stratified for residents and gastroenterologists

<table>
<thead>
<tr>
<th>Performance of surveillance interval agreement in patients with or without diminutive SSPs stratified for residents and gastroenterologists</th>
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<tbody>
<tr>
<td>Patients with diminutive and synchronous larger polyps (N = 1,295)</td>
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<tr>
<td>Pooled surveillance interval agreement (%)</td>
</tr>
<tr>
<td>Overall</td>
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<tr>
<td>Residents</td>
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<td>Gastroenterologists</td>
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Surveillance interval agreement

A total of 1,295 patients with at least 1 diminutive polyp were included for the analysis of the surveillance interval agreement (Figure 1). In 12.0% (156 of 1,295) of included patients, a diminutive SSP was detected. Overall, diminutive SSPs determined the advised surveillance interval in 6.9% (CI: 5.3 – 8.3) of recommendations, according to the 2012 USMSTF surveillance guideline. Overall, an optical diagnosis strategy for diminutive polyps would have resulted in an accurate surveillance interval assignment in 75.2% (CI: 72.9 – 77.6) of included patients (Table 2). The calculated surveillance interval agreement was significantly lower for patients with diminutive SSPs compared to those without diminutive SSPs (53.3% vs. 78.1%, P<0.01). Of these 69 patients with diminutive SSPs that would have received an inaccurate surveillance interval based on the optical diagnosis, 60 patients would have received a delayed surveillance of 5-10 years (55.0%) or 10 years (45.0%). For patients with diminutive polyps only (N = 908), surveillance interval agreement for patients with diminutive SSPs was 28.4% compared to 72.3% for those without diminutive SSPs (p<0.01). No difference in surveillance interval agreement was found between residents and gastroenterologists (Table 2).

Figure 2 | Accuracy of optical diagnosis of diminutive sessile serrated polyps stratified for polyp location

Figure 2
Table 3 | Performance of pooled negative predictive value in patients with or without diminutive SSPs stratified for residents and gastroenterologists

<table>
<thead>
<tr>
<th>Performance of pooled negative predictive value (%)</th>
<th>Patients without diminutive SSPs</th>
<th>Patients with diminutive SSPs</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>84.3%</td>
<td>50.0%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Residents</td>
<td>87.5%</td>
<td>46.9%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Gastroenterologists</td>
<td>83.7%</td>
<td>61.5%</td>
<td>&lt;0.01</td>
</tr>
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Trends in optical diagnosis of diminutive polyps over time

Overall accuracy of optical diagnosis of diminutive polyps increased from 62.5% in 2011 to 77.0% in 2014 (p<0.01) (Figure 3). From 2011 to 2014, the rate of accurately identified diminutive SSPs increased from 0% in 2011 to 47.1% in 2014 (p=0.02). The same trend was seen for adenomas, as the accuracy improved from 54.0% in 2011 to 89.3% in 2014 (p<0.01). All these trends were observed for both gastroenterologists as well as residents.

Pathology review

In total, 98 diminutive serrated polyps were reviewed by an independent expert gastrointestinal pathologist. The original diagnosis of those lesions showed 79 HPs and 19 SSPs. Review of those pathology slides by an expert pathologist (LK) resulted in disagreement in 11 of 98 lesions (11.2%, CI: 5.0 – 17.4). Eight of 79 initially diagnosed HPs were reviewed as SSPs. Vice versa, three of 19 SSPs were reviewed as HPs. Polyp histology review was interpreted at substantial agreement as the corresponding kappa statistic was calculated at 0.67 (CI: 0.58 – 0.76).

DISCUSSION

In this study we demonstrated that the endoscopic characterization of diminutive SSPs in daily practice is challenging as only 24.4% of diminutive SSPs were accurately identified. As a result,
incorporating SSPs in an optical diagnosis strategy for diminutive polyps has considerable impact. Diminutive SSPs determined 6.9% (CI: 5.5 – 8.2%) of post-polypectomy surveillance assignments using the 2012 USMTF surveillance guideline. The accuracy of post-polypectomy surveillance assignments based on an optical diagnosis strategy were significantly lower for patients with diminutive SSPs compared to those with diminutive SSPs (53.3% vs. 78.1%, p<0.01). Furthermore, the pooled NPV per polyp for diminutive neoplastic histology in the recto-sigmoid was significantly lower in patients with diminutive SSPs than in patients without diminutive SSPs (50.0% vs 84.3%; p<0.01). Although the overall accuracy of optical diagnosis of diminutive SSPs was only 24.4%, accurate endoscopic characterization of diminutive SSPs improved over time from 0% in 2011 to 47.1% in 2014 (p=0.02).

To our knowledge, this is the first study that evaluated the incorporation of the optical diagnosis of SSPs in a daily colonoscopy practice. This study represents prospectively collected data of a large sample of colonoscopies performed in low-risk patients in an ambulatory endoscopy center. In our outpatient colonoscopy center, the general colonoscopy quality as well as the adenoma and proximal serrated polyp detection rates of our endoscopists are high\textsuperscript{20}. In addition, all lesions were assessed by experienced gastrointestinal pathologists. The prevalence of diminutive SSPs, as reported in this study (7.1%, CI: 6.2 – 8.0) might be perceived as high, but is in line with several recent reports\textsuperscript{12,13}. To further increase credibility, we performed a random blinded pathology review of 10% of diminutive serrated polyps. The resulting kappa statistic (0.67, CI: 0.58 – 0.76) confirmed substantial agreement between the primary histology reading and the blinded expert pathology review, comparable with the agreement among expert pathologists in two earlier reports\textsuperscript{21,22}. A recent study showed that adenomas do not harbor any of the major histological criteria of SSPs, as evaluated by a panel of expert pathologists\textsuperscript{21}. Therefore, substantial variability between pathologists in the differentiation
Optical diagnosis of sessile serrated polyps in daily practice

between serrated polyps and adenomas was not expected and therefore adenomas were not centrally revised.

An expert panel of the American Society of Gastrointestinal Endoscopy (ASGE) has proposed the “Preservation and Incorporation of Valuable endoscopic Innovations” (PIVI) document. In this document, it is stated that only those predictions that are issued with high-confidence should be taken into account when implementing a strategy based on optical diagnosis of diminutive polyps. First, the agreement in recommended surveillance intervals between optical diagnosis and definite histopathology should be at least 90%. Second, to leave non-neoplastic diminutive polyps in the recto-sigmoid in situ, the NPV for adenomatous histology should exceed 90%. As shown in a recently published meta-analysis, histology predictions assessed with high confidence were more likely to be correct. Furthermore, our endoscopists could use NBI at their discretion but the proportion of assessments based on NBI was unknown. Multiple studies have demonstrated that the use of NBI significantly increases the overall performance of optical diagnosis. Both lack of confidence levels and lack of standardized NBI polyp assessment might explain why the performance thresholds for both PIVI thresholds were not reached in our study and are the main limitations of our study. If a high percentage of the incorrectly diagnosed diminutive polyps would have been assessed with low confidence, those polyps would have been sent for pathologic diagnosis. Eventually, the correct surveillance interval could have been assigned or the polyp could not have been left in situ in the recto-sigmoid. Without knowing the confidence levels for each optical diagnosis, our results could be subject to change. However, the aim of the current study was to assess the influence of diminutive SSPs on the overall performance of optical diagnosis strategies in daily practice, rather than to make a formal comparison with the PIVI performance thresholds. The absolute values of performance, as presented in this study should therefore be interpreted with caution.

It is important that SSPs are included in schemes and studies for optical diagnosis for several reasons. Nowadays, SSPs are recognized as precursor lesions for CRC and should be managed accordingly. Second, the presence of a SSP increases the risk of future CRC. Patients should therefore receive appropriate and tailored surveillance. One of the benefits of optical diagnosis is the ability to inform patients of their follow-up at discharge when only diminutive polyps are detected. In our study, only 28.4% of these patients with ≥1 diminutive SSP would have received an accurate surveillance recommendation at discharge. In order to safely implement optical diagnosis, accurate identification of diminutive SSP seems of importance but is dependent on the guideline used in the study. Currently, the 2012 USMSTF surveillance guideline is the only guideline in which surveillance for patients with SSPs of any size is advised. Many gastroenterologists in the United States use the expert panel statement on serrated polyps for surveillance interval recommendations. In the expert panel statement, surveillance for diminutive HPs is only advised when at least 4 diminutive HPs are detected proximal to the sigmoid. Because of this large number of proximal diminutive HPs we think the results will not differ much when using the expert statement. Last, diminutive recto-sigmoid SSPs
that are endoscopically characterized as HPs could remain in situ and potentially lead to interval CRCs. We observed a difference in accurate differentiation between SSPs located proximal to the recto-sigmoid and those located in the recto-sigmoid (29% vs. 5%). Most SSPs are located in the proximal colon and endoscopists might therefore be more aware of SSPs. Likewise, HPs are more prevalent in the distal colon and serrated appearing polyps are more likely to be diagnosed as HPs rather than SSPs. For all these reasons, future prospective studies should focus on evaluation and improvement of the performance of optical diagnosis of all diminutive polyps in general colonoscopy practice, using classification systems that enable the identification of adenomas, HPs as well as SSPs. Only then the performance of endoscopists can be evaluated and compared with the above mentioned PIVI thresholds. For this purpose, our research group has recently proposed the “Workgroup serrAted polyPs and Polyposis” (WASP) classification\textsuperscript{26}. This NBI classification algorithm combines the NICE classification with earlier described specific SSP features. These include a cloud-like surface, dark spots inside the crypts, irregular shape and indistinctive borders. After a brief training the pooled accuracy for all polyps increased significantly, SSPs included. As this study was performed ex-vivo with pre-selected images, future research is needed to verify whether WASP classification can be used for in-vivo optical diagnosis of diminutive polyps.

In our study, only 24.4% (CI: 18.5 – 30.3) of 202 diminutive SSPs were accurately diagnosed based on their endoscopic appearance. More importantly, 41.3% (CI: 34.5 – 48.1) of SSPs were falsely characterized as innocuous HPs. This is in line with a previous post-hoc analysis from a prospective study of NBI characterization by community gastroenterologists in daily practice\textsuperscript{27}. Kumar et al. described that up to one third of SSPs were misclassified as HPs when using the NICE classification\textsuperscript{28}. Of 71 diminutive SSPs, 27 (38%) had all three NICE features of HPs\textsuperscript{27}. Several groups have tried to increase the performance of optical diagnosis of SSPs with variable levels of success\textsuperscript{28-30}. In the largest study to date, Yamada et al. used magnifying NBI to differentiate HPs from SSPs\textsuperscript{31}. In this in-vivo validation study, they described “dilated and branching vessels” as a specific feature of SSPs\textsuperscript{31}. Nevertheless overall accuracy of 62% for differentiating SSPs from HPs was insufficient\textsuperscript{31}.

The results of our study are the first to show that the pooled performance of optical diagnosis for SSPs improves over time. In a similar fashion, accurate endoscopic characterization of diminutive adenomas also increased significantly over time. The improvement for accurate differentiation of diminutive adenomas over time has been observed previously by Ladabaum et al. In their study on the real-time assessments of colonic polyps, the optical diagnosis was predicted by community-based gastroenterologists using NBI\textsuperscript{32}. When comparing the first batch of 20 diminutive polyps per endoscopist with the last batch of 20 diminutive polyps diagnosed during endoscopy, the sensitivity for adenomas increased from 76.6% to 90.2% (p=0.04)\textsuperscript{32}. Although this is speculative, a reason for this gradual improvement over time might be the accumulation of experience in the use of NBI during the time-frame of this study. Besides, the increased awareness of SSPs and their clinical relevance in the last few years could also explain this improvement. Overall, these data might indicate that the PIVI
performance thresholds could potentially be met, including diminutive SSPs, especially when specific
attention and training to accurately diagnose SSPs would be given.

In summary, we determined that the optical diagnosis of SSPs tends to be difficult in daily practice,
decreasing overall endoscopist performance in patients with diminutive SSPs. Although the accuracy
of optical diagnosis for diminutive SSPs improved over time, the overall performance remained
unsatisfactory. Before the paradigm of optical diagnosis can replace histological analysis of diminutive
polyps in daily practice, future studies should use validated classification algorithms for training to
improve the performance of optical diagnosis in general colonoscopy practices.
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