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Clinical validation of the SIMPLE classification for optical diagnosis of colorectal polyps

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ABSTRACT

Background and study aims A novel endoscopic optical diagnosis classification system (SIMPLE) has recently been developed. This study aimed to evaluate the SIMPLE classification in a clinical cohort.

Patients and methods All diminutive and small colorectal polyps found in a cohort of individuals undergoing screening, diagnostic, or surveillance colonoscopies underwent optical diagnosis using image-enhanced endoscopy (IEE) and the SIMPLE classification. The primary outcome was the agreement of surveillance intervals determined by optical diagnosis compared with pathology-based results for diminutive polyps. Secondary outcomes included the negative predictive value (NPV) for rectosigmoid adenomas, the percentage of pathology exams avoided, and the percentage of immediate surveillance interval recommendations. Analysis of optical diagnosis for polyps ≤ 10 mm was also performed.

Results 399 patients (median age 62.6 years; 55.6 % female) were enrolled. For patients with at least one polyp ≤ 5 mm undergoing optical diagnosis, agreement with pathology-based surveillance intervals was 93.5 % (95 % confidence interval [CI] 91.4–95.6). The NPV for rectosigmoid adenomas was 86.7 % (95 %CI 77.5–93.2). When using optical diagnosis, pathology analysis could be avoided in 61.5 % (95 %CI 56.9–66.2) of diminutive polyps, and post-colonoscopy surveillance intervals could be given immediately to 70.9 % (95 %CI 66.5–75.4) of patients. For patients with at least one ≤ 10 mm polyp, agreement with pathology-based surveillance intervals was 92.7 % (95 %CI 89.7–95.1). NPV for rectosigmoid adenomas ≤ 10 mm was 85.1 % (95 %CI CI 76.3–91.6).

Conclusions IEE with the SIMPLE classification achieved the quality benchmark for the resect and discard strategy; however, the NPV for rectosigmoid polyps requires improvement.

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Introduction

Advances in endoscopic video optics have enabled visualization of mucosal and vascular surface patterns of colorectal polyps in a way that allows their pathology to be predicted [1, 2]. This is achieved by using virtual electronic chromoendoscopy modes, such as narrow-band imaging, I-SCAN, and flexible spectral imaging color enhancement [1, 3–9]. These modalities are referred to as image-enhanced endoscopy (IEE), and their use can potentially replace pathology examinations for diminutive (≤ 5 mm) and small (≤ 10 mm) colorectal polyps [10, 11]. Such use of IEE instead of pathology is referred to as the "resect and discard strategy" [12–14]. Clinical implementation of this approach would reduce colonoscopy-associated costs [1, 10].

Optical polyp diagnosis and the "resect and discard strategy" should only be used if certain quality benchmarks with regard to surveillance interval assignment and diagnostic accuracy are met [1, 15]. Several classification systems that use surface, vessel, and lesion patterns to classify colorectal polyps have been developed. However, until recently, no specific classification was available for the novel Pentax Optivista system. This led an expert team to develop a specific classification for this IEE system named the "Simplified Identification Method for Polyp Labeling during Endoscopy (SIMPLE) classification" [5]. The SIMPLE classification includes diagnostic criteria for sessile serrated adenomas (SSA) and has demonstrated a high degree of accuracy in assessing small and diminutive polyps [5]. However, this assessment was only conducted in a setting where experts used photo documentation of polyps for optical diagnosis. Thus, the next logical step is to test the SIMPLE classification in a patient cohort during live endoscopies. The aim of our study, therefore, was to conduct a prospective clinical validation study of the SIMPLE classification.

Patients and methods

Study design

This was a single-center, prospective, clinical study conducted at Montreal University Hospital Center (CHUM) between March 2018 and March 2019. The study was planned and executed as sub-study within a larger randomized controlled trial that was approved by the Montreal University Hospital Research Center (CRCHUM) Institutional Review Board (IRB Nr CER 17.135) and registered at ClinicalTrials.gov (NCT03515343).

Patients

Eligible study patients included adults aged between 45 and 80 years presenting for screening, surveillance, or diagnostic colonoscopy at CHUM. All study patients signed a written informed consent form prior to study participation. Exclusion criteria included known inflammatory bowel disease, active colitis, coagulopathy, familial polyposis syndrome, poor general health (American Society of Anesthesiologists class > 3), and emergency colonoscopies (procedures in the emergency or intensive care unit or patients with active upper or lower gastrointestinal bleeding). All polyps with missing (e. g. specimen not retrieved) or nondefinitive (e. g. non-polyp) pathology and colorectal cancers (CRCs) we excluded from the final analysis.

Procedures

All patients received a standard of care bowel preparation and standard premedication and sedation (e. g. fentanyl and midazolam) for their colonoscopies. Patients underwent colonoscopy using one of two IEE systems – Optivista EPK-i7010 or I-SCAN (both Pentax Medical, Tokyo, Japan) – for optical diagnosis of colorectal polyps. Any polyps detected during the colonoscopy were measured, and their size and anatomical location were documented. All polyps were resected according to standard practice and sent for pathological analysis in order to obtain a reference standard with which to compare optical diagnosis.

Classification and assignment of surveillance intervals

Reference pictures of the SIMPLE classification and criteria were available to the endoscopists during colonoscopy and were shown to the endoscopist upon request during an optical polyp diagnosis. The ten experienced gastroenterologists did not routinely perform optical diagnosis in their endoscopic practice and did not have any specific training in the use of the SIMPLE classification. Prior to the study, all participating endoscopists had completed a 30-minute presentation on optical diagnosis using the Optivista IEE followed by an image-based optical diagnosis test [11, 16].

Polyp morphology was described and classified using the SIMPLE classification (**Supplemental Table 1**). Endoscopists were asked to assign "yes" or "no" to each of the SIMPLE classification criteria when assessing each polyp with IEE, and polyps were then assigned the SIMPLE diagnosis (i. e. hyperplastic polyp, SSA, or adenoma) based on these documented criteria. In cases of unclear diagnosis, a "low confidence" diagnosis was assigned.

Surveillance intervals were calculated for all patients based on the pathology prediction when using the SIMPLE classification and then compared with the surveillance intervals based on pathology results. Surveillance intervals based on pathology results were considered the reference standard. Surveillance intervals for the primary outcome were assigned based on the 2012 US Multi-Society Task Force (USMSTF) guidelines, taking account of first-degree family history of CRC, inadequate preparation, and histopathological results of other polyps detected in the same patient [17, 18]. In cases where polyp pathology was missing, the polyp was excluded from the analysis. Surveillance intervals were only determined for high-confidence optical diagnoses. In cases of a low-confidence optical diagnosis, the pathology result was used to complete surveillance interval assignment.

Outcomes

The primary outcome of the study was the agreement between SIMPLE-based surveillance intervals and pathology-based intervals for patients with polyps 1 to 5 mm. Secondary outcomes were: 1) the proportion of correct optical polyp diagnoses; 2) the specificity, negative predictive value (NPV), and positive

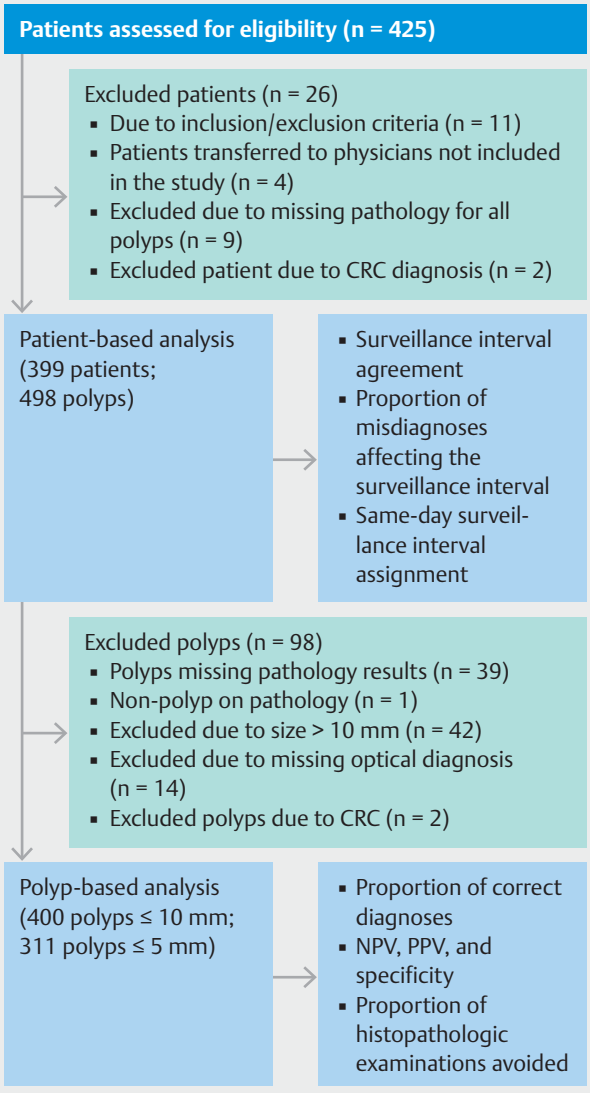
predictive value (PPV) of optical diagnosis for different polyp entities; 3) the proportion of histopathological examinations that could be avoided (i. e. the percentage of polyps where the pathology exams would have been replaced by a high confidence optical diagnosis); 4) the proportion of inaccurate diagnoses affecting surveillance interval assignment; 5) the proportion of patients with same-day surveillance interval assignment. All analyses were conducted for both diminutive (≤ 5 mm) and small (≤ 10 mm) polyps.

The American Society for Gastrointestinal Endoscopy (ASGE) Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) guideline benchmark of ≥ 90 % was used for the agreement between SIMPLE-based surveillance intervals and pathology-based intervals (needed for implementation of 'resect and discard' strategies), and the NPV for diagnosis of rectosigmoid adenomas (needed for implementation of 'diagnose and leave' strategies) [1]. As the USMSTF guideline was revised in 2020, we analyzed surveillance intervals based on both the 2012 and revised 2020 guidelines, as well calculating the percentage of patients affected by the revised guidelines [17, 18].

Sample size and statistical analysis

Using previously published diagnostic accuracy figures for SIMPLE, and adherence to pathology-based surveillance intervals using optical diagnosis, we assumed a 94 % adherence with pathology-based surveillance intervals for SIMPLE [19–21]. To detect a difference with the 90 % ASGE PIVI thresholds at a two-sided alpha of 0.05 and power of 0.8, we needed to include at least 388 patients in our study cohort.

Descriptive analysis with presentation of crude numbers, proportions or medians with interquartile range (IQR) were used to present patient, procedure, and polyp outcomes. Agreement between the optical diagnosis and pathology-based recommendations were presented as proportions with a two-sided 95 % Confidence Interval (CI). For polyp-based outcomes, we computed sensitivity, specificity, NPV, and PPV of each polyp type, along with 95 % 2-sided confidence intervals. All analyses were performed using Stata v.16 (Statacorp, USA).



▶ **Fig. 1** Study enrollment diagram. CRC, colorectal cancer; NPV, negative predictive value; PPV, positive predictive value.

Results

A total of 399 patients (median age 62.6 years; 55.6 % female) with a total of 498 polyps were included. The adenoma detection rate and polyp detection rate in the cohort was 38.8 % and 58.6 %, respectively. The final polyp-based analysis included 311 diminutive polyps and 400 small polyps. Patient inclusions and exclusions are shown in ▶ **Fig. 1**. Detailed information on patient and polyp characteristics is provided in ▶ **Table 1**.

Surveillance agreement

Diminutive polyps (≤ 5 mm)

For the primary outcome, and based on the 2012 USMSTF guidelines, the agreement between the SIMPLE classification-based surveillance intervals and those determined by histopathological results for patients with diminutive polyps was 93.5 % (95 %CI 91.4–95.6). Use of the SIMPLE classification led to shorter surveillance intervals being assigned for 4.8 % (95 %CI 2.9–7.3) of patients and longer surveillance intervals for 1.7 % (95 %CI 0.7–3.6) ▶ **Fig. 2**). Detailed information on correct and incorrectly assigned surveillance intervals is provided in ▶ **Table 2**.

When applying the 2020 guidelines as reference, the agreement between the SIMPLE classification-based surveillance intervals and those determined by histopathological results for patients with diminutive polyps was 99.5 % (95 %CI 98.2–99.9). Use of the SIMPLE classification led to shorter surveillance intervals being assigned for 0.0 % (95 %CI 0.0–0.9) of patients and longer surveillance intervals for 0.5 % (95 %CI 0.1–1.8) compared with the pathology-based assignment (▶ **Fig. 2**, ▶ **Table 2**).

▶ **Table 1** Patient, procedure, and small polyp characteristics.

Age, median (IQR)	62.6 (56.2 – 68.4)
Sex, female (%)	55.6
Adequate bowel preparation[1], (%)	86.5
Polyp detection rate [2] , (%)	58.6
Adenoma detection rate [2] , (%)	38.8
Polyp size, median (IQR)	4.0 (2.7 – 5.0)
Paris Classification, (%)	
▪ Is	94.3
▪ Ip	2.2
▪ ≥IIa	3.5
Segment, (%)	
▪ Proximal to rectosigmoid	59.3
▪ Rectosigmoid	40.7
Polyp type, (%)	
▪ Hyperplastic	42.7
▪ Adenoma[3]	53.8
▪ SSA	3.5
▪ HGD	0.75

IQR, interquartile ratio; SA, sessile serrated adenoma; HGD, high-grade dysplasia.
[1] Defined as a total Boston score ≥ 6 and a score per section ≥ 2.
[2] Defined as percentage of patients where at ≥ 1 polyp/adenoma was found.
[3] Includes tubular, villous, and tubulovillous adenomas.

Small polyps (≤ 10 mm)

Based on the 2012 guidelines, the agreement between the SIMPLE classification-based surveillance intervals and those determined by histopathological results for patients with small polyps was 92.7 % (95 %CI 89.7–95.1). When applying the 2020 guidelines, the agreement was 98.2 % (95 %CI 96.4–99.3) (▶ **Fig. 2**, ▶ **Table 2**).

Effect of incorrect optical diagnosis on surveillance interval assignment

Diminutive polyps (≤ 5 mm)

Optical diagnosis of diminutive polyps was performed in 189 patients out of 399 (47.4 %), 187 of whom (98.9 %) were assigned a surveillance interval in agreement with the pathology-based surveillance interval. A total of 110 patients (58.2 %) had one or more misdiagnosed polyp that did not affect surveillance interval, whereas 2 patients (1.1 %) had at least one misdiagnosis that affected the surveillance interval (▶ **Table 3**). Overall, 77 patients (40.7 %) had a correct diagnosis for all polyps.

For 303 patients out of 399 (75.9 %), assignment of the surveillance interval was determined by factors other than exclusive optical diagnosis. Use of optical diagnosis of diminutive polyps would have allowed 70.9 % (95 %CI 66.5–75.4) of patients to receive an immediate post-colonoscopy surveillance interval recommendation.

Small polyps (≤ 10 mm)

Optical diagnosis of small polyps was performed in 204 of 399 patients (51.1 %), 197 of whom (96.6 %) were assigned a surveillance interval in agreement with the pathology-based surveillance interval. A total of 115 patients (56.4 %) had one or more misdiagnosed polyp that did not affect the surveillance interval, whereas seven patients (3.4 %) had at least one misdiagnosis that affected the surveillance interval (▶ **Table 3**). Overall, 82 patients (40.2 %) had a correct diagnosis for all polyps.

For 274 patients out of 399 (68.7 %), assignment of the surveillance interval was determined by factors other than exclusive optical diagnosis. Use of optical diagnosis of small polyps would have allowed 76.7 % of patients (95 %CI 72.5–80.8) receive an immediate post-colonoscopy surveillance interval recommendation.

Polyp-based analysis

Diminutive polyps (≤ 5 mm)

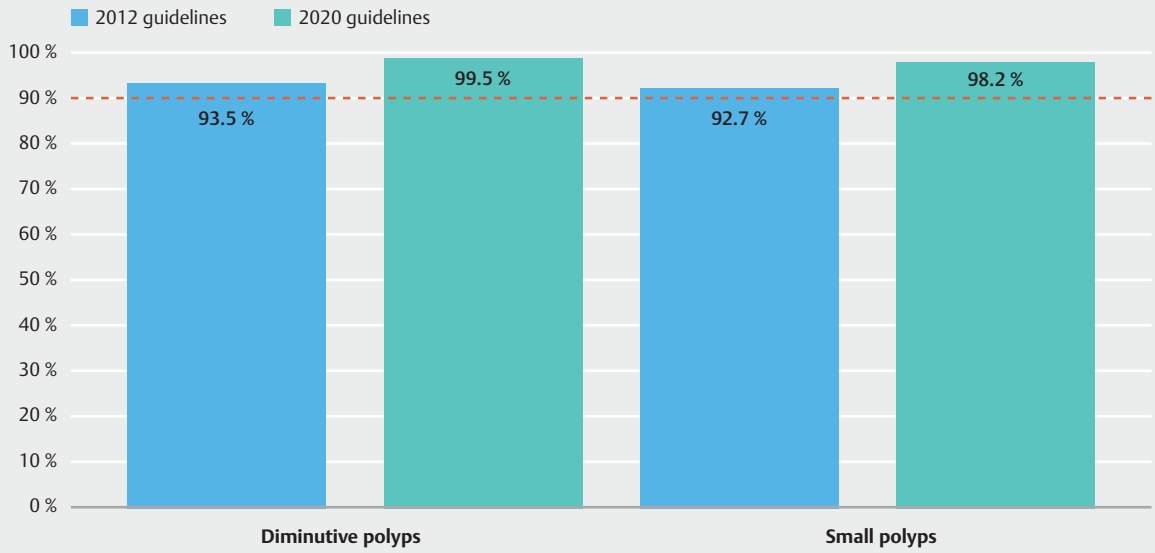
When using the SIMPLE classification for optical diagnosis of diminutive polyps, the rate of high-confidence diagnoses was 79.5 % (221/278). The rate of correct diagnoses for high-confidence optical diagnosis was 67.9 % (95 %CI 61.7–74.0). The general NPV of optical diagnosis for diminutive rectosigmoid adenomatous polyps was 86.7 % (95 %CI 77.5–93.2) (▶ **Table 4**). Use of the SIMPLE classification alone for high-confidence optical diagnosis of diminutive polyps would have resulted in a 61.5 % (95 %CI 56.9–66.2) reduction in pathology examinations.

Small polyps (≤ 10 mm)

When using the SIMPLE classification for optical diagnosis of small polyps, the rate of high-confidence diagnoses was 78.3 % (285/364). The rate of correct diagnoses for high-confidence polyps was 66.7 % (95 %CI 61.2–72.1). The NPV of optical diagnosis for small rectosigmoid adenomas was 85.1 % (95 %CI 76.3–91.6) (▶ **Table 4**). Use of the SIMPLE classification alone for high-confidence optical diagnosis of small polyps would have resulted in a 75.7 % (95 %CI 71.6–79.8) reduction in pathology examinations.

Effect of USMSTF update on surveillance agreement

For agreement between the optical diagnosis surveillance interval and the pathology-based surveillance interval in diminutive polyps, the guideline modifications affected only 24 patients (6.0 %) and there was one (0.3 %) fewer assignment with high discrepancy (i. e., a 10-year interval assigned using optical diagnosis when the pathology-based interval was 1–3 years) when using the 2020 guidelines (▶ **Table 2**). Use of the 2020 guidelines also resulted in five fewer optical diagnosis-based surveillance intervals that were longer (1.3 %) and 19 fewer



Surveillance interval	2012 Guidelines	2020 Guidelines	2012 Guidelines	2020 Guidelines
Correct, n (%) [95% CI]	373 (93.5) [91.4 – 95.6]	397 (99.5) [98.2 – 99.9]	370 (92.7) [89.7 – 95.1]	392 (98.2) [96.4 – 99.3]
Shorter, n (%) [95% CI]	19 (4.8) [2.9 – 7.3]	0 (0.0) [0 – 0.9]*	22 (5.5) [3.5 – 8.2]	2 (0.5) [0.1 – 1.8]
Longer, n (%) [95% CI]	7 (1.7) [0.7 – 3.6]	2 (0.5) [0.1 – 1.8]	7 (1.7) [0.7 – 3.6]	5 (1.2) [0.4 – 2.9]

*One sided 97.5 % confidence interval

▶ **Fig. 2** Surveillance intervals determined with optical diagnosis and the SIMPLE classification compared with histopathology (n = 399 patients).

that were shorter (4.8 %) compared with pathology-based intervals.

For small polyps, application of the 2020 guidelines affected 22 patients (5.5 %), and there was one (0.3 %) with high discrepancy compared with the pathology (▶ **Table 2**). There were two fewer assignments (0.5 %) that were longer and 20 fewer assignments (5.0 %) that were shorter.

Discussion

For diminutive and small colorectal polyps, the agreement between optical diagnosis using the SIMPLE classification and histopathology-based surveillance intervals was above the ≥ 90 % quality benchmark recommended by the ASGE [1]. This quality benchmark was reached regardless of whether the 2012 or 2020 USMSTF guidelines were used as the reference standard to assign surveillance intervals [17, 22].

The main differences in the 2020 recommendations compared with the 2012 guidelines include modified surveillance intervals for patients with serrated polyps, three to four adenomas < 10 mm, and > 10 adenomas. In general, patients with serrated polyps will be assigned longer surveillance intervals with the 2020 guidelines compared with 2012 guidelines. Thus, application of the SIMPLE classification for optical diagnosis of small and diminutive polyps using Optivista or I-SCAN IEE in combination with the 2020 USMFT guidelines becomes even more feasible. We found a 67.9 % accuracy of optical diagnosis made with high confidence for diminutive polyps. The initial validation study by Iacucci et al. showed a higher accuracy of 94 % [5]; however, the study was conducted in a setting where experts used the classification to assign polyp diagnosis based on images [5]. Our lower accuracy is most likely explained by the fact that a nonexpert group (not having previously used SIMPLE) performed optical diagnosis during live endoscopies. Breakdown of our endoscopist performance showed high heterogeneity in key quality indicators and diagnostic accuracy with all but one meeting quality indicator minimums for ADR, however the best performing endoscopist was only able to predict correct histology in 80 % of cases. Iacucci et al. showed that training increased accuracy of expert endoscopists from 83 % to 94 %. Hence, with appropriate training using a dedicated training module for the IEE platform and classification to be used, the accuracy of using the SIMPLE classification in clinical setting could potentially be further improved. In our study, the rectosigmoid NPV for SIMPLE optical diagnosis was 85.1 % and 86.7 % for diminutive and small rectosigmoid adenomas, respectively, which did not reach the ≥ 90 % quality benchmark recommended by the PIVI guidelines. Similarly, the rectosigmoid NPV of 89 % described by Iacucci et al. also fell short of the ≥ 90 % PIVI benchmark [1, 5]. More development and research is required before the system can be used routinely for the "diagnose and leave" strategy [1].

Use of IEE and the SIMPLE classification in routine clinical practice would allow surveillance intervals to be assigned immediately for most patients. We found that when using optical diagnosis of diminutive polyps, 70.9 % of patients could be giv-

▶ **Table 2** Surveillance interval agreement between optical diagnosis of small and diminutive polyps using the SIMPLE classification and the pathology-based reference standard, based on 2012 and 2020 US Multi-Society Task Force guidelines[1]

Optical diagnosis	Pathology-based reference standard				Total, n
	1 year	3 years	5 years	10 years	
Polyps ≤ 5 mm					
2012 guidelines					
▪ 1 year	**52**	0	0	0	52
▪ 3 years	0	**53**	1	0	54
▪ 5 years	0	3	**78**	18	99
▪ 10 years	0	2	2	**190**	194
▪ Total, n	52	58	81	208	399
2020 guidelines					
▪ 1 year	**52**	0	0	0	52
▪ 3 years	0	**47**	0	0	47
▪ 5 years	0	0	**87**	0	87
▪ 10 years	0	1	1	**211**	213
▪ Total, n	52	48	88	211	399
Polyps ≤ 10 mm					
2012					
▪ 1 year	**52**	0	0	0	52
▪ 3 years	0	**52**	1	0	53
▪ 5 years	0	5	**79**	21	105
▪ 10 years	0	1	1	**187**	189
▪ Total, n	52	58	81	208	399
2020					
▪ 1 year	**52**	0	0	0	52
▪ 3 years	0	**46**	0	0	46
▪ 5 years	0	0	**85**	2	87
▪ 10 years	0	2	3	**209**	214
▪ Total, n	52	48	88	211	399

[1] Bold cells show concordant surveillance intervals.

▶ **Table 3** Optical diagnosis of small and diminutive polyps using the SIMPLE classification according to the 2020 US Multi-Society Task Force guidelines.

	Patients, n (%)	
	Diminutive polyps	Small polyps
Optical diagnosis attempted	189/399 (47.4)	204/399 (51.1)
Surveillance interval in agreement with histopathology	187 (98.9)	197 (96.6)
≥ 1 misdiagnosed polyp that did not affect surveillance interval	110 (58.2)	115 (56.4)
≥ 1 misdiagnosed polyp that affected surveillance interval	2 (1.1)	7 (3.4)
All polyps diagnosed correctly	77 (40.7)	82 (40.2)

▶ **Table 4** Sensitivity, specificity, negative and positive predictive values for small and diminutive polyps according to optical diagnosis.[1]

SIMPLE diagnosis	Accuracy of optical diagnosis, n/N (%) [95%CI]				
	Sensitivity	Specificity	NPV	PPV	Rectosigmoid NPV[2]
Diminutive polyps					
▪ Hyperplastic polyps	98/126 (77.8) [69.5–84.7]	76/125 (60.8) [51.7–69.4]	76/104 (73.1) [63.5–81.3]	98/147 (66.7) [58.4–74.2]	–
▪ Adenomas	66/120 (55.0) [45.7–64.1]	121/131 (92.4) [86.4–96.3]	121/175 (69.1) [61.7–75.9]	66/76 (86.8) [77.1–93.5]	72/83 (86.7) [77.5–93.2]
▪ Sessile serrated adenomas	2/5 (40.0) [0.5–85.3]	220/246 (89.4) [84.9–93.0]	220/223 (98.7) [96.1–99.7]	2/28 (7.1) [0.9–23.5]	–
Small polyps					
▪ Hyperplastic polyps	107/144 (74.3) [66.3–81.2]	118/173 (68.2) [60.7–75.1]	118/155 (76.1) [68.6–82.6]	107/162 (66.0) [58.2–73.3]	–
▪ Adenomas	91/161 (56.5) [48.5–64.3]	145/156 (92.9) [87.7–96.4]	145/215 (67.4) [60.7–73.7]	91/102 (89.2) [81.5–94.5]	80/94 (85.1) [76.3–91.6]
▪ Sessile serrated adenomas	8/12 (66.7) [34.9–90.1]	260/305 (85.2) [80.8–89.0]	260/264 (98.5) [96.2–99.6]	8/53 (15.1) [6.7–27.6]	–

NPV, negative predictive value; PPV, positive predictive value.
[1] For high-confidence diagnoses.
[2] Adenomas and sessile serrated adenomas were considered to be equivalent.

en an immediate surveillance interval recommendation. When using optical diagnosis for diminutive and small polyps, this is possible for 76.7% of patients. In contrast, when using pathology diagnosis, immediate surveillance interval assignment is only possible for 46.3% of patients. These results strengthen the positive impact of optical diagnosis and the support for implementation of the "resect and discard strategy," both in terms of cost-effectiveness of the procedure (estimated annual cost savings of US$ 1 billion dollars in the United States [10]) and by making it possible to provide the majority of patients with immediate surveillance interval recommendations without waiting for pathology results [1, 10]. Furthermore, our current practice of waiting and assigning surveillance intervals based on pathology results is far from perfect. A recent meta-analysis investigating the concordance of pathology-based surveillance intervals with published guidelines showed that for the North American guidelines, the concordance was only 44.7% for low-risk adenomas and 37.1% for hyperplastic polyps [23]. Thus, using optical diagnosis instead of pathology for diminutive polyps could potentially improve surveillance interval assignment given that pathology-based assignment in clinical practice does not always adhere to the guidelines.

The low incidence of high-grade dysplasia (HGD) and villous polyp features found in diminutive polyps suggests that optical diagnosis can most likely be implemented safely despite the very low possibility that an incorrect diagnosis will delay surveillance. In our study, we found 0% and 0.07% cases of HGD and 0.9% and 1.3% of villous adenomas among diminutive and small polyps, respectively; therefore, the risk of missing a cancer among diminutive polyps seems negligibly low. As advanced pathology is so rare among diminutive polyps, the use of optical diagnosis is most likely a safe approach [24]. More research is needed to determine whether optical diagnosis can be extended to small polyps; however, a recent publication yielded good outcomes similar to our cohort [25]. In our study, the rate of advanced pathology among polyps 6 to 10 mm was 2.8% for HGD, 0.9% for traditional serrated adenoma, and 2.8% for villous adenomas and tubulovillous pathology. One study found that when optical diagnosis was extended to small polyps, there were a higher reduction in histology (45.9% vs. 30.5%) and a higher proportion of immediate surveillance assignment (15.6% vs. 7.3%) compared with optical diagnosis in only diminutive polyps; however, T1 cancer was diagnosed in 0.33% of small polyps and 71% of these would have been discarded without pathological examination [25]. A recent study including 2 532 298 colonoscopies showed that the best predictor of advanced pathology is indeed a larger polyp size [26]. The concern with extending the use of optical diagnosis to polyps 6–10 mm is the increasing risk that advanced pathology or even cancer might be present, and the absence of pathological assessment might result in delayed treatment and follow-up.

Another crucial factor for clinical implementation of the resect and discard strategy is incomplete polyp resection. Reliable complete polyp resection will further mitigate the risks associated with optical polyp diagnosis, such as the removal of a polyp with advanced pathology and delays to surveillance due to an incorrect diagnosis. Unfortunately, a recent meta-analysis showed that the incomplete resection rate was 15.9% for polyps 1 to 10 mm, 9.9% for forceps removal of polyps 1 to 5 mm, and 4.4% for snare polypectomy of polyps 1 to 5 mm [27]. This suggests the use of cold snare polypectomy in conjunction with optical diagnosis for diminutive polyps.

Many recent guidelines tend to recommend 10-year surveillance intervals for patients with 1–2 tubular adenomas, hyper-

plastic polyps, or normal colonoscopies [17, 18, 28]. In this context, it becomes often unnecessary to know the optical polyp diagnosis as 10 years will often be an appropriate surveillance interval independent of optical or pathology-based diagnosis. Indeed, a recent study showed that an inaccurate optical diagnosis does not always lead to an incorrectly assigned surveillance interval. A significant proportion of patients may be assigned correct surveillance intervals despite one or more incorrect optical polyp diagnoses [29]. However, the problem remains that it would be preferable to reliably identify polyps with villous or HGD features, and the SIMPLE optical diagnosis classification only includes criteria for identification of serrated polyps but not sub-entities such as distinction of traditional serrated adenoma from SSA or high-grade from low grade dysplasia. The development of computer-aided diagnosis for colonoscopy could help nonexpert endoscopists to accurately assess polyps. Gross et al. showed an accuracy of 93.1 % for computer-aided diagnosis, which was superior to that for nonexperts; however, computer-aided diagnosis is still in its nascent stage and many years away from routine clinical implementation [30].

Some strengths and limitations of our study should be mentioned. This is the first clinical validation study of the SIMPLE classification. The prospective design of the study allowed high-quality data to be collected for a clinical cohort of patients. In addition, multiple endoscopists were involved in the study allowing for better external validity of the results. The heterogeneous performance of endoscopists with regards to key quality indicators also improves the generalizability to real-life performance in other endoscopic practices. Study limitations include the moderate sample size, and further studies should be performed in larger cohorts. Second, although this was a multi-endoscopist study, the number of optical diagnoses was not balanced among the endoscopists. This limits our ability to evaluate the influence of different training levels and interrater variability among endoscopist when using the classification. Third, no specific training module for I-SCAN or Optivista IEE is currently available. The training module that was used in the study was based on narrow-band imaging pictures, and a training module specific to I-SCAN/Optivista with the SIMPLE classification could improve the results. This is especially important as the NPV to diagnose rectosigmoid polyps did not achieve the recommended benchmark for the "diagnose and leave" strategy. Another limitation of this study is the overall low number of SSA/P which limits interpretation of results for these polyps. Colon segment was determined by endoscopists which could have led to errors in identifying specific segments; however, this did not affect our study's main outcomes.

Conclusions

In conclusion, results from this first clinical validation demonstrated that optical polyp diagnosis reaches the required benchmarks for surveillance interval assignment when the SIMPLE classification was used in a certain set of conditions. Future larger studies should compare the SIMPLE classification with other classification systems, and specific training modules for use of the SIMPLE classification with IEE platforms should be developed in order to further increase optical diagnosis accuracy and NPV for rectosigmoid polyps.

Competing interests

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