Accuracy in optical diagnosis for polyps between 5 and 15 mm and its implications on surveillance. A prospective, multicenter study. (POPS study)

Eduardo Redondo-Cerezo[1] · Clara Heredia-Carrasco[1] · Carlos Alegría-Motte[2] · Antonio Caballero-Mateos[2] · Francisco Vadillo-Calles[3] · Eva Julissa Ortega-Suazo[1] · Virgilio Martos-Ruiz[2] · Jose Luis Ariza-Fernández[4] · Elisabet López-González[5] · Juan Gabriel Martínez-Cara[1] · Francisco Valverde-Lopez[1] · Mercedes López de Hierro[1] · Damián Sánchez-Capilla[1] · Javier Luis López-Hidalgo[6] · Rita Jimenez-Rosales[1]

Abstract

Background and aims Polyps histology and diameter up to 1 cm determine whether a patient needs a colonoscopy after 3 years or less, or far ahead. Endoscopists' and pathologists' size estimations can be imprecise. Our aim was to assess endoscopist ability to correctly recommend surveillance colonoscopies for patients with polyps around the 10 mm threshold, based on its endoscopic sizing and optical diagnosis by NBI.

Methods NBI-assisted diagnosis and endoscopist estimation of polyp size were compared with reference standard, considering this as the post resection polyp measurements by the nurse assistant and the pathologic results, in a prospective, multicenter, real life study, that recruited adults undergoing colonoscopy in five hospitals. By comparing the endoscopic and pathologist size estimation, with polyps' measurement after resection, and optical and histological diagnoses in patients with polyps between 5 and 15 mm, sensitivity was assessed at the patient level by means of two characteristics: the presence of adenoma, and the surveillance interval. Surveillance intervals were established by the endoscopist, based on optical diagnosis, and by another gastroenterologist, grounded on the pathologic report. Determinants of accuracy were explored at the polyp level.

Results 532 polyps were resected in 451 patients. Size estimation was *more precise* for the endoscopist. Endoscopist sensitivity for the presence of adenoma or carcinoma was 98.7%. Considering the presence of high-grade dysplasia or cancer, sensitivity was 82.6% for the endoscopic optical diagnosis. Sensitivity for a correct 3-year surveillance interval was 91.5%, specificity 82.3%, with a PPV of 93.2% and NPV of 78.5% for the endoscopist. 6.51% of patients would have had their follow-up colonoscopy delayed, whereas 22 (4.8%) would have it been performed earlier, had endoscopist recommendations been followed.

Conclusion Our study observes that NBI optical diagnosis can be recommended in routine practice to establish surveillance intervals for polyps between 5 and 15 mm.

Clinical Trials Registration Number: NCT04232176

Keywords Adenomatous polyps · Colon neoplasms · Colonoscopy · NBI · Small polyps

✉ Eduardo Redondo-Cerezo
eredondoc@gmail.com

1 Endoscopy Unit, Department of Gastroenterology and Hepatology, "Virgen de Las Nieves" University Hospital, Avenida de las Fuerzas Armadas 2, 18014 Granada, Spain

2 Internal Medicine Service, Hospital Comarcal "Santa Ana", Motril, Spain

3 Internal Medicine Service, Hospital Comarcal "Virgen del Puerto", Plasencia, Spain

4 Gastroenterology Service, Hospital Comarcal de Poniente, El Ejido, Spain

5 Internal Medicine Service, Hospital Comarcal "Vega Baja", Orihuela, Spain

6 Pathology Department, "Virgen de Las Nieves" University Hospital, Granada, Spain

Endoscopic resection of adenomatous colorectal polyps has demonstrated to reduce mortality from cancer of the colorectum [1]. Traditionally, the gold standard for the diagnosis of a colorectal adenoma is ex vivo histopathologic microscopy; however, 43% of resected polyps are identified as benign, and up to 1% have already undergone malignant transformation [2]. Indeed, some reports have observed that the pathologic diagnosis is not accurate in up to 10% of cases, when they are reviewed by a second expert pathologist [3, 4].

The possibility of a purely optical biopsy has widely been addressed, and even the AGSE established thresholds for adopting real-time endoscopic assessment of the histology of diminutive colorectal polyps, with the main purposes of reducing the total costs of colonoscopy, without affecting its efficacy or diagnostic accuracy, and shifting towards a paradigm of 'diagnosing and leave', in which the endoscopist leaves in situ diminutive hyperplastic colorectal polyps, or a 'resect and discard' strategy, in which polyps are resected after endoscopic assessment of histology [5].

However, being those goals of great interest, there is an essential threshold in this setting that has not been addressed in depth. A single adenoma of 1 cm or bigger needs a 3 years follow-up colonoscopy, whereas 4 or fewer adenomas smaller than 1 cm could undergo colonoscopy after 7–10 years [6]. Moreover, most of the recent studies about polyps usually lack information about how polyps were measured, assuming that the endoscopist is precise when measuring polyps optically, and focusing the study just on polyps' histological nature. When deciding whether the patients will be rescheduled for a colonoscopy in 3 or more years, size matters and has an impact on patients and costs. Previous evidence has shown that visual size estimation is suboptimal, even with the open forceps method, usually with a tendency to overestimate polyp size [7–11]. To avoid this, many authors and endoscopists consider the pathologic measurements as the gold standard, although those sizes are sometimes a mere estimation or approximate. Even more, it has been observed a retraction of the polyps size of 12–18% after formalin fixation [7].

Although many papers have focused on the ability of the endoscopist to accurately diagnose diminutive colorectal polyps, no previous research has focused on the 1 cm threshold in polyp diagnosis. The 1 cm threshold implies a significant difference regarding the endoscopic unit workload, being accuracy essential to correctly categorize patients. More, a correct recommendation from the endoscopy suite, immediately after the procedure, might lead to the avoidance of a subsequent outpatient visit relieving GI office workload and eluding patients' unnecessary visits. A quick check to the pathologic diagnosis, which might be highly concordant with endoscopic evaluation would be sufficient in most cases. A small proportion of patients would need to be about a change in the previous endoscopic diagnosis.

For this purpose, we designed a prospective multicenter study on patients submitted for colonoscopy, to assess endoscopists ability to correctly perform an optical NBI diagnosis of polyps between 5 and 15 mm. *We chose this size interval intending to include all the lesions of 10 mm, which size might be underestimated or overestimated, provided that the inclusion in the study was made after endoscopist sizing estimation.* The main outcomes of the study were precision on optical diagnosis, size estimation, and recommendations regarding the surveillance when compared to the pathologic gold standard.

Methods

Study design

We performed a prospective, multicenter, observational study at five institutions in Spain involving patients who had been sent for a colonoscopy for different indications, including CCR screening program. All colonoscopies were performed by gastroenterologists who had been trained as endoscopists in a single academic institution, with an 'in vivo' dedicated training program in NBI. All of them had performed at least 100 complete average risk screening colonoscopies with adequate bowel preparation, before the beginning of patients' enrollment. The study period extended from December 2019 to October 2020.

Patients selection

Inclusion in the study was offered to all the patients older than 18 years old, with a colonic polyp with a size between 5 and 15 mm, as estimated by the endoscopist, who accepted to be included in the study and signed the informed consent were included. All patients with inadequate bowel preparation or incomplete colonoscopy were excluded from the study. We also excluded individuals with polyps that could not be resected or were not recovered for histological analysis, with polyps that were resected by piecemeal resection, or patients who had polyposis syndromes, in which the histology of the polyps is known in advance (Fig. 1).

During the endoscopic procedure, the endoscopist performed white light examination and real-time NBI optical diagnosis, and estimated the polyp size. A nurse assistant took note about location, size, NBI-NICE o WASP criteria and Paris Classification before the retrieval of the endoscope. Afterwards, the polyps were recovered avoiding aspiration through the biopsy channel, *spread out* on a cellulose layer and *were measured with an analogical caliper* and registered by the nurse assistant *before introducing them in a formalin container*. Subsequently, the resected specimens were processed into the Pathology department as usual. All

Fig. 1 Patient's recruitment
flow diagram
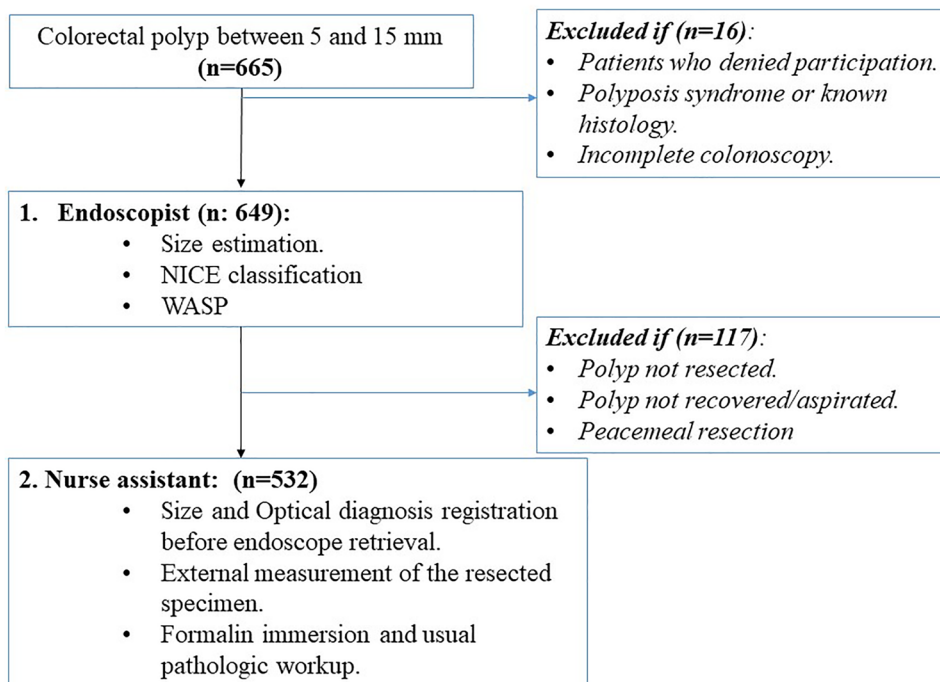
polyps were resected by snare polypectomy, with electrosurgical power or cold-snare polypectomy.

Adequacy of bowel preparation by BBPS, retrieval time, date of the procedure, name of the endoscopist, hospital setting and patients' demographic data were also recorded.

Every colonoscopy was performed with Olympus CF-H190L colonoscopes and Evis-Exera III processors.

After the procedure, in view of patients' characteristics and optical diagnosis, the endoscopist stated a follow-up interval in accordance with the available guidelines [6, 12]. At the time of the inclusion of the histologic results in the database, a follow-up interval was established relying on the pathologic results.

Pathologic samples were studied by pathologists with expertise in Gastroenterology, in a centralized lab that usually receive samples from three of the five centers involved. Being a real life study, we did not include in the requirements two pathologists for every sample, but an external expert gastrointestinal pathologist performed random revisions of approximately 20% of the samples.

Definitions

Advanced adenoma included adenoma ≥ 1 cm, tubulovillous or villous adenomas, and adenomatous polyps with high-grade dysplasia. Adenomatous specimens included tubular, tubulovillous, or villous adenomas and adenomatous polyps with high-grade dysplasia. Clinically

significant serrated polyps (SSPs) were defined as any sessile serrated polyp/adenoma, traditional serrated polyp, hyperplastic polyps ≥ 1 cm anywhere in the colon, or hyperplastic polyp ≥ 5 mm located proximally to the sigmoid colon. We chose this definition based on the expert consensus on serrated polyp by Rex et al. [13], which recommended shorter screening intervals for any hyperplastic polyp > 5 mm located proximally to the sigmoid colon.

Polyps were classified under the *NBI International Colorectal Endoscopic Classification* (NICE), as well as with the *Workgroup on serrAted PolypS and Polyposis* (WASP) to avoid NICE classification failure to detect serrated polyps [14, 15].

En-block resection was stated when the polyp was completely resected in a single time and the endoscopist had no doubts about left polyp tissue in the resection site. If the endoscopist did not resect the whole polyp in a single specimen, or had doubts regarding the persistence of adenomatous tissue in the site of resection, requiring additional treatment, we considered it a piecemeal resection and excluded the patient from the analysis.

Low-risk adenoma (LRA) was considered when patients had 1–2 tubular adenomas < 10 mm in diameter. High-risk adenoma (HRA) refers to patients with tubular adenoma ≥ 10 mm, 3 or more adenomas, adenoma with villous histology, or high-grade dysplasia (HGD). Advanced neoplasia is defined as adenoma with size ≥ 10 mm, villous histology, or HGD [12].

Data collection

Data were initially documented on a data sheet in the endoscopy suite, and completed with demographic information including patient sex and age. Data regarding polyp size, location within the colon, optical diagnosis, resection technique, complications and polyp size immediately after resection were also collected at the patient's bedside, still in the endoscopy suite.

The database was completed after receiving the definitive pathologic report, with the estimated size by the pathologist, histologic diagnosis, and follow-up schedule in view of the pathologic results.

Additional information about the endoscopist who performed the colonoscopy, participant hospital, BBPS score, type of resection and snares, complications, patients' comorbidities and treatments was collected.

Outcome definition

Polyp based analysis was made in what referred to size and optical diagnosis. Patient's based analysis was performed when making follow-up recommendations.

The first outcome is the accuracy of the endoscopist to provide the patients with correct recommendations about subsequent follow-up colonoscopies after the procedure. These recommendations are based on two main characteristics: Optical diagnosis and size estimation. Regarding optical diagnosis, pathologic diagnosis was considered the gold standard, whereas the post-resection measurement of the polyp before fixation was considered the gold standard for polyp size estimation.

Time interval to the following colonoscopy was calculated for the endoscopist diagnosis and the pathologic diagnosis, following available guidelines [6, 12]. The endoscopist follow-up interval was established immediately after the colonoscopy, taking into account optical diagnosis and endoscopist sizing. Pathologic follow-up was stated with the pathologic report, considering pathologic sizing and diagnosis. Finally, actual (reference standard) surveillance recommendations were established considering post-resection measurements by the nurse assistant and histologic results.

Additionally, we calculated the diagnosis accuracy of the endoscopist in the different settings studied and overall.

When a colorectal carcinoma or a large polyp (> 15 mm) was found, the additional polyps observed, that had the criteria for their inclusion in the study, were considered for the polyp-based analysis, but the follow up recommendations were not considered for analysis, and the patient was referred for surgical treatment.

Sample size estimation

The study was designed to estimate a test sensitivity of 95%, based on a sample size of 302 polyps assuming a concordance in endoscopic and pathologic recommendations above 90%, and 5% precision (d^2).

Statistical analysis

Categorical variables were described as number and percentage, and qualitative variables as mean (standard deviation) or median (interquartile range) depending on their parametricity as studied previously with the Kolmogoronov-Smirnov test and graphic analysis of the variables.

For mean size comparisons we used the Wilcoxon Rank Sum Test, studying correlations between different measurements by means of the Spearman test. Precision with respect to the beforehand established as the real diameter, the post-resection sizing, was studied with Bland–Altman plots, which give us graphically the mean bias ± SD between actual (real) an endoscopist or pathologist estimations.

When addressing optical diagnosis and follow-up recommendations, we established as the gold standard the pathologic diagnosis, and recommendations based on the after resection diameter (real diameter), and on pathologic diagnosis for follow-up intervals calculations [7]. Thereafter, we calculated in tables 2×2 Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and overall accuracy. More, to study agreement between each endoscopist or pathologist reports and actual surveillance recommendations we used also the weighted kappa coefficient and the contingency coefficient C.

Missing data regarding polyps histology were excluded from the final analysis.

Ethics

The study protocol was approved by the Human Research Ethics Committee of 'Virgen de las Nieves' University Hospital, the 11th of December 2019. Written informed consent was required to every patient included in the study. Indeed, the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in a prior approval by the institution's human research committee.

Results

Patients characteristics

532 polyps were resected in 451 patients submitted to our endoscopy units during the study period. Patients' mean age was 64 years (69.2% male). 85% were ASA I or II, being the

leading indication for colonoscopy a positive occult blood test (47.4%) followed by a follow-up colonoscopy after colorectal cancer resection or a previous polypectomy. Most of our patients (80%) had no previous history of colorectal cancer (CRC), 6.8% had suffered colorectal cancer, 5.1% a high-risk adenoma, 4.7% a low-risk adenoma and 2.6% a CRC plus an adenoma. 75% of patients had no previous colonoscopy, whereas 25% had undergone at least one previous procedure,

Colonoscopy characteristics

Colonoscopies were performed with Olympus Exera III platform and H190L colonoscopes. Cecal intubation was achieved in 98% of procedures, a good or excellent colonic cleansing (Boston Score ≥ 6) was achieved in 91%.

Polyp characteristics

36.1% of polyps were located in the right colon, with sigmoid as the main location within the colon (29%) (Table 1). Most of the polyps were sessile (Paris 0-Is; 58%), pedunculated (0-Ip, 15%) or subpedunculated (0-Isp; 13.6%) 81.6% of the polyps were considered NICE 2, 14.3% NICE 1 and only 3.8% NICE 3. 8% were found to have WASP criteria. 10 mm or 15 mm snares were used in 84% of patients as the main resection tool, and cold snare polypectomy was performed in 45% of cases, with submucosal injection for endoscopic mucosal resection in 25%. Added to the polyps included in the study, additional large polyps (> 15 mm) or CRC were found in 23% of patients. Endoscopists optical diagnosis and Pathologic diagnosis are shown in Table 1. Dysplasia of any grade was found in 6% of all resected polyps. Median polyps size was 7 mm for the endoscopist, in the after resection on site measurement and in the Pathology laboratory. Complications were observed in 9 patients (1.7%), 8 immediate minor bleeding, self-contained or treated with hemoclips, and 1 perforation endoscopically resolved by clipping. All of our patients could be discharged the same day with no further need for admission or endoscopic therapy.
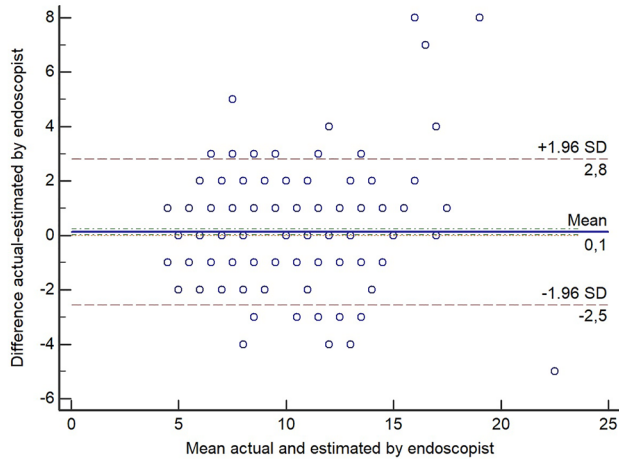
Size measurement

We found significant differences between endoscopist size estimation and actual size measurement (7.71 ± 3.0 mm vs. 7.85 ± 3.07 mm; $p = 0.018$), as well as between pathologist sizing and actual size measurement (7.39 ± 3.38 mm vs. 7.85 ± 3.07 mm; $p < 0.0001$). Subsequently, we explored the correlation between the endoscopist size estimation and actual size (Spearman coefficient: 0.88; $p < 0.0001$) and

Table 1 Patients and polyps characteristics

Polyps	N	Percent (%)
Small (< 10 mm)	377	71
Large (≥ 10 mm)	154	29
Larger polyps (> 15 mm)	113	21.4
Colorectal cancer	10	1.9
NICE 1	76	14.3
NICE 2	434	81.6
NICE 3	20	3.8
Polyp location		
Cecum	47	8.8
Ascendent	82	15.4
Hepatic flexure	28	5.3
Transverse proximal	35	6.6
Transverse médium	23	4.3
Transverse distal	25	4.7
Splenic flexure	27	5.1
Descendent	62	11.7
Sigmoid	153	28.8
Rectum	50	9.4
Cononoscopy		
Incomplete	1.5%	
Boston Score > 6	92%	484
Pathologic diagnosis		
Hyperplastic	65	12.3
Tubular adenoma	354	66.6
Tubulo-Villous	60	11.3
Serrated adenoma	15	2.8
HGD	22	4.2
Submucosal carcinoma on adenoma	6	1.2
Mixed serrated/adenoma	5	0.9
Patients		
Age (median, IQR)	63	51–73
Gender (% female)	164	36.3
Smoker		
Alcohol use		
ASA Score (%3–4)	76	14.3
Medications		
NSAIDS	13	2.5
Aspirin	96	18
Statin	133	25
Anticoagulants	29	5.9
Primary reason for colonoscopy		
BCSP	252	47.4
Rectal bleeding	38	7.1
Change in bowel habit	37	7
Iron deficiency anemia	102	19.1
Previous CRC/polyps	103	19.4
Previous colonoscopy (10 yrs)	132	24.8
CRC	36	6.8
High risk adenoma	27	5.1
Low risk adenoma	25	4.7

Table 1 (continued)

Polyps	N	Percent (%)
CRC + adenoma	14	2.6
Other (Hyperplastic)	1	0.2

Fig. 2 Endoscopist size estimation vs. real diameter. Bland–Altman plot

Fig. 3 Pathologist size measurement vs. real diameter. Bland–Altman plot

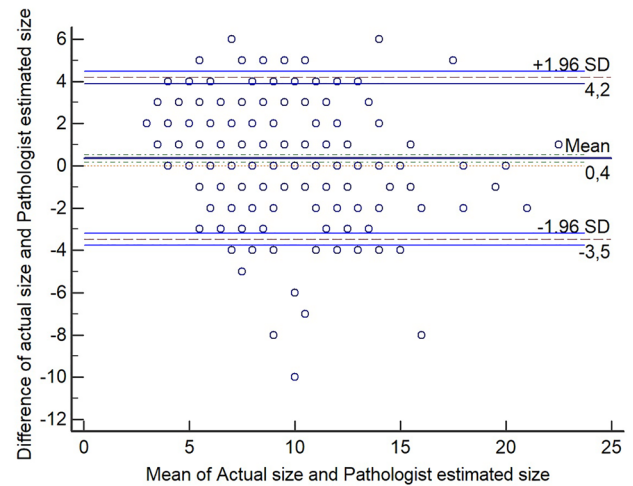the pathologist measurement (Spearman coefficient: 0.75; $p < 0.0001$).

We categorized polyps' sizes above or below the threshold of 10 mm, according to the polypectomy revision schedule and our study hypothesis, with an analysis of the kappa coefficient between actual size and endoscopist estimation (Kappa = 0,85; $p < 0.0001$) and pathologist measurement (Kappa = 0,68; $p < 0.0001$).

Finally, the Bland–Altman plot showed the mean bias ± SD between actual and endoscopist estimated sizes as 0.1 ± 1.33 mm, and the limits of agreement were − 2.5 mm and 2.8 mm (Fig. 2). With regard to actual vs pathologist measurements the mean bias ± SD was 0.4 ± 1.94 mm, being the limits of agreement -3.5 mm and 4.2 mm (Fig. 3).

Optical diagnosis

We found a majority of NICE 2 polyps (82%) followed by NICE 1 (14%) and NICE 3 (4%). 8% had WASP criteria for serrated histology.

Differentiation between adenoma or carcinoma vs. hyperplastic polyps was studied for endoscopy, comparing its results with the definitive histological diagnosis. 97.2% of sensitivity and 67.6% specificity was observed, with positive predictive value (PPV) of 94.5%, negative predictive value (NPV) of 80.6% and accuracy of 92.8%. Kappa index between both test was 0.69 (CI 95% 0.60–0.79) (Table 2).

Table 2 Test performance summary on optical diagnosis

Endoscopy vs. Pathologic results		
Adenoma/Carcinoma vs. Hyperplastic/Serrated		
Sensitivity	97.2%	95.1–98.4%
Specificity	67.6%	56.3–77.1%
Positive predictive value	94.5%	91.9–96.3%
Negative Predictive value	80.6%	69.1–88.6%
Accuracy	92.8%	90.2–94.7%
Wasp criteria for SSP diagnosis		
Surveillance (3 years/more)		
Sensitivity	38.9%	20.3–61.4%
Specificity	92.8%	90.4–95,0%
Positive predictive value	17.1%	8.5–1.3%
Negative predictive value	97.6%	95.8–98.7%
Accuracy	91.1%	88.3–93.3%

When considering WASP criteria and the pathological diagnosis of serrated adenomas, we found a poor sensitivity (38.9%) but a good specificity (92.8%) with a PPV of 17.1% and a NPV of 97.6% and overall accuracy of 91.1% (Kappa 0.20; CI 95% 0.10–0.42) However, if we contemplate the possibility of misclassification of serrated adenomas and hyperplastic polyps and consider them together, sensitivity fell to 27.5%, specificity was 95.5%, PPV 53.7% and NPV 87.5%. In this last comparison, kappa rose to 0.29 (CI 95% 0.14–0.43) (Tables 2, 3 4).

There were only two cases of colorectal carcinoma in this series of small polyps, all correctly diagnosed by the endoscopist.

When considering cancer and high-grade dysplasia together, endoscopist sensitivity was 82.6%, specificity

Table 3 Test performance summary. Surveillance recommendations

Endoscopy vs. Reference standard		
Surveillance (3 years/more)		
Sensitivity	91.5%	88.0–94.1%
Specificity	87.1%	74.6–88%
Positive predictive value	93.2%	90.0–95.5%
Negative predictive value	78.5%	70.6–80.4%
Accuracy	89%	85.8–95.6%
Pathology vs. Reference standard		
Surveillance (3 years/more)		
Sensitivity	89.9%	86.1–92.7%
Specificity	87.9%	81–92.5%
Positive predictive value	95.1%	92.1–97.0%
Negative predictive value	76.8%	69.2–82.9%
Accuracy	89.3%	86.1–91.9%

97.9%, PPV 65.5% and NPV 99.2% with an overall accuracy of 97.2% (Kappa 0.72 (CI 95% 0.57–0.86)).

Follow-up recommendations

We compared follow-up recommendations made by the endoscopist immediately after the procedure and the real recommendations after the pathologic results, with the post-resection size of the polyp as the real size for follow-up considerations [7]. In this sense, the weighted kappa coefficient between both variables was 0.68 (CI 95% 0.632–0.739), and the contingency coefficient C was 0.82 (Calculated Cmax was 0.894). In the case of the follow-up recommendations based only on the pathologist report, we found a weighted kappa coefficient of 0.663 and a contingency coefficient C of 0.80.

For the endoscopists, based on the presence of criteria for deciding a 3 years or less follow up or not, when compared with the reference standard, endoscopic sensibility was 91.5%, specificity 82.3%, with a PPV of 93.2% and NPV of 78.5%. Overall accuracy was 89%. *In this regard, 28 (6.51%) patients would have had their follow-up colonoscopy delayed if only the endoscopic report had been taken into account, whereas 22 (4.8%) would have had their colonoscopy performed earlier than by-protocol established.* When considering the need of follow up or not, sensitivity was 96%, specificity 73%, PPV 98.1% and NPV 56.4%, with an overall accuracy of 94.5%. (Table 3). *Interestingly, 17 patients who needed follow-up were not considered so by the endoscopist. Conversely, 8 patients who did not need endoscopic follow up were considered for it after endoscopic evaluation.*

As we had established that the pathologist was not exactly the gold standard, we compared the recommendations considering only the sizing and diagnosis of the pathologic report, with the independent 'real' follow-up based on the pathologic diagnosis and the post-resection measured size of the polyps. When considering the targeted threshold of the 3 years or less follow-up schedule, information provided by the pathologic report had a sensitivity of 89.9%, specificity of 87.9%, PPV of 95.1% and NPV of 76.8%, with an overall accuracy of 89.3% (Table 3). However, regarding the need or not of a follow-up, sensitivity was 97.8%, specificity 35.9%, PPV 94.1%, NPV 60.9% and accuracy 92.4%.

Discussion

This multicenter prospective real-live study on small polyps, between 5 and 15 mm, evaluates the precision of follow-up recommendations given by average gastroenterologists not usually dedicated to endoscopy. Our data show that, even not reaching the ASGE PIVI thresholds [5], recommendations regarding surveillance offered even by non-specifically dedicated endoscopists are the most reliable with respect to patients' follow-up.

The Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) statement released by the American Society of GI Endoscopy has issued advice on acceptable performance thresholds for real-time endoscopic assessment of diminutive polyps required before optical diagnosis should be recommended for routine clinical practice [5]. The PIVI statement established that optical diagnosis for small (6–9 mm) polyps can be used to determine

Table 4 Pathologist vs. Optical diagnosis results

Endoscopist optical diagnosis	Pathologic results *n* (%)					
	Hyperplastic	Serrated	Tubular adenoma	Advanced adenoma	Carcinoma	Total
Hyperplastic	41 (63.2%)	5 (33.3%)	5 (1.4%)	0	0	51
Serrated	2 (3%)	6 (40%)	6 (1.7%)	1 (1.1%)	0	15
Adenoma	21 (32,3%)	0	278 (78.5%)	33 (37.9%)	2 (33.3%)	334
Advanced adenoma	1 (1,5%)	4 (26,6%)	65 (18.4%)	52 (59.8%)	2 (33.3%)	124
Carcinoma	0	0	0	1 (1.1%)	2 (33.3%)	3
Total	*65*	*15*	*354*	*87*	*6*	527

surveillance. In expert hands, optical diagnosis using white light and NBI has been shown to be comparable to histology [16, 17]. However, every study on optical diagnosis considers endoscopist accuracy on sizing the polyps as adequate, whereas some evidence points to, at least, a substantial variability [7–11]. In this sense, polyp measurement is of paramount importance, especially around the 10 mm frontier, which marks the difference of the 3 years surveillance vs. the 7–10 years follow-up colonoscopy [6]. Our results observe that the endoscopist is more accurate than the pathologist when estimating the polyp size. For this reason, the practice in some centers that follow the pathologic report to offer surveillance recommendations is inaccurate and should not be endorsed. Moreover, the practice of systematically measuring the polyp by a technician before fixation could reduce inaccuracy in this matter, as well as devices such as the graduated measurement ones that can be passed down the biopsy channel and placed alongside the lesion to aid measurement as previously described [18]. However, some years after their first description those devices have not been widely adopted by endoscopists for several reasons, and we could state from our results that endoscopist precision sizing polyps can be considered acceptable.

When considering optical diagnosis in those lesions, an interest about the coincidence with the pathologic report has arisen in several papers, whereas the main concerns for the patient is, first, whether a cancer is found and second, when the next colonoscopy should be performed. After excluding malignancy, the patient needs to know the subsequent surveillance schedule. In this regard, our results show a good performance for the endoscopist when ruling out a malignancy, with very good results in the differentiation between adenoma or cancer and hyperplastic lesions. Indeed, sensitivity for the diagnosis of adenoma reached 98.7%, with an overall accuracy of 92.2%, comparable to what has been previously described in a meta-analysis [19]. Although other previous studies did not reach similar results, the procedures in our study were performed with HD colonoscopes and mostly by general gastroenterologist who had undergone a similar structured training in NBI with 'in vivo' cases in the same referral center.

Ours is a real life study, and we should consider the possibility of pathologic misdiagnoses, although the coincidence between diagnoses in the samples selected to perform a quality control were very good. However, it has been previously observed pathologic misdiagnoses in adenoma, especially when the endoscopist diagnosis of adenoma based on NBI is made with a good level of confidence [4]. Our results with sessile serrated polyps were discouraging, although there are two reasons to take those results with caution, first is the low impact on follow-up recommendations, and second, the recognized suboptimal ability of pathologists in the diagnosis of those lesions

[20, 21]. Indeed, the rate of SSPs in our study was remarkably high when compared with the reported prevalence of 0.3–0.5% [22], which might rise concerns about an endoscopic and pathologic overdiagnosis. In this regard, maybe both endoscopist and pathologist are still quite inaccurate.

The most interesting results of our research are related to surveillance recommendations. Previously, we established the immediate after-resection sizing by the technician as the gold standard for polyp diameter, following former reports that have launch this method to avoid the recognized endoscopists' subjectivity [7, 11], and the usual inaccuracy of the pathologic report in this regard. Overall, we observed that endoscopists recommendations regarding the 3-year colonoscopy follow-up threshold, given on the basis of the estimated sizing and the optical diagnosis, were more accurate than the ones provided when following the pathologic report. We should also highlight that the overall NPV for adenomatous histology we found was above the PIVI thresholds, even in a sample from quite different clinical settings, academical and community based [5, 23]. These observations have two main consequences in daily clinical practice: First, endoscopist immediate recommendations after polyp resection should be enough to offer a reliable surveillance plan in most cases, and second, the pathologic report should not be the gold standard for those recommendations. This has a direct impact on patients' management, with no need for follow-up visits to the Gastroenterologist office, but maybe just a pathologic report check and an appointment for patients with an optical misdiagnosis. There can also be a number of procedure implications, especially on polyps sizing, that could be done after polyp retrieval with no added length to the endoscopic procedure, as well as on the diagnosis accuracy of SSPs, which remains as an important diagnostic challenge. Certainly, an optical diagnosis-based protocol might lead to considerable less outpatient visits and a more appropriate indication for the colonoscopy surveillance interval.

The main limitations of our study is the heterogeneity of the researchers, that might bias the results. However, it can be also considered a strength, because it shows the real life experience in different endoscopy settings. Moreover, the similar previous training for all the endoscopist involved in the study confirm findings on previous reports that point to an improvement in optical diagnosis when a structured training program is implemented [24]. Another limitation relies on the high proportion of SSPs pathologically confirmed and endoscopically suspected. In this regard, we believe more diagnostic tools are needed to improve the endoscopic suspicion and the pathologic diagnosis of those lesions. Finally, polyps' measurement after resection by our nurses might bear some bias when spreading the tumor or including normal tissue in the measurements. However, nurses were taught to perform it properly before including patients, and

it has been previously recognized as a gold standard for polyps' sizing [9, 18].

In conclusion, our paper shows that optical diagnosis is adequate and enough to establish a surveillance protocol in patients with polyps of around 10 mm in most circumstances, in real life endoscopy. Indeed, endoscopist based recommendations are more accurate than the ones based on the pathologic report, mainly due to a *more precise* estimation of the polyp size, as well as to an optical diagnosis that reach the PIVI thresholds. The main impact of those findings lies on the need of outpatient visit to a gastroenterology clinic for surveillance advice based on the pathologic results, and a more accurate scheduling of follow-up colonoscopies.

Declarations

References

1. Zauber AG, Winawer SJ, O'Brien MJ, Lansdorp-Vogelaar I, van Ballegooijen M, Hankey BF, Shi W, Bond JH, Schapiro M, Panish JF, Stewart ET, Waye JD (2012) Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med 366:687–696

2. Qumseya BJ, Coe S, Wallace MB (2012) The effect of polyp location and patient gender on the presence of dysplasia in colonic polyps. Clin Transl Gastroenterol 3:e20

3. Rees CJ, Rajasekhar PT, Wilson A, Close H, Rutter MD, Saunders BP, East JE, Maier R, Moorghen M, Muhammad U, Hancock H, Jayaprakash A, MacDonald C, Ramadas A, Dhar A, Mason JM (2017) Narrow band imaging optical diagnosis of small colorectal polyps in routine clinical practice: the detect inspect characterise resect and discard 2 (DISCARD 2) study. Gut 66:887–895

4. Ponugoti P, Rastogi A, Kaltenbach T, MacPhail ME, Sullivan AW, Thygesen JC, Broadley HM, Rex DK (2019) Disagreement between high confidence endoscopic adenoma prediction and histopathological diagnosis in colonic lesions. Endoscopy 51 221 226

5. Committee AT, Abu Dayyeh BK, Thosani N, Konda V, Wallace MB, Rex DK, Chauhan SS, Hwang JH, Komanduri S, Manfredi M, Maple JT, Murad FM, Siddiqui UD, Banerjee S (2015) ASGE Technology Committee systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting real-time endoscopic assessment of the histology of diminutive colorectal polyps. Gastrointest Endosc 81:502 e501–502 e516

6. Gupta S, Lieberman D, Anderson JC, Burke CA, Dominitz JA, Kaltenbach T, Robertson DJ, Shaukat A, Syngal S, Rex DK (2020) Recommendations for follow-up after colonoscopy and polypectomy: a consensus update by the us multi-society task force on colorectal cancer. Am J Gastroenterol 115:415–434

7. Gopalswamy N, Shenoy VN, Choudhry U, Markert RJ, Peace N, Bhutani MS, Barde CJ (1997) Is in vivo measurement of size of polyps during colonoscopy accurate? Gastrointest Endosc 46:497–502

8. Rex DK, Rabinovitz R (2014) Variable interpretation of polyp size by using open forceps by experienced colonoscopists. Gastrointest Endosc 79:402–407

9. Morales TG, Sampliner RE, Garewal HS, Fennerty MB, Aickin M (1996) The difference in colon polyp size before and after removal. Gastrointest Endosc 43:25–28

10. Elwir S, Shaukat A, Shaw M, Hughes J, Colton J (2017) Variability in, and factors associated with, sizing of polyps by endoscopists at a large community practice. Endosc Int Open 5:E742–E745

11. Chaptini L, Chaaya A, Depalma F, Hunter K, Peikin S, Laine L (2014) Variation in polyp size estimation among endoscopists and impact on surveillance intervals. Gastrointest Endosc 80:652–659

12. Lieberman DA, Rex DK, Winawer SJ, Giardiello FM, Johnson DA, Levin TR (2012) Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US multi-society task force on colorectal cancer. Gastroenterology 143:844–857

13. Rex DK, Ahnen DJ, Baron JA, Batts KP, Burke CA, Burt RW, Goldblum JR, Guillem JG, Kahi CJ, Kalady MF, O'Brien MJ, Odze RD, Ogino S, Parry S, Snover DC, Torlakovic EE, Wise PE, Young J, Church J (2012) Serrated lesions of the colorectum: review and recommendations from an expert panel. Am J Gastroenterol 107:1315–1329; quiz 1314, 1330

14. Ij JE, Bastiaansen BA, van Leerdam ME, Meijer GA, van Eeden S, Sanduleanu S, Schoon EJ, Bisseling TM, Spaander MC, van Lelyveld N, Bargeman M, Wang J, Dekker E, Dutch Workgroup serrAted polyp S, Polyposis (2016) Development and validation of the WASP classification system for optical diagnosis of adenomas, hyperplastic polyps and sessile serrated adenomas/polyps. Gut 65:963–970

15. Hewett DG, Kaltenbach T, Sano Y, Tanaka S, Saunders BP, Ponchon T, Soetikno R, Rex DK (2012) Validation of a simple classification system for endoscopic diagnosis of small colorectal polyps using narrow-band imaging. Gastroenterology 143:599–607 e591

16. Ignjatovic A, East JE, Suzuki N, Vance M, Guenther T, Saunders BP (2009) Optical diagnosis of small colorectal polyps at routine colonoscopy (Detect InSpect ChAracterise Resect and Discard; DISCARD trial): a prospective cohort study. Lancet Oncol 10:1171–1178

17. Rex DK (2009) Narrow-band imaging without optical magnification for histologic analysis of colorectal polyps. Gastroenterology 136:1174–1181

18. Leng Q, Jin HY (2015) Measurement system that improves the accuracy of polyp size determined at colonoscopy. World J Gastroenterol 21:2178–2182

19. McGill SK, Evangelou E, Ioannidis JP, Soetikno RM, Kaltenbach T (2013) Narrow band imaging to differentiate neoplastic and non-neoplastic colorectal polyps in real time: a meta-analysis of diagnostic operating characteristics. Gut 62:1704–1713

20. Schachschal G, Sehner S, Choschzick M, Aust D, Brandl L, Vieth M, Wegscheider K, Baretton GB, Kirchner T, Sauter G, Rosch T (2016) Impact of reassessment of colonic hyperplastic polyps by expert GI pathologists. Int J Colorectal Dis 31:675–683

21. Gourevitch RA, Rose S, Crockett SD, Morris M, Carrell DS, Greer JB, Pai RK, Schoen RE, Mehrotra A (2018) Variation in pathologist classification of colorectal adenomas and serrated polyps. Am J Gastroenterol 113:431–439

22. East JE, Vieth M, Rex DK (2015) Serrated lesions in colorectal cancer screening: detection, resection, pathology and surveillance. Gut 64:991–1000

23. Mason SE, Poynter L, Takats Z, Darzi A, Kinross JM (2019) Optical technologies for endoscopic real-time histologic assessment of colorectal polyps: a meta-analysis. Am J Gastroenterol 114:1219–1230

24. Rastogi A, Rao DS, Gupta N, Grisolano SW, Buckles DC, Sidorenko E, Bonino J, Matsuda T, Dekker E, Kaltenbach T, Singh R, Wani S, Sharma P, Olyaee MS, Bansal A, East JE (2014) Impact of a computer-based teaching module on characterization of diminutive colon polyps by using narrow-band imaging by non-experts in academic and community practice: a video-based study. Gastrointest Endosc 79:390–398