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New Paradigms for Colonoscopic Management of Diminutive Colorectal Polyps: Predict, Resect, and Discard or Do Not Resect?

Cesare Hassan¹, Alessandro Repici¹, Angelo Zullo¹ and Prateek Sharma²

¹Digestive Endoscopy Unit, Istituto Clinico Humanitas, Milan, Italy, ²Division of Gastroenterology, University of Kansas Medical Center, Kansas City, KS, USA

The possibility to predict *in vivo* the histology of colorectal polyps by advanced endoscopic imaging has resulted in the implementation of a more conservative management for diminutive lesions detected at colonoscopy. In detail, a predict-and-do-not-resect strategy has been proposed for diminutive lesions located in the rectosigmoid tract, whilst a predict-resect-and-discard policy has been advocated for nonrectosigmoid diminutive polyps. Recently, the American Society for Gastrointestinal Endoscopy set required thresholds to be met, before allowing the adoption of these policies in the clinical field. The ability of current endoscopic imaging in reaching these thresholds would depend on a complex interaction among the accuracy of advanced endoscopic imaging in differentiating between adenomatous and hyperplastic lesions, the prevalence of (advanced) neoplasia within diminutive lesions, and the type of surveillance intervals recommended. Aim of this review is to summarize the data supporting the application of both a predict-and-do-not-resect and a predict-resect-and-discard policies, also addressing the potential pitfalls associated with these strategies.

Key Words: Electronic chromoendoscopy; Colonoscopy; Polypectomy; Narrow band imaging; Preservation and incorporation of valuable endoscopic innovation

INTRODUCTION

Any decision-making process in clinical medicine may be simplified in a series of sequential steps that cumulatively lead to a clinical diagnosis or intervention. Thus, the additional benefit of any step must be balanced with the associated exploitation of medical and economic resources. When limiting our focus to diagnostic process, the additional value of any subsequent test will depend on the absolute increase in accuracy as compared with what was achieved prior to the test.

Histological examination of colorectal lesions has been considered in the last decades as a critical step in the decision-making process, because of its contribution in differentiating between nonneoplastic and neoplastic lesions, and - among

those neoplastic - between noninvasive and invasive lesions.^{1,2} The relevance of postpolypectomy histological examination has been intimately related with the lack of any alternative in characterizing polypoid or nonpolypoid lesions prior to the pathological examination itself.^{1,2} Despite histological characterization of colorectal polyps has been generally considered as a gold-standard, some pitfalls may be identified. First, not all the removed polyps are actually retrieved, resulting into a complete loss of information in 10% to 20% of cases.³ Secondly, a high interobserver variability in the diagnosis of the degree of dysplasia and villous component - i.e., the unfavourable features discriminating between advanced and nonadvanced neoplasia - has been shown.⁴ Third, the same differentiation between hyperplastic and adenomatous histotypes is not perfect, with adenomatous tissue hidden in the nonexamined part of the embedded specimen. Fourth, there is no general consensus on the clinical meaning of histological characterization with divergent recommendations according to different guidelines.^{5,6}

The need of postpolypectomy histological examination causes a substantial exploitation of medical and economic resources. It may be estimated that roughly one in every two

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Correspondence: Cesare Hassan

Division of Gastroenterology, Ospedale Nuovo Regina Margherita Hospital, Via E. Morosini 30, I-00153 Rome, Italy

Tel: +39-3387922296, Fax: +39-3387922296, E-mail: cesareh@hotmail.com

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patients undergoing screening or diagnostic colonoscopy are diagnosed with at least one polyp, thus requiring postpolypectomy pathological examination.^{7,8} Secondly, the vast majority of these polyps are diminutive (≤ 5 mm) with a very low prevalence of advanced neoplasia, marginalizing the clinical impact of pathological examination.⁷⁻⁹ Third, the estimated cost of the pathological examination is of the same magnitude with that of colonoscopy, heavily affecting the cost of colonoscopy screening without adding an equivalent contribution to colonoscopy efficacy.¹⁰⁻¹² Fourth, the need of a new visit for communicating the postpathological surveillance interval generates a substantial and avoidable loss of productivity for the society, especially when considering that roughly 60% of the United States population undertakes a screening colonoscopy every 10 years.¹³

In order to address these pitfalls, a policy of discarding the postpolypectomy pathological examination has been proposed, also named as predict-resect-and-discard policy.¹⁴⁻¹⁶ Its main assumption is that if endoscopy may predict *in vivo* the histotype of the polyp, the additional value of histological examination may be marginalized, becoming inefficient and/or cost-ineffective.¹⁰⁻¹² Predict-resect-and-discard policy has been mainly prompted by the technical evolution of endoscopic imaging, leading to a new field defined as advanced endoscopic imaging, with the main aim of differentiating between hyperplastic and neoplastic, as well as between noninvasive and invasive neoplastic lesions.^{17,18} However, before implementing a predict-resect-and-discard policies, several issues need to be addressed. First, *in vivo* prediction of polyp histology is required to reach an adequate level of accuracy, in order to minimize the possible contribution of postpolypectomy histological examination to the decision-making process. Secondly, a high degree of inter and intraobserver agreement is required, in order to assure its reproducibility. Third, a feasible training and learning curve must be in place, in order to result into an adequate generalizability of the predict-resect-and-discard strategy. Fourth, advanced imaging techniques need to be supported by the available endoscopic systems. Fifth, the appropriateness of the clinical recommendations - i.e., the postpolypectomy surveillance intervals - should not be deteriorated by the exclusion of pathological examination. Sixth, a standardized and formal reporting of *in vivo* histological prediction must be in place, in order to prevent misuse or eventual medical litigations related with the implementation of this policy.

Aim of this review is to address the pros and cons of a predict-resect-and-discard policy based on the data available in the literature.

ADVANCED ENDOSCOPIC IMAGING

Standard white light endoscopy has been regarded as inaccurate to accurately predict *in vivo* the histological features of colorectal lesions. Sensitivity has been shown to broadly range between 60% and 90%, with specificity ranging between 40% and 90%.¹⁹⁻²¹ The evolution from standard to high-definition endoscopy disappointingly failed to meaningfully improve the suboptimal white light accuracy in characterizing colorectal polyps.¹⁹ The possibility to *in vivo* differentiate among different histotypes has been initially shown by Japanese endoscopists.^{2,17,18,22,23} Briefly, it was exploited the ability of some dyes - such as indigo carmine and methylene blue - to highlight the pit pattern of colorectal lesions at high-(optical) magnification endoscopy.^{2,17,18,22,23} The pit pattern of both polypoid and nonpolypoid lesions was shown to be intimately associated with the progressive distortion and elongation of colonic glands during colorectal cancer (CRC) carcinogenesis or, alternatively, with the evolution towards a serrated - mainly hyperplastic - histotypes.^{2,17,18,22,23} However, dye-chromoendoscopy failed to be successfully implemented in Western countries for several reasons. First, Japanese endoscopists appeared to be more prone to implement chromoendoscopy in colonoscopy, because chromoendoscopy had already been routinely adopted for population-based gastric cancer screening.²⁴ Secondly, dye spraying has been generally discarded as time-consuming and inconvenient, also when considering the intensive volume of screening colonoscopies performed in Western countries.¹³ Thirdly, dye-chromoendoscopy requires a long-lasting learning curve, possibly including several hundreds of examinations.^{2,16,17,21,22} Fourth, chromoendoscopy has been primarily exploited for differentiating between endoscopically and surgically resectable submucosal cancer in nonpolypoid lesions rather than for discriminating between nonneoplastic and neoplastic lesions.^{2,16,17,21,22} Fifth, an excessive dye spraying may substantially reduce the visibility of the mucosa surrounding the targeted lesion, potentially affecting the detection rate of more serious lesions.

For all these reasons, there was the need of a major breakthrough to expand the success of advanced endoscopic imaging to Western countries. As detailed by Rastogi et al. in this issue of *Clinical Endoscopy*, the advent of electronic chromoendoscopy (EC) - such as narrow band imaging, Fuji intelligent color enhancement, and Pentax I-Scan - opened the door for the *in vivo* prediction of polyp histology in Western countries. First, EC has shown a promising accuracy in differentiating between adenomatous and hyperplastic polyps in several studies (Table 1),^{9,14-16,19-21,25-52} owing to the advantage of being extremely simple and fast to be activated. Secondly, the level of confidence of the operator in the *in vivo* prediction has

Table 1. Studies Reporting Accuracy of Electronic Chromoendoscopy in Differentiating between Adenomatous and Hyperplastic Lesions

Author	Country	Setting	No. of points	No. of polyps	No. of polyps <10 mm	Aden. prevalence, %	Endoscopist	Optical magnification	Pit pattern	Vascular pattern	Sensitivity, %	Specificity, %
Machida et al. ²⁵	Japan	Artificial	34	43	-	79	-	High	Yes	Yes	100	75
Chiu et al. ²⁰	Taiwan	Artificial	133	180	-	78	Experienced	High	No	Yes	91	80
Chiu et al. ²⁰	Taiwan	Artificial	133	180	-	78	Experienced	Low	Yes	No	84	71
Su et al. ²¹	Taiwan	Artificial	78	110	40	59	Experienced	High	No	Yes	96	87
Hirata et al. ⁵¹	Japan	Retrospective	99	148	-	89	-	High	Yes	No	99	94
East et al. ²⁶	UK	Artificial	20	31	33	64	Experienced	High	Yes	Yes	77	50
Tischendorf et al. ²⁷	Germany	Artificial	52	100	75	63	Experienced	High	Yes	Yes	91	89
Rastogi et al. ¹⁴	USA	Screening/Surveillance	40	123	-	59	Experienced	Low	Yes	No	97	86
Sikka et al. ⁴¹	USA	Artificial	63	80	-	61	Inexperienced	Low	No	Yes	86	97
Rogart et al. ⁴⁰	USA	Unselected	131	265	251	49	Inexperienced	Low	Yes	Yes	95	90
East et al. ²⁸	UK	High-risk	62	116	116	43	Experienced	High	Yes	Yes	98	88
Sano et al. ²⁹	Japan	Screening/Surveillance	92	150	-	74	Experienced	High	No	Yes	96	92
Rex ¹⁶	USA	Unselected	136	451	428	51	Experienced	Low	Yes	Yes	96	92
van den Broek et al. ³⁰	The Netherlands	Artificial	32	50	45	44	Experienced	High	Yes	No	88	56
Wada et al. ³¹	Japan	Unselected	495	617	-	95	Inexperienced	High	Yes	No	90	55
Tischendorf et al. ³³	Germany	Artificial	131	100	80	58	Experienced	High	No	Yes	91	97
Buchner et al. ⁴²	USA	Unselected	75	119	-	68	Experienced	Low	-	-	77	71
Ignjatovic et al. ¹⁵	UK	High-risk	130	278	278	71	Exp. and inexp.	Low	No	Yes	94	89
Tischendorf et al. ³²	Germany	Artificial	223	209	-	77	Experienced	High	No	Yes	94	86
Henry et al. ⁴³	USA	Unselected	52	126	-	53	Experienced	Low	No	Yes	92	88
Ignjatovic et al. ⁴⁴	UK	Artificial	-	630	630	50	Exp. and inexp.	Low	Yes	Yes	87	84
Ignjatovic et al. ³⁵	UK	Artificial	-	80	80	50	Experienced	Low	No	Yes	74	56
Kuiper et al. ³²	The Netherlands	High-risk	-	238	-	49	Experienced	Low/High	Yes	No	87	63
Sato et al. ³⁶	Japan	Unselected	183	424	-	80	Exp. and inexp.	High	No	Yes	91	76
Rastogi et al. ⁴⁵	USA	Screening/Surveillance	-	-	-	-	Experienced	Low	Yes	Yes	90	68
Gross et al. ³⁴	Germany	Artificial	214	434	434	59	Exp. and inexp.	High	No	Yes	93	92
Gross et al. ³⁴	Germany	Artificial	214	434	434	59	Exp. and inexp.	High	No	Yes	86	88

Table 1. Continued

Author	Country	Setting	No. of points	No. of polyps	No. of polyps <10 mm	Aden. prevalence, %	Endoscopist	Optical magnification	Pit pattern	Vascular pattern	Sensitivity, %	Specificity, %
Gupta et al. ⁴⁶	USA	Screening/Surveillance	410	1,254	1,121	64	Experienced	Low	Yes	Yes	94	72
Takemura et al. ³⁹	Japan	Artificial	-	371	-	87	Experienced	High	Yes	Yes	98	99
Kuiper et al. ³⁸	The Netherlands	Unselected	64	154	-	37	Experienced	High	Yes	No	81	93
Hewett et al. ⁴⁷	USA	Unselected	108	236	236	63	Experienced	Low	Yes	Yes	98	69
Kuiper et al. ⁴⁸	The Netherlands	Unselected	308	108	308	46	Inexperienced	Low	Yes	No	77	79
Hewett et al. ⁹	USA	Screening/Surveillance	31	235	231	16	Experienced	Low	Yes	Yes	94	98
Yoo et al. ³⁷	Korea	Unselected	68	107	-	93	Experienced	High	Yes	No	89	87
Yoo et al. ³⁷	Korea	Unselected	68	107	-	93	Experienced	High	No	Yes	92	87
Paggi et al. ⁵⁰	Italy	Unselected	286	511	511	69	Experienced	Low	Yes	Yes	95	66
Longcroft-Wheaton et al. ¹⁹	UK	Unselected	51	150	150	64	Experienced	Low	Yes	Yes	83 ^{a)}	82
Ladabaum et al. ⁴⁹	USA	Unselected	1,673	2,596	2,405	65	Inexperienced	Low	Yes	Yes	93 ^{b)}	81
											91	40

Exp., experienced; inexp., inexperienced.

^{a)}Standard definition; ^{b)}High-definition.

been associated with EC accuracy, so that - by restricting the analysis only to the high-confidence diagnosis - EC accuracy may be further improved.^{9,15,16,47-49} Third, EC is available on the new generation of endoscopes, so that a widespread implementation of this technique may be expected. Fourth, a very fast and simple training and learning curve has been shown to be feasible, also leading to acceptable rates of inter and intraobserver agreements, thus assuring the generalizability and reproducibility of the *in vivo* characterization.^{25,47,53}

PREDICT-RESECT-AND-DISCARD AND PREDICT-AND-DO-NOT RESECT POLICIES

The efficacy and safety of strategies based on *in vivo* characterization of colorectal lesions depends on a complex interaction between the accuracy values of EC, the expected prevalence of disease, and the types of surveillance intervals recommended. The main criticism to EC-based prediction is its inability in discriminating between nonadvanced and advanced neoplasia.^{9,14-16,19-21,25-50,54} Since unfavourable histological features - such as high-grade dysplasia or >20% villous component - predict a higher risk of metachronous advanced neoplasia,⁵⁵ the identification of unfavourable histological features actually results into the assignment of a more intensive postpolypectomy surveillance (i.e., 3-years vs. -5/10-years).^{5,6} Therefore, EC-based policies should be implemented only when the risk of advanced neoplasia may be marginalized. When comparing the prescreening prevalence of advanced neoplasia - ranging between 4% and 10% - with that of sub-centimetric polyps, such prevalence would appear to be marginal - i.e., $\leq 1\%$ - in diminutive lesions, whilst ranging between 1% and 5% in 6 to 9 mm lesions.^{7,8,56} Consequently, the actual drawback of a predict-resect-and-discard policy for diminutive lesions would be the lack of characterization of one case of advanced neoplasia every ≥ 100 predictions, resulting into a 2/7-year delay in the postpolypectomy surveillance interval. Suggestively, the predict-resect-and-discard policy would still appear safer than the actual nonreferral policy implemented by computed tomography colonography and colon capsule, according to which diminutive lesions, irrespectively of whether (advanced) adenomatous or hyperplastic, should not even sent to post-test polypectomy.^{57,58} On the other hand, the application of EC-based policies to 6 to 9 mm lesions appears to be more controversial, because of the higher prevalence of advanced neoplasia within these lesions.^{7,46} However, the much lower prevalence of 6 to 9 mm as compared with ≤ 5 mm lesions in the general population would marginalize the impact of these lesions over the efficiency of EC-policies.⁸ The second criticism to *in vivo* prediction of polyp histology is the

possibility of EC-false-negatives/positives results when discriminating between hyperplastic and adenomatous polyps (Table 1).^{9,14-16,19-21,25-52} This would result in the risk of either anticipating the postpolypectomy surveillance interval in those with an hyperplastic lesion misclassified at EC as adenomatous or delaying it in those with an EC-misclassified adenomatous lesion. The clinical consequences of EC-misclassification would mainly depend on two variables, namely prevalence of adenomatous histotype and type of guidelines adopted. Similarly to advanced neoplasia prevalence, relative prevalence of adenomatous histotype within colorectal lesions is intimately related with polyp size, being about 50% and about 65% in diminutive and small lesions, respectively.^{7,59,60} Based on these values, when assuming a 90% EC-based sensitivity for adenomatous histotype, the negative predictive value for adenomatous histology would equalize a 90% threshold for diminutive lesions, but it would be substantially inferior for 6 to 9 mm polyps. When limiting our analysis to diminutive lesions, polyp prevalence is also likely to be related with polyp location. Because of the well-known prevalence of several tiny hyperplastic lesions in the rectosigmoid tract, the relative prevalence of adenomatous histotype may be expected to be further reduced in this tract, as compared with the remaining colon. In a consecutive series of 235 distal polyps - including 220 \leq 5 mm lesions - only 38 were actually adenomatous, corresponding to a 16% overall frequency of the adenomatous histotype.⁹ Because of the inverse relationship between adenomatous prevalence and negative predictive value, the very low disease prevalence in the rectosigmoid tract further reassures on the safety of EC-based policies in this location. The clinical impact of eventual false-positive/negative results at EC would also depend on the type of guidelines adopted. According to the United States and European-based guidelines, patients with one to two tubular subcentimetric adenomas should have their next surveillance examination at 5 to 10 years and 10 years, respectively.⁵ The impact of this 5 to 10 year difference on the implementation of EC-based policies is dramatic. If a 5-year interval is chosen, any false-positive/negative result at EC would cause an inappropriate anticipated/delayed surveillance interval for hyperplastic and adenomatous lesions, respectively, underlining the necessity for an optimal EC-accuracy in this scenario. On the other hand, if a 10 year interval for patients with one to two tubular subcentimetric adenomas is adopted, any false-positive/negative result would not affect the 10-year surveillance interval, since adenomatous and hyperplastic lesions would share a common 10-year interval recommendation in this scenario. The final criticism to EC-based policies is represented by the impossibility of differentiating between hyperplastic and nonhyperplastic serrated lesions - such as sessile serrated polyps or sessile serrated adenomas

lesions - at EC, because of the similar EC characteristics of these lesions.¹⁴ However, prevalence of sessile or traditional serrated adenoma has been shown to be very low in subcentimetric lesions, being cumulatively present in 0.3% to 0.5% and 0.8% to 1.3% of diminutive and small lesions, respectively.^{7,60} Moreover, these lesions seem to be associated with a higher risk of synchronous or metachronous advanced neoplasia only when located in the proximal colon or larger than 10 mm.⁶¹

Based on all these considerations, the American Society for Gastrointestinal Endoscopy (ASGE) recently developed a preservation and incorporation of valuable endoscopic innovations (PIVI) statement for real-time endoscopic assessment of the histology of diminutive colorectal polyps.⁶² In detail, it was determined that:

1) 'For colorectal polyps <5 mm in size to be resected and discarded without pathologic assessment, endoscopic technology (when used with high confidence) used to determine histology of polyps <5 mm in size, when combined with histopathologic assessment of polyps >5 mm in size, should provide a >90% agreement in assignment of postpolypectomy surveillance intervals when compared with decisions based on pathology assessment of all identified polyps.'

2) 'For a technology to be used to guide the decision to leave suspected rectosigmoid hyperplastic polyps <5 mm in size in place (without resection), the technology should provide >90% negative predictive value (when used with high confidence) for adenomatous histology.'

The ASGE, therefore, recommended two different EC-based policies, namely a predict-resect-and-discard strategy for nonrectosigmoid <5 mm lesions characterized at EC with high-confidence, and a predict-and-do-not-resect policy for rectosigmoid diminutive polyps predicted as hyperplastic at EC with high confidence. The overall algorithm is summarized in Fig. 1.⁶²

The ability of EC to meet with the 1° PIVI has been tested in a few series (Table 2).^{9,15,16,19,25,46-50} When recommending a 5-year interval surveillance for low risk subcentimetric adenomas,⁵ the majority of the available series failed to match the 1° PIVI, especially when EC was performed by less experienced endoscopists. On the other hand, when adopting a 10-year schedule, most of the studies succeeded in meeting the 1° PIVI. Intriguingly, when considering a 10 year interval for low-risk subcentimetric adenomas, a different strategy, in theory, would be to do-not-predict-resect-and-discard one to two diminutive lesions without EC-based prediction, reserving EC differentiation only to patients with at least three lesions. However, it is unclear whether the medical community would be ready to resect and discard lesions without having received any prediction about its histology.¹¹

The 2° PIVI is rather innovative, since it introduces the predict-and-do-not-resect strategy based on the main assumption that - after EC-prediction of hyperplastic histotype - the possibility of leaving *in situ* a ≤ 5 mm adenoma is too low to warrant the cost of polypectomy itself. Therefore, the predict-and-do-not-resect policy represents a dramatic step forward in rationalizing the exploitation of medical and economic resources at colonoscopy, since it does not only exclude the pathological examination, but also the polypectomy itself from the colonoscopy procedure. When considering the low prevalence of adenomatous component among subcentimetric rectosigmoid lesions, it was not unexpected that the ma-

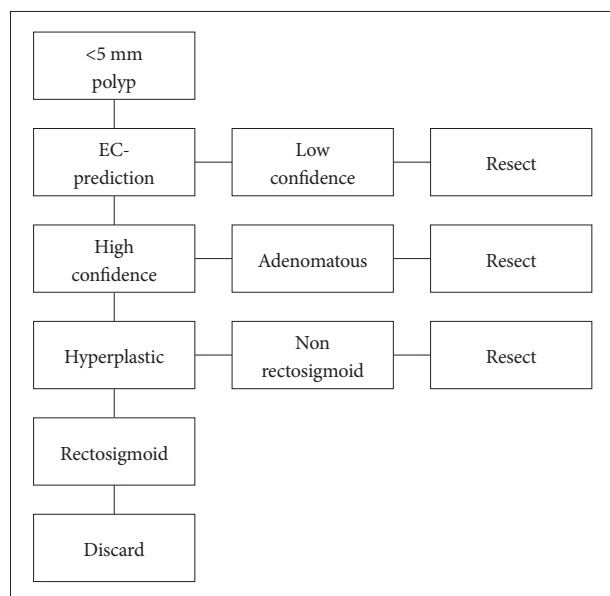


Fig. 1. Summary algorithm of the electronic chromoendoscopy (EC)-based proposed strategies according to American Society for Gastrointestinal Endoscopy recommendations.⁶²

majority of the available studies consistently validated the feasibility of this policy, resulting into >90% negative predictive values. The exclusion from this strategy of nonrectosigmoid lesions may be also expected to marginalize the risk of leaving high-risk serrated lesions *in situ*. However, it could also be argued that the drawback of this policy is to accept that 1 in every 10 patients with a rectosigmoid polyp discarded at EC would remain *in situ*, resulting into the risk of progression of one unresected diminutive EC-misclassified adenoma. At this regard, previous studies addressed the natural history of unresected diminutive or larger lesions in the recto-sigmoid tract, reassuring on the very low risk of progression of these lesions. In detail, Hoff et al.⁶³ and Hofstad et al.⁶⁴ followed up 194 diminutive and 253 ≤ 10 mm polyps detected for 3 and 2 years, respectively. No diminutive polyp reached a >5 mm size and only 0.5% of ≤ 10 mm polyps eclipsed the 10-mm threshold after a 1-year time interval, and no case of severe dysplasia or carcinoma was registered.^{63,64} In a recent Japanese study only 2.9% of 408 subcentimetric lesions followed up for 43.1 months reached a ≥ 10 mm size, without the occurrence of any invasive cancer.⁶⁵ Overall these data may be reassuring, when considering the very low risk of discarding an (advanced) adenoma in the rectosigmoid colon.

CONCLUSIONS

The increasing volume of colonoscopy procedures - related with a growing awareness of the efficacy of CRC screening - in a period of economic constraint requires a rational exploitation of the limited medical and financial resources. This is further worsened by the additional volume of surveillance procedure generated by the detection of neoplastic lesions at the screening examination, especially when considering the

Table 2. Studies Reporting Accuracy of Electronic Chromoendoscopy in Matching the Desired Thresholds for the Two Porposed Preservation and Incorporation of Valuable Endoscopic innovations (see text)

Author	Country	No. of points	No. of polyps	High/low confidence	1° PIVI	2° PIVI
Rex ¹⁶	USA	136	451	Yes	Yes	-
Ignjatovic et al. ¹⁵	UK	130	278	Yes	Yes	Yes
Rastogi et al. ⁴⁵	USA	-	-	No	No	No
Gupta et al. ⁴⁶	USA	410	1,254	No	No/Yes	Yes
Hewett et al. ⁴⁷	USA	108	236	Yes	-	Yes
Kuiper et al. ⁴⁸	The Netherlands	308	108	Yes	No	-
Hewett et al. ⁹	US	31	235	Yes	-	Yes
Paggi et al. ⁵⁰	Italy	286	511	Yes	No	-
Longcroft-Wheaton et al. ¹⁹	UK	51	150	No	No/Yes	No
Longcroft-Wheaton et al. ¹⁹	UK	50	143	No	Yes	No
Ladabaum et al. ⁴⁹	USA	1,673	2,596	Yes	No/Yes	Yes

PIVI, preservation and incorporation of valuable endoscopic innovation.

increase in adenoma detection rate with the evolution of endoscopic technology and the development of quality assurance programs. For this reason, any policy that may simplify and rationalize colonoscopy procedure or work up is useful. Predict-resect-and-discard and predict-and-do-not-resect policies offer the advantage of saving the cost for polypectomy or postpolypectomy pathological examination in a substantial percentage of the cases, as well as to recommend on the same day of the colonoscopy procedure the recommended surveillance interval. In order to meet the desired clinical thresholds, however, EC-based policies require a careful reassessment of the current postpolypectomy surveillance guidelines. When considering the intrinsic limit of EC-accuracy, the recommendation of a 10-year interval for low-risk adenomas would minimize any risk of EC-based false-positive/negative result, prompting for an immediate implementation of these new policies in clinical practice.

Conflicts of Interest

The authors have no financial conflicts of interest.

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