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RETROSPECTIVE STUDY

Virtual chromoendoscopy in small bowel capsule endoscopy: New light or a cast of shadow?

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Abstract

AIM: To evaluate whether virtual chromoendoscopy can improve the delineation of small bowel lesions previously detected by conventional white light small bowel capsule endoscopy (SBCE).

METHODS: Retrospective single center study. One hundred lesions selected from forty-nine consecutive conventional white light SBCE (SBCE-WL) examinations were included. Lesions were reviewed at three Flexible Spectral Imaging Color Enhancement (FICE) settings and Blue Filter (BF) by two gastroenterologists with experience in SBCE, blinded to each other's findings, who ranked the quality of delineation as better, equivalent or worse than conventional SBCE-WL. Inter-observer percentage of agreement was determined and analyzed with Fleiss Kappa (κ) coefficient. Lesions selected for the study included angioectasias (*n* = 39), ulcers/erosions (*n* = 49) and villous edema/atrophy (*n* = 12).

RESULTS: Overall, the delineation of lesions was improved in 77% of cases with FICE 1, 74% with FICE 2, 41% with FICE 3 and 39% with the BF, with a percentage of agreement between investigators of 89% (κ = 0.833), 85% (κ = 0.764), 66% (κ = 0.486) and 79% (κ = 0.593), respectively. FICE 1 improved the delineation of 97.4% of angioectasias, 63.3% of ulcers/erosions and 66.7% of villous edema/atrophy with a percentage of agreement of 97.4% (κ = 0.910), 81.6% (κ = 0.714) and 91.7% (κ = 0.815), respectively. FICE 2 improved the delineation of 97.4% of angioectasias, 57.1% of ulcers/erosions and 66.7% of villous edema/atrophy, with a percentage of agreement of 89.7% (κ = 0.802), 79,6% (κ = 0.703) and 91.7% (κ = 0.815), respectively. FICE 3 improved the delineation of 46.2% of angioectasias, 24.5% of ulcers/erosions and none of the cases of villous edema/atrophy, with a percentage of agreement of 53.8% [κ = not available (NA)], 75.5% (κ = NA) and 66.7% (κ = 0.304), respectively. The BF improved the delineation of 15.4% of angioectasias, 61.2% of ulcers/erosions and 25% of villous edema/atrophy, with a percentage of agreement of 76.9% (κ = 0.558), 81.6% (κ = 0.570) and 25.0% (κ = NA), respectively.

CONCLUSION: Virtual chromoendoscopy can improve the delineation of angioectasias, ulcers/erosions and villous edema/atrophy detected by SBCE, with almost perfect interobserver agreement for FICE 1.

Key words: Capsule endoscopy; Virtual chromoendoscopy; Small bowel enteroscopy; Flexible Spectral Imag-

ing Color Enhancement Endoscopy; Imaging review

Core tip: One of the recent technical advances of small bowel capsule endoscopy (SBCE) technology is the possibility to enhance endoscopic imaging with computed virtual chromoendoscopy, using the Flexible Spectral Imaging Color Enhancement (FICE) or the Blue Filter modes. In our study, virtual chromoendoscopy, particularly FICE 1, improved the delineation of three main types of small bowel mucosal lesions: vascular (angioectasias), mucosal breaks (ulcers and erosions) and villous pattern (edema and atrophy), with substantial inter-observer agreement. Thus, we support the use of virtual chromoendoscopy as a complement to conventional white light SBCE for the evaluation of difficult to interpret endoscopic images.

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INTRODUCTION

Small bowel capsule endoscopy (SBCE) is a well established diagnostic procedure for the evaluation of small bowel diseases, with a high diagnostic yield when compared to other small bowel imaging modalities[1-5]. Recently, SBCE diagnostic abilities have been further expanded with the incorporation of virtual chromoendoscopy into the versions 6, 7 and 8 of RAPID® Reader (Given® Imaging Ltd, Yoqneam, Israel)[6-8], using the Flexible Spectral Imaging Color Enhancement (FICE, Fujinon Corporation®, Saitama, Japan) and the Blue Filter (BF). FICE uses a spectral estimation technology, narrowing the bandwidth of white light that permits an automatic reconstruction of pre-acquired conventional endoscopic images into virtual images with different wavelengths of red, green and blue, in order to enhance vascular contrast and the resolution of surface patterns[9,10]. The BF is another setting of virtual chromoendoscopy consisting of colour enhancement within a short wavelength range (490-430 nm). Virtual chromoendoscopy works with the convenience of a quick push-button switch between white light and chromoendoscopy with no need for dye spraying[11]. Virtual chromoendoscopy has been extensively investigated in the upper and lower GI tract[9,12-14], and recently in double-balloon enteroscopy[15]. Despite the conflicting data, most studies support its use to improve the evaluation of size, borders and mucosal pattern of different types of lesions[9,11,16-18]. However, it is currently controversial whether virtual chromoendoscopy may increase the diagnostic yield and diagnostic accuracy of SBCE, and what are the optimal wavelength filters to be used[7,11,19].

The aim of this study was to evaluate whether the currently available virtual chromoendoscopy settings may improve the delineation of the most frequent small bowel mucosal lesions detected by conventional white light SBCE (SBCE-WL).

MATERIALS AND METHODS

Type of study and selection of participants

We conducted a retrospective single center study, which included forty nine consecutive SBCE examinations for the investigation of patients with iron deficiency anemia, overt or occult obscure digestive bleeding and suspected or known Crohn's disease.

Procedures

All patients followed a 24 h clear liquid diet and 12 h fasting prior to SBCE (PillCam® SB, Given® Imaging Ltd Yoqneam, Israel). No oral purge was administered. All videos were reviewed with conventional white light by a gastroenterologist with extensive experience on SBCE (> 500 procedures), who selected 100 consecutive lesions to enter the study, including vascular lesions (angioectasias, $n = 39$), mucosal breaks (ulcers/erosions, $n = 49$) and villous morphology changes (villous edema/atrophy, $n = 12$) (Figure 1). All lesions were described using the terminology proposed by the Given Capsule Endoscopy working group[20]. According to the methodology of the study, two gastroenterologists with experience in SBCE (more than 200 examinations) reviewed the selected lesions using all three FICE settings and the BF, and were blinded to each other's evaluation. The settings used in the study were: FICE 1 (wavelength red 595 nm, green 540 nm, blue 535 nm), FICE 2 (wavelength red 420 nm, green 520 nm, blue 530 nm), FICE 3 (wavelength red 595 nm, green 570 nm, blue 415 nm) and BF (wavelength 490-430 nm). The sequence used by the reviewers was uniform, starting with FICE 1, then FICE 2, FICE 3 and finally the BF.

Variables and outcomes

SBCE-WL and virtual chromoendoscopy images were compared regarding the contrast of mucosal surface and clear demarcation of the borders of the lesions. Each investigator rated the delineation of lesions with each setting of FICE and BF mode as follows: +2 (remarkably better delineation with enhanced delineation of lesion surface and/or borders), +1 (slight improvement), 0 (equivalent to conventional SBCE-WL), -1 (worse delineation or inability to characterize a specific lesion). Finally, the scores attributed by the investigators were added for each lesion, such that a final score $\geqslant 2$ was classified as better delineation, a score between 0 and 1 was considered equivalent to conventional SBCE-WL, and a score $\leqslant -1$ indicated worse delineation with virtual chromoendoscopy.

Statistical analysis

Inter-observer percentage of agreement was determined

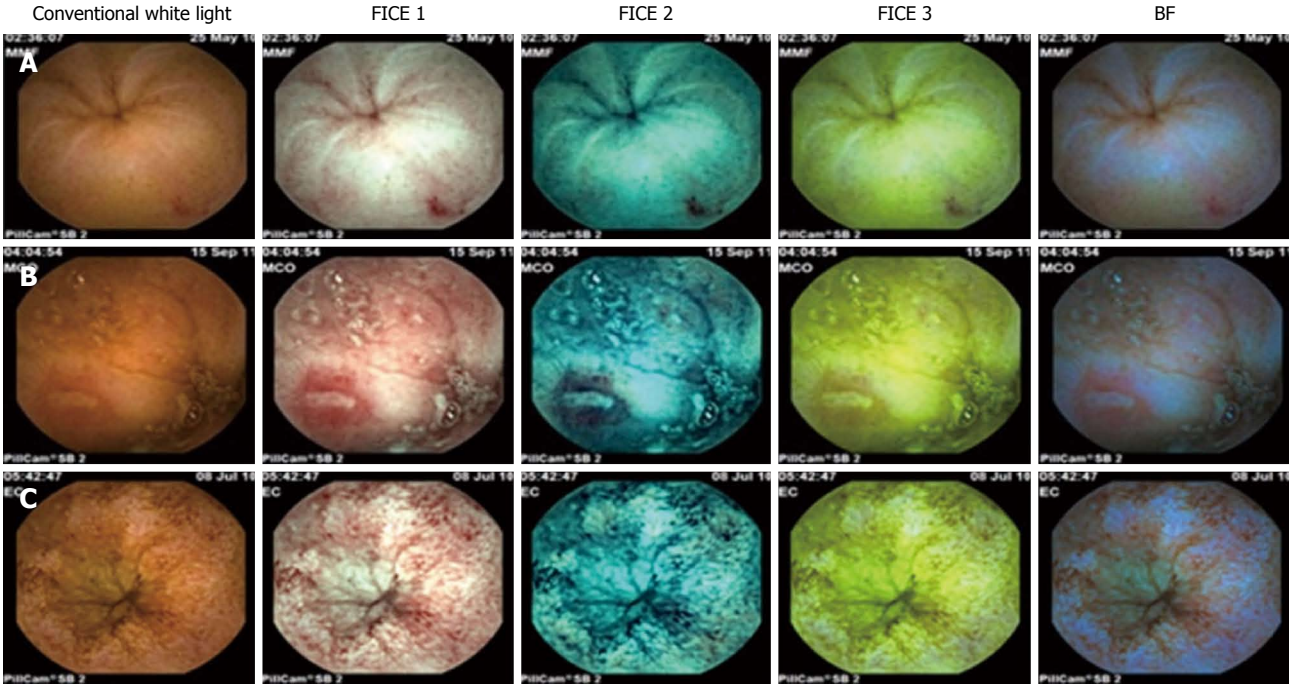

Figure 1 Small bowel mucosal lesions under conventional white light and virtual chromoendoscopy. A: Angioectasia; B: Ulcer; C: Villous edema.

Table 1 Summary of results

	Angioectasias (*n* = 39)	Ulcers/erosions (*n* = 49)	Villous edema/atrophy (*n* = 12)	Overall (*n* = 100)
FICE 1				
Improved delineation	38/39 (97.4%)	31/49 (63.3%)	8/12 (66.7%)	77/100 (77.0%)
Percentage of agreement, κ	97.4%, κ = 0.910	81.6%, κ = 0.714	91.7%, κ = 0.815	89.0%, κ = 0.833
FICE 2				
Improved delineation	38/39 (97.4%)	28/49 (57.1%)	8/12 (66.7%)	74/100 (74.0%)
Percentage of agreement, κ	89.7%, κ = 0.802	79.6%, κ = 0.703	91.7%, κ = 0.815	85.0%, κ = 0.764
FICE 3				
Improved delineation	18/39 (46.2%)	12/49 (24.5%)	0/12 (0.0%)	41/100 (41.0%)
Percentage of agreement, κ	53.8%, κ = NA	75.5%, κ = NA	66.7%, κ = 0.304	66.0%, κ = 0.486
BF				
Improved delineation	6/39 (15.4%)	30/49 (61.2%)	3/12 (25.0%)	39/100 (39.0%)
Percentage of agreement, κ	76.9%, κ = 0.558	81.6%, κ = 0.570	25.0%, κ = NA	79.0%, κ = 0.593

FICE: Flexible Spectral Imaging Color Enhancement; BF: Blue Filter; NA: Not available.

and analyzed using Fleiss *Kappa* coefficient, such that κ *(k)* < 0 indicated poor agreement, 0.00-0.20 slight agreement, 0.21-0.40 fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 substantial agreement, and 0.81-1.00 almost perfect agreement[21].

RESULTS

Overall, the delineation of small bowel mucosal lesions was improved in 77% of cases with FICE 1, 74% with FICE 2, 41% with FICE 3 and 39% with the BF, with a percentage of agreement between the two investigators of 89% [κ = 0.833 (*P* < 0.001), 95%CI: 0.741-0.925], 85% [κ = 0.764 (*P* < 0.001), 95%CI: 0.654-0.874], 66% [κ = 0.486 (*P* < 0.001), 95%CI: 0.345-0.627] and 79% [κ = 0.593 (*P* < 0.001), 95%CI: 0.438-0.748], respectively (Table 1). FICE 1 improved the delineation of 97.4% of vascular lesions (angioectasias), 63.3% of mucosal breaks (ulcers/erosions) and 66.7% of villous morphology changes (edema/atrophy), with a percentage of agreement of 97.4% [κ = 0.910 (*P* < 0.001), 95%CI: 0.736-1.084], 81.6% [κ = 0.714 (*P* < 0.001), 95%CI: 0.543-0.885 and 91.7% [κ = 0.815 (*P* < 0.001), 95%CI: 0.470-1.160], respectively. FICE 2 improved the delineation of 97.4% of angioectasias, 57.1% of ulcers/erosions and 66.7% of villous edema/atrophy, with a percentage of agreement of 89.7% [κ = 0.802 (*P* < 0.001), 95%CI: 0.620-0.984], 79.6% [κ = 0.703 (*P* < 0.001), 95%CI: 0.540-0.866] and 91.7% [κ = 0.815 (*P* < 0.001), 95%CI: 0.470-1.160], respectively. FICE 3 improved the delineation of 46.2% of angioectasias, 24.5% of ulcers/erosions and none of the cases of villous edema/atrophy, with a percentage of agreement of 53.8% (κ = NA), 75.5% (κ = NA) and 66.7% [κ = 0.304 (*P* = 0.098), 95%CI: -0.091-0.700],

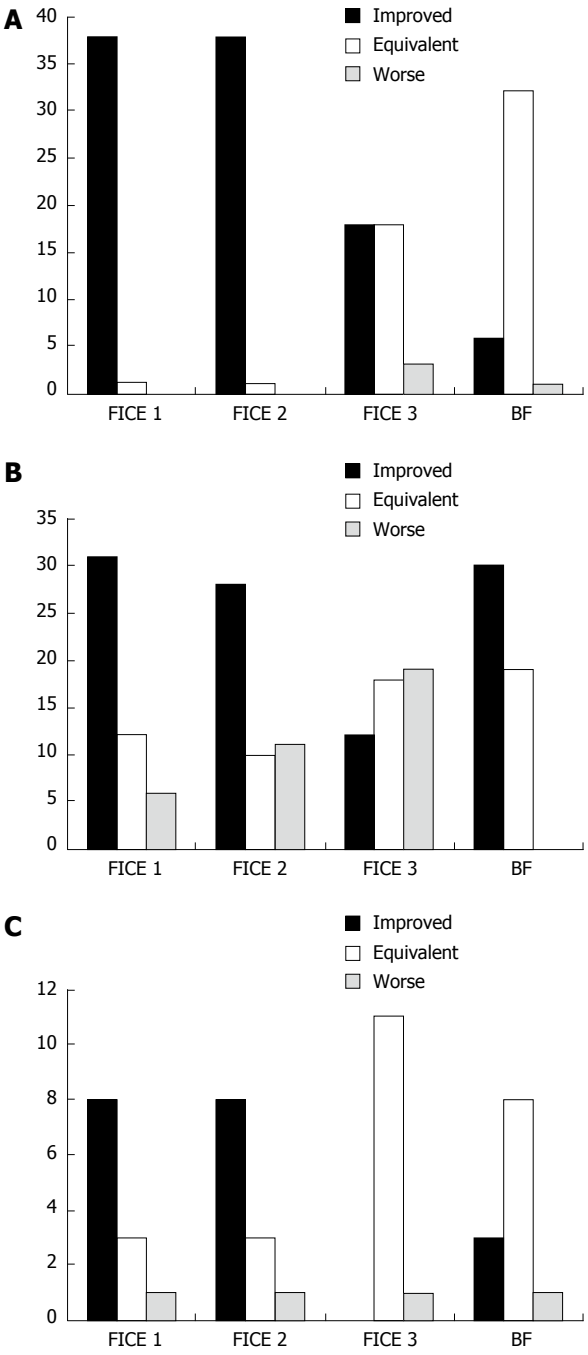

Figure 2 Delineation. A: Of angioectasias with all different settings of virtual chromoendoscopy: comparison with conventional white light; B: Of ulcers or erosions with all different settings of virtual chromoendoscopy: comparison with conventional white light; C: Of villous edema or atrophy with all different settings of virtual chromoendoscopy: comparison with conventional white ligh.

respectively. The BF improved the delineation of 15.4% of angioectasias, 61.2% of ulcers/erosions and 25% of villous edema/atrophy, with a percentage of agreement of 76.9% [κ = 0.558 (P < 0.001), 95%CI: 0.264-0.852], 81.6% [κ = 0.570 (P < 0.001), 95%CI: 0.333-0.807] and 25.0% (κ = NA), respectively. The detailed outcomes in terms of quality of delineation per type of lesion with each setting of virtual chromoendoscopy are summarized in graphical representation for angioectasias (Figure 2A), ulcers/erosions (Figure 2B) and villous edema/atrophy (Figure 2C).

DISCUSSION

Currently available data on the use of virtual chromoendoscopy on SBCE are scarce, with conflicting results reported in the literature regarding its accuracy and clinical value[7,11,22-24]. Moreover, there is ongoing discussion on what should be the optimal settings to improve the detection and/or delineation of different types of lesions[7,19]. Some important questions have been addressed[11], such as whether virtual chromoendoscopy may improve the detection rate of clinically relevant lesions, and whether it may contribute to a better characterization of lesions detected with conventional SBCE-WL. We should underline that a significant number of non-pathological or clinically irrelevant lesions may be detected when FICE is used, such as small red spots or prominent folds that may be erroneously interpreted as angioectasias when FICE is used[22]. Our study did not address this issue, since we did not perform a comparative evaluation of the full video using white light *vs* virtual chromoendoscopy; indeed, all images of the lesions selected to enter the study had been previously identified with SBCE-WL, as we aimed to evaluate whether virtual chromoendoscopy could improve the delineation of the most common lesions in the small bowel detected by the capsule.

We observed that, overall, FICE 1 and FICE 2 improved the delineation of small bowel lesions in up to 77% and 74% of the cases, respectively, with almost perfect interobserver agreement for FICE 1 [κ = 0.833 (P < 0.001), 95%CI: 0.741-0.925] and substantial interobserver agreement for FICE 2 [κ = 0.764 (P < 0.001), 95%CI: 0.654-0.874]. Conversely, the interobserver agreement was moderate with FICE 3 [κ = 0.486 (P < 0.001), 95%CI: 0.345-0.627)] and BF [κ = 0.593 (P < 0.001), 95%CI: 0.438-0.748], and these settings only improved the delineation of lesions in 41% and 39%, respectively. FICE 1 and FICE 2 were particularly useful improving the delineation of angioectasias (97.4% with both settings) and, to a lesser degree, ulcers/erosions (63.3% and 57.1%, respectively) and villous edema/atrophy (66.7% with both settings). Overall, FICE 1 and FICE 2 were superior to FICE 3 and BF for all types of lesions, which is in line with other published data[6,7,25] (Table 2). Interestingly, in the case of ulcers/erosions, the BF yielded good results, comparable to FICE 1 and FICE 2, improving the delineation of 61.2% of lesions, although with a lower interobserver agreement [κ = 0.570 (P < 0.001), 95%CI: 0.333-0.807].

The outcomes per type of lesion may be summarized as follows: the delineation of angioectasias was improved with either FICE 1 or FICE 2 in almost all cases (97.4%); the delineation of ulcers/erosions was improved in 57%-63% of the cases with either FICE 1 (63.3%), FICE 2 (57.1%) or BF (61.2%); the delineation of villous edema/atrophy was improved with either FICE 1 or FICE 2 in approximately two thirds (66.7%) of the cases. As in other published studies[7,19,23], we found FICE 3 to

Table 2 Summary of publications on small bowel capsule endoscopy-virtual chromoendoscopy

Ref.	Center	Study type	No. of patients	Outcome	Results
Imagawa *et al*[7]	Single center	Retrospective	122 patients	Delineation	145 lesions FICE 1: improved delineation in 87.0% (20/23) of angioectasias, 53.3% (26/47) of ulcers/erosions and 25.3% (19/75) of tumors FICE 2: improved delineation in 87.0% (20/23) of angioectasias, 25.5% (12/47) of ulcers/erosions and 20.0% (15/75) of tumors FICE 3: no improvement
Imagawa *et al*[6]	Single center	Prospective	50 patients	Detection rate	FICE 1: increased detection rate of angioectasias (48 *vs* 17, $P = 0.0003$) FICE 2: increased detection rate of angioectasias (45 *vs* 17, $P < 0.0001$) FICE 3: increased detection rate of angioectasias (24 *vs* 17, P = ns) Detection of ulcers, erosions and tumors did not differ significantly between conventional SBCE-WL and SBCE-FICE
Gupta *et al*[22]	Single center	Retrospective	60 patients	Detection rate	157 lesions detected with SBCE-FICE *vs* 114 with SBCE-WL ($P = 0.15$) 5/55 angioectasias were better characterized with SBCE-FICE More P0 diagnosed with SBCE-FICE (39 *vs* 8, $P < 0.001$) Intra-class κ correlations with SBCE-FICE: 0.88 (P2 lesions); 0.61 (P1 lesions) Intra-class κ correlations with SBCE-WL: 0.92 (P2 lesions); 0.79 (P1 lesions) For P2 lesions, the sensitivity was 94% *vs* 97% and specificity was 95% *vs* 96% for SBCE-FICE and SBCE-WL, respectively
Krystallis *et al*[19]	Single center	Retrospective	200 patients	Delineation	167 lesions including angioectasias ($n = 18$), erosions/ulcers ($n = 60$), villi oedema ($n = 17$), cobblestone ($n = 11$), blood lumen ($n = 15$), lesions of unknown clinical significance ($n = 46$) FICE 1: improved delineation in 34%; κ = 0.646 FICE 2: improved delineation in 8.6%; κ = 0.617 FICE 3: improved delineation in 7.7%; κ = 0.669 Blue mode: improved delineation in 83%; κ = 0.786
Duque *et al*[8]	Single center	Prospective	20 patients	Detection rate	150 lesions SBCE-FICE: increased detection rate (95 *vs* 75), κ = 0.650 SBCE-FICE did not miss any lesion identified by CE-WL and allowed the identification of a higher number of angioectasias (35 *vs* 32, $P = 0.25$) and erosions (41 *vs* 24, $P < 0.001$)
Nakamura *et al*[25]	Single center	Prospective	50 patients	Detection rate (QuickView)	SBCE-WL: sensitivity 80%, specificity 100% SBCE-FICE: sensitivity 91% specificity 86% SBCE-FICE resulted in more false positive findings and lower specificity
Sakai *et al*[26]	Single center	Prospective	12 patients	Detection rate	142 lesions including angioectasias ($n = 60$) and ulcers/erosions ($n = 82$) Angioectasias were detected with CE-WL (26/60), SBCE-FICE 1 (40/60), SBCE-FICE 2 (38/60), SBCE-FICE 3 (31/60) Ulcers/erosions were detected with SBCE-WL (38/82), SBCE-FICE 1 (62/82), SBCE-FICE 2 (60/82), SBCE-FICE 3 (20/82) SBCE-FICE 1and 2 significantly increased the detection rate of angioectasias ($P = 0.0017$ and $P = 0.014$, respectively) and ulcers/erosions ($P = 0.0012$ and $P = 0.0094$, respectively) In poor bowel visibility conditions, SBCE-FICE yielded a high rate of false-positive findings
Cotter *et al*	Single center	Retrospective	49 patients	Delineation	100 lesions including angioectasias ($n = 39$), ulcers/erosions ($n = 49$), villous edema/atrophy ($n = 12$) FICE 1: image improvement in 77% (κ = 0.833) FICE 2: image improvement in 74% (κ = 0.764) FICE 3: image improvement in 66% (κ = 0.486) BF: image improvement in 79% (κ = 0.593) FICE 1 improved the delineation of 97.4% of angioectasias, 63.3% of ulcers/erosions and 66.7% of villous edema/atrophy FICE 2 improved the delineation of 97.4% of angioectasias, 57.1% of ulcers/erosions and 66.7% of villous edema/atrophy FICE 3 improved the delineation of 46.2% of angioectasias, 24.5% of ulcers/erosions and none of the cases of villous edema/atrophy BF improved the delineation of 15.4% of angioectasias, 61.2% of ulcers/erosions and 25.0% of villous edema/atrophy

FICE: Flexible Spectral Imaging Color Enhancement; BF: Blue Filter; SBCE-WL: White light small bowel capsule endoscopy.

be ineffective for the vast majority of small bowel mucosal lesions. The results of our study suggest that FICE 1 (wavelengths red 595 nm, green 540 nm, blue 535 nm) seems to achieve the optimal appearance of vascular and mucosal contrast for small bowel lesions, with the highest interobserver agreement among all settings of FICE, and thus it should generally be the setting of choice when using virtual chromoendoscopy. Imagawa *et al*[7] had reported that both FICE 1 and FICE 2 could improve the delineation of ulcers and erosions, however the detection

rate of such lesions was similar between white light and virtual chromoendoscopy[6]. Similarly to our study, Krystallis *et al*[19] reported a better delineation of ulcers using the BF. Duque *et al*[8] reported an improvement in the diagnosis of erosions using FICE 2, due to the enhancement of its inflammatory halo. Regarding villous edema/atrophy, in our study it was better visualized with FICE 1 and FICE 2, while other authors[19] have found edema to be better visualized with the BF mode.

In summary, our results suggest that virtual chromoendoscopy, and particularly FICE 1, may be used in those cases where the characterization or interpretation of small bowel lesions is not straightforward with conventional SBCE-WL. On the other hand, in our study virtual chromoendoscopy did not lead to reclassification of any of the lesions detected with conventional SBCE-WL, and we did not evaluate whether it could contribute to increase the diagnostic yield of SBCE by identifying new lesions previously undetected with SBCE-WL, as we evaluated pre-selected lesions, which had already been previously diagnosed. Moreover, in the absence of a gold standard, it is not possible to accurately assess the false positives rate of these new techniques. Thus, at this point, although virtual chromoendoscopy has been shown to improve the delineation of small bowel lesions previously diagnosed by conventional SBCE-WL, the impact of this technology on the detection rate, accuracy of diagnosis and improved clinical outcome warrants further investigation. Our data support the current use of virtual chromoendoscopy as a complement to conventional white light SBCE for the evaluation of difficult to interpret endoscopic images.

COMMENTS

Background

One of the recent technical advances of small bowel capsule endoscopy (SBCE) is the possibility to enhance endoscopic imaging with computed virtual chromoendoscopy, using the Flexible Spectral Imaging Color Enhancement (FICE) or the Blue Filter (BF) modes. However, it is currently controversial whether virtual chromoendoscopy may increase the diagnostic yield and diagnostic accuracy of SBCE, and what are the optimal wavelength filters to be used.

Research frontiers

The authors aimed to evaluate whether different settings of FICE or the Blue Filter could improve the delineation of the most frequent small bowel mucosal lesions detected by conventional white light small bowel capsule endoscopy (SBCE-WL), namely the three main types of small bowel mucosal lesions: vascular (angioectasias), mucosal breaks (ulcers and erosions) and villous pattern (edema and atrophy).

Innovations and breakthroughs

Virtual chromoendoscopy improved the delineation of three main types of small bowel mucosal lesions: vascular (angioectasias), mucosal breaks (ulcers and erosions) and villous pattern (edema and atrophy). FICE 1 (wavelengths red 595 nm, green 540 nm, blue 535 nm) seems to achieve the optimal appearance of vascular and mucosal contrast for small bowel lesions, with the highest interobserver agreement among all settings of FICE, and thus it should generally be the setting of choice when using virtual chromoendoscopy.

Applications

The results suggest that virtual chromoendoscopy, and particularly FICE 1, may be used in those cases where the characterization or interpretation of small bowel lesions is not straightforward with conventional SBCE-WL. Authors' support the use of virtual chromoendoscopy as a complement to conventional white light SBCE for the evaluation of difficult to interpret endoscopic images.

Terminology

FICE (Fujinon Corporation®, Saitama, Japan) is a computed virtual chromoendoscopy modality that uses a spectral estimation technology, narrowing the bandwidth of white light that permits an automatic reconstruction of pre-acquired conventional endoscopic images into virtual images with different wavelengths of red, green and blue, in order to enhance vascular contrast and the resolution of surface patterns. BF is a different setting of virtual chromoendoscopy consisting of colour enhancement within a short wavelength range (490-430 nm).

Peer review

In a retrospective study, the authors have evaluated virtual chromoendoscopy SBCE in the delineation of small bowel lesions previously detected by white light SBCE. The virtual chromoendoscopy included 3 types of FICE and a blue filter. This is an interesting report.

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