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Brief Report - Clinical

Dysplasia detection using high-definition scopes with dye vs virtual chromoendoscopy in IBD: A meta-analysis of randomized clinical trials

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Lay Summary

This meta-analysis of 8 randomized controlled trials compares the effectiveness of using high-definition scopes with virtual chromoendoscopy vs dye chromoendoscopy for detecting dysplasia in inflammatory bowel disease patients. Overall, the odds of dysplasia detection were not significantly different between dye chromoendoscopy and virtual chromoendoscopy.

Key words: chromoendoscopy, ulcerative colitis, Crohn's disease, meta-analysis, high-definition

Introduction

Patients with inflammatory bowel disease (IBD) are at increased risk of colon cancer, and IBD-associated colon cancers tend to occur at a younger age with worse outcomes than the general population.[1,2] American Gastroenterological Association guidelines in 2021 stated that dye chromoendoscopy (DCE) to enhance dysplasia detection should be considered, particularly if standard-definition white light endoscopy (SD-WLE) is used, and that virtual chromoendoscopy (VCE) can be a suitable alternative to DCE if high-definition white light endoscopy (HD-WLE) is used.[3] This is primarily based on a 2020 meta-analysis of randomized controlled trials by El-Dallal et al.[4] even though guidelines also state that earlier studies have not been favorable for VCE. More studies on this topic have since been published. A recent meta-analysis concluded DCE was superior to HD-WLE with biopsies.[5] The purpose of this study was to perform an updated systematic review and meta-analysis on the effectiveness of DCE and VCE for dysplasia detection in IBD patients undergoing HD-WLE.

Methods

We comprehensively searched the databases PubMed, EMBASE, and Cochrane Library from inception to March 31, 2024. A combination of keywords, free text, and medical subject headings terms were used to include variations of the terms "inflammatory bowel disease," "virtual chromoendoscopy," and "dye chromoendoscopy." An additional manual search and review of the reference lists of included and relevant studies was performed. We followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria. We only included articles written in the English language. M.F.H.M., A.B., and K.A. independently reviewed and performed data abstraction on retrieved articles guided by predefined criteria. The author S.A.S. adjudicated any discrepancies.

We included studies that met the following criteria: (1) randomized controlled trials (RCTs); (2) HD-WLE was used for all study participants; (3) the primary study comparison was between DCE and VCE, which included narrow band imaging (NBI), iSCAN, autofluorescence imaging (AFI), and flexible spectral imaging color enhancement (FICE); and (4) the primary outcome was dysplasia detection, defined as the number of patients with at least 1 dysplastic lesion detected, including adenomatous lesions. Studies were excluded if the study population had non-IBD patients or used SD-WLE.

Data were abstracted onto predesigned data collection forms. Cochrane risk of bias tool for randomized trials (RoB-2) was used to assess quality and risk of bias, and GRADE (Grading of Recommendations, Assessment, Development and Evaluation) criteria were used to rate the certainty of evidence.

We performed a comparative effectiveness meta-analysis utilizing the random effects model with the primary outcome of

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Key Messages

What is already known?
Dye chromoendoscopy is superior to high-definition white light endoscopy for dysplasia detection in inflammatory bowel disease patients.

What is new here?
When using high-definition scopes, this meta-analysis shows no significant differences in dysplasia detection in inflammatory bowel disease patients between dye chromoendoscopy and virtual chromoendoscopy.

How can this study help patient care?
Previous data suggest that dye chromoendoscopy is superior to high-definition white light endoscopy for dysplasia detection. Still, the superiority of virtual chromoendoscopy over high-definition white light endoscopy is not established. This study suggests that virtual chromoendoscopy could be a viable alternative to dye chromoendoscopy when dye chromoendoscopy is not available.

per-patient dysplasia detection. We used odds ratios (ORs) for comparison with 95% confidence intervals (CIs). I^2 was used to assess heterogeneity.

Results

After removing duplicates, 360 studies were reviewed for inclusion. Of these, 308 studies were excluded after initial screening; of the remaining 52 studies, 17 were not the correct study design, 14 were not the correct study population, 4 were not the correct study outcome, and 9 were excluded for other reasons. Ultimately, 8 studies met our inclusion/exclusion criteria, of which 7 were published as full papers at the time of review (Table 1). Risk of bias was low overall. Pellise et al. had some concern in terms of bias from the randomization process. Watanabe et al. had some concern in terms of bias from deviation from intended intervention, missing outcome data, measurement of outcome, and selection of reported results. Gulati et al. had some concern in terms of bias from the randomization process, deviation from intended intervention, missing outcome data, and selection of reported results.

Three RCTs used NBI, 3 used iSCAN, 1 used FICE, and 1 used AFI. Overall, odds of dysplasia detection were not significantly different between DCE and VCE (OR, 1.2; 95% CI, 0.86-1.7; $P = .275$; $I^2 = 12.5\%$) (Figure 1A). This was still true when we limited our analysis to full-text articles (n = 7) (OR, 1.3; 95% CI, 0.87-1.9; $P = 0.200$; $I^2 = 16.6\%\%$) (Figure 1B).

GRADE assessment demonstrated low certainty of evidence both overall and when only full-text studies were included. Overall, 1152 patients were included in analysis with a relative effect of 1.162 (95% CI, 0.880-1.532) and an absolute difference of 25 more patients with dysplasia detected per 1000 patients, favoring DCE. In full-text studies only, 889 patients were included with a relative effect of 1.217 (95% CI, 0.888-1.666) and an absolute difference of 36 more patients with dysplasia was detected per 1000 patients, favoring DCE. Certainty of evidence was downgraded 2 levels due to imprecision.

Table 1. Description of all studies included for meta-analysis.

Author	Country	Sample size	Mean age (y)	Female	IBD type	Mean disease duration (y)	VCE	DCE	Publication type
Bisschops (2018)[12]	Canada	131	52.3	58 (44)	UC	15	NBI	0.1% methylene blue	Full
Pellise (2011)[6]	Spain	60	48.3	27 (45)	42 UC/19 CD	15.9	NBI	Indigo carmine	Full
Watanabe (2016)[7]	Japan	263	51	127 (48)	UC	13	NBI	Indigo carmine	Abstract
Iacucci (2018)[13]	Canada	180	48.7	122 (45)	129 UC/136 CD/5 IC	17.7	iSCAN	0.04% methylene blue or 0.03% of indigo carmine	Full
González-Bernardo (2021)[14]	Spain	129	50.4	62 (48)	UC/CD	17.7	iSCAN	0.03% indigo carmine	Full
Jans (2024)[15]	European multicentric trial	131	50 y	79 (60)	UC	17.2	iSCAN	Methylene blue (0.1%)	Full
Gulati (2018)[8]	United Kingdom	48	44.9 y	18 (37.5)	45 UC/3 CD	14.5	FICE	Indigo carmine	Full
Vleugels (2018)[16]	The Netherlands and United Kingdom	210	56.2 y	88 (42)	UC	20.8	AFI	0.1% methylene blue solution or 0.2% indigo carmine solution	Full

Values are n or n (%), unless otherwise indicated.
Abbreviations: AFI, autofluorescence imaging; CD, Crohn's disease; DCE, dye chromoendoscopy; FICE, flexible spectral imaging color enhancement; IBD, inflammatory bowel disease; IC, indeterminate colitis; NBI, narrow-band imaging; UC, ulcerative colitis; VCE, virtual chromoendoscopy.

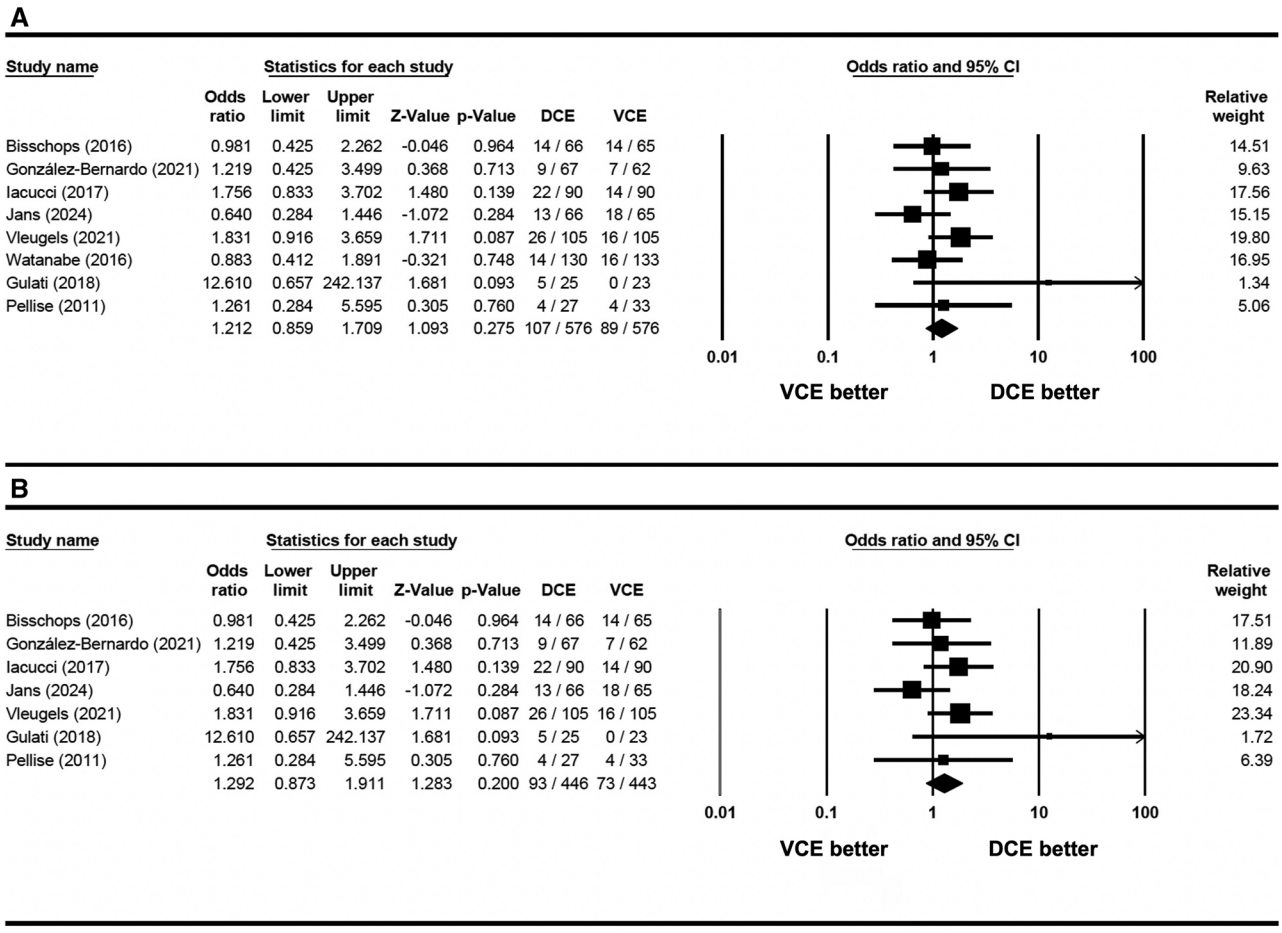

Figure 1. Forest plots of (A) all studies and (B) full-text studies only, comparing outcome of dysplasia detection between dye chromoendoscopy (DCE) and virtual chromoendoscopy (VCE). CI, confidence interval.

Discussion

With the advent of newer technologies, updated guidelines are needed to standardize our approach to surveillance colonoscopies for IBD patients. In our previous meta-analysis of RCTs, we demonstrated that DCE was superior to HD-WLE, but we did not examine VCE.[5] For this current meta-analysis, we show that DCE and VCE are not significantly different in terms of dysplasia detection.

Prior meta-analyses on this topic have differed in terms of their conclusions. Similar to our analysis, El-Dallal et al. found no significant difference in dysplasia detection between VCE and DCE in a per-patient analysis. In contrast, 2 network meta-analyses by Shehab et al. and Sinopoulou et al.[0] have concluded that DCE is superior to other endoscopy types, including VCE, in terms of dysplasia detection. However, for Shehab et al.this conclusion appears to have been made based on a per-lesion analysis. In their per-patient analysis, DCE was inconsistently better than VCE, with no significant difference noted between DCE and FICE or AFI, while outperforming NBI and iSCAN. Additionally, this meta-analysis included older studies that used SD-WLE, which is established to be inferior to HD-WLE. For Sinopoulou et al. this conclusion was made based on a comparison of chromoendoscopy types against HD-WLE, with no direct comparison made between DCE and VCE.

The strength of this study is in its inclusion criteria. We included RCTs only, reducing bias present in other study types. The quality of included studies was moderate. Additionally, as discussed previously, we only included studies that directly compared DCE with a VCE modality. We also only included studies that evaluated HD-WLE, which are more commonly used as compared with SD-WLE. However, the limitation of this approach is that the number of studies included is small, making it more likely to miss a difference in effect.

The findings of this study have important implications for clinical practice. In comparison with DCE, VCE may be more accessible to the gastroenterologist. It is simpler to perform, which can reduce the amount of time needed to learn and perform chromoendoscopy. This may also reduce operator variability based on expertise and experience. Additionally, DCE effectiveness is arguably more dependent on the quality of the bowel preparation compared with VCE. In S.A.S.'s practice, DCE is the preferred method for surveillance colonoscopies for IBD patients, often in conjunction with VCE, as it can lead to a more thorough evaluation of the mucosa during the second pass. Using dye spray can help ensure that all of the mucosa has been examined because missed areas would not have been stained. Furthermore, while our previous meta-analysis demonstrated that chromoendoscopy is superior to HD-WLE with random biopsies, there still may be some benefit of random biopsies in addition to targeted bi-

opsies with chromoendoscopy. A meta-analysis by Gao et al.[1] demonstrated an approximately 7% additional yield of random biopsies in a per-patient analysis for patient receiving advanced modalities, including chromoendoscopy. Patients with primary sclerosing cholangitis particularly seem to benefit from random biopsies. In our practice, we have utilized random biopsies on top of target biopsies with chromoendoscopy in select patient populations at high risk of dysplasia, such as patients with primary sclerosing cholangitis, previous dysplasia, pseudopolyps, and foreshortened gut.

Conclusions

Previously, we have shown that DCE is superior to HD-WLE alone. This meta-analysis demonstrates no significant difference in dysplasia detection for IBD patients between DCE and VCE. Gastroenterologists should select the chromoendoscopy technique with which they are most comfortable for surveillance in IBD. Future research should evaluate long-term outcomes for DCE and VCE, such as cancer diagnosis and mortality.

Author contributions

M.F.H.M.—study concept and design, acquisition of data, analysis of data, manuscript revision. J.J.C.—analysis of data, manuscript drafting, manuscript revision. A.B.—acquisition of data, analysis of data, manuscript revision. T.N.—analysis of data, manuscript revision. K.A.—acquisition of data, manuscript revision. S.A.S.—study concept and design, analysis of data, manuscript revision, study supervision.

Conflicts of interest

S.A.S. has served on the advisory board for Pfizer and as a consultant for Roche Information Systems. All other authors disclose no conflicts.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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