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Endocuff Vision is safe to use for dysplasia surveillance in patients with ulcerative colitis: a feasibility study

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ABSTRACT

Background and study aims Endocuff Vision improves adenoma detection rates in patients without inflammatory bowel disease. This study aimed to investigate the safety and feasibility of Endocuff Vision-assisted high-definition white light endoscopy (HDWLE) with dye-spray chromoendoscopy for detection of dysplasia in patients with ulcerative colitis.

Patients and methods Patients with clinically inactive ulcerative colitis due for dysplasia surveillance were recruited. Procedural endpoints included safety, cecal intubation rate (CIR), terminal ileum intubation rate (TIR), withdrawal time, polyp detection rate, dysplasia detection rate (DDR), and sessile serrated lesion detection rate.

Results Twenty-five patients (9 female, median age 57 [range 28–82] years) were studied. Endocuff Vision-assisted HDWLE was completed in all participants, with a CIR of 100%, in a median 4 minutes (range 2–16), and a TIR of 88% in a median of 6.5 minutes (range 3–19). Median withdrawal time was 18 minutes (range 10–55), including application of dye-spray, biopsies and polypectomy. The Mayo Endoscopic subscore was 0 in 11, 1 in 9, and 2 in 5 patients. The DDR was 24% (6 patients had a total of 12 dysplastic lesions) and sessile serrated lesion detection rate was 12% (3 patients had a total of 4 sessile serrated polyps). No serious adverse events occurred, with one patient developing clinically insignificant minor mucosal bleeding.

Conclusion Endocuff Vision-assisted HDWLE is feasible and safe in patients with ulcerative colitis undergoing dysplasia surveillance. Further studies are required to assess superiority of this technique compared with standard high-definition white light endoscopy with chromoendoscopy.

Introduction

Risk of developing colorectal cancer (CRC) in patients with ulcerative colitis (UC) is estimated at 1.5 to 2.4 times the background population [1,2], with most cancers arising from endoscopically visible dysplastic lesions [3,4]. Surveillance colonoscopy with dye-spray chromoendoscopy is currently recommended for detection and subsequent endoscopic removal of dysplastic lesions in patients with UC [1,2,5]. Furthermore, detection of CRC at an early stage via endoscopic surveillance has been demonstrated to reduce morbidity and mortality [6].

Dysplastic lesions in patients with UC are often flat and therefore more likely missed during routine inspection [7,8]. With evolving endoscopic technologies, miss rates for such lesions in comparison with standard-definition, white-light endoscopy (WLE) have been reduced [9–12]. Current international consensus guidelines recommend use of high-definition WLE (HDWLE) and chromoendoscopy to optimize detection of colitis-associated dysplasia [1]. Nonetheless, the cost-effectiveness of these approaches, along with precise surveillance intervals, is still poorly characterized. Improvements in techniques that enable detection and removal of dysplastic lesions, along with therapeutic developments to optimize disease control,

may enable extension of surveillance intervals while still reducing risk of CRC.

Endocuff Vision (ARC Medical Design Ltd) is a distal colonoscopic attachment with soft, finger-like projections that aims to flatten mucosal folds and has been shown to improve adenoma detection rate (ADR) in patients without inflammatory bowel disease (IBD) undergoing CRC screening [13–18]. This device is not currently recommended in patients with severe colitis due to concerns regarding mucosal trauma [19] but has not previously been studied in patients with clinically inactive IBD undergoing surveillance colonoscopy for detection of dysplasia.

The aims of this pilot study were, therefore, to assess the safety and feasibility of Endocuff Vision-assisted HDWLE and chromoendoscopy in patients with clinically quiescent UC undergoing dysplasia surveillance.

Patients and methods

Consecutive patients with clinically inactive UC (Simple Clinical Colitis Activity Index (SCCAI) [20] < 3) who met criteria for dysplasia surveillance according to national and international guidelines [1, 5,21,22] were invited to participate in this prospective observational study. Exclusion criteria are outlined in ▶ **Table 1**.

All procedures were performed by one of two experienced colonoscopists with subspecialty interest in IBD and endoscopy, and trained in use of Endocuff Vision (MG and DvL). Patients received split-dose bowel preparation using sodium picosulfate/magnesium oxide/citric acid (Picoprep, Fresenius Kabi Australia Pty Ltd) and macrogol/sodium sulphate/sodium chloride/potassium chloride/ascorbic acid (Glycoprep-C, Fresenius Kabi) and underwent propofol-based deep sedation administered by a specialist anesthetist. Quality of bowel preparation was graded using the Boston Bowel Preparation Scale (BBPS), a score calculated by the summation of three individual colonic segment scores (from the right, transverse, and left colon) to indicate the degree of bowel visualization [23]. Chromoendoscopy was performed during withdrawal using 0.02 % methylene blue and sprayed to coat the pan-colonic mucosal surface using a foot pump. It was pre-specified that the colonoscope was to be withdrawn and Endocuff Vision removed in case of a fixed sigmoid colon with acute angulation, severe (Mayo Endoscopic Subscore 3) colitis, severe diverticulosis, identification of a new colonic stricture and/or obstructive cancer. Procedural endpoints included adverse events (including minor mucosal bleeding), cecal intubation rate (CIR) and time, terminal ileum intubation rate (TIR) and time, total withdrawal time, polyp detection rate, dysplasia detection rate, sessile serrated lesion detection rate, and requirement for removal of Endocuff Vision.

Participants were contacted by telephone to ascertain post-procedural complications including pain and rectal bleeding at days 1, 7 and 21.

Role of the funding source

This was an investigator-initiated study with an unrestricted grant from Norgine Pty Ltd, Australia. Endocuff Vision devices were provided by Norgine for free. No representatives from Norgine were involved in development of the study protocol or performance, collation or analysis of data, or manuscript preparation.

▶ **Table 1** Exclusion criteria.

Pregnancy
Known cancer or polyposis syndrome
Colonoscopy to remove known dysplastic or serrated lesion
Known colonic strictures
Known severe diverticular disease
Prior colonic resection
Clinically active UC (SCCAI ≥ 3)
Clopidogrel, warfarin, direct-acting anticoagulants (DOACs) unable to be withheld prior to the procedure

UC, ulcerative colitis

Statistical analysis

Data analyses were performed using Stata v12 (StataCorp, 2011), and SPSS (22.0, IBM Corp, 2013). As this was a pilot feasibility study, a specific sample size calculation was not performed.

Ethical considerations

All subjects provided written informed consent prior to participation in the study. This study was approved by the Office of Research and Ethics at Eastern Health (LR 90/2016).

Results

Twenty-seven patients were recruited, with one patient withdrawn due to the presence of clinically active disease (SCCAI ≥ 3) at time of procedure and a second patient excluded from analyses due to evidence of terminal ileitis noted at the colonoscopy, requiring change of diagnosis to Crohn's disease. Patient and disease characteristics are presented in ▶ **Table 2**.

Endocuff Vision-assisted HDWLE was completed in all participants. Most colonoscopies were performed by a single proceduralist (MG, 23 of 25). Key outcomes are outlined in ▶ **Table 3**. Nineteen patients (76 %) had excellent preparation as per Boston Bowel Preparation Score (BBPS) of 9, with one patient having inadequate preparation (BBPS 3). Cecal intubation was achieved in all patients (100 %). The terminal ileum (TI) was intubated to a depth of 5 cm or more in 11 patients (44 %), with a short intubation able to be performed in another 11 patients, and no views of the terminal ileum in three patients.

Safety

One patient was noted to have minor superficial linear mucosal bleeding in the rectum noted upon withdrawal in a segment of Mayo 1 inflammation, with no bleeding or other clinical sequelae. No other cases of mucosal trauma were noted. Endocuff Vision did not require removal in any patient, and no inadver-

▶ **Table 2** Baseline patient and disease characteristics.

Median Age (range)	57 years (29 – 82)
Female: Male	9:16
Montreal Classification at diagnosis[1]	(N = 25)
▪ Disease extent: E1:E2:E3	4:9:12
▪ Disease severity: S1:S2:S3	21:3:1
Median disease duration, y (range)	15 (8 – 42)
Median clinic SCCAI[2] (range)	0 (0 – 1)
Median pre-procedure SCCAI (range)	0 (0 – 2)
Previous abdominal surgery[3]	N = 10

[1] Montreal classification: UC disease extent: E1 – proctitis, E2 – left sided colitis, E3 – extensive colitis; UC disease severity: S1 – clinical remission, S2 – mild UC, S3 – moderate UC, S4 – severe UC.
[2] SCCAI: Simple Clinical Colitis Activity Index
[3] Any previous laparoscopic or open abdominal surgery related, or not related to inflammatory bowel disease

▶ **Table 3** Procedural outcome measures.

Procedural Outcomes	Number (n = 25)	Percentage
Adequate bowel preparation (BBPS ≥ 6)	24	96 %
Cecal Intubation Rate	25	100 %
Terminal ileum intubation rate	22	88 %
	Median	**Range**
Cecal insertion time (min)	4	2 – 16
Ileal insertion time (min)	6.5	3 – 19
Withdrawal time (min), unadjusted (inclusive of biopsies and polypectomy)	18	10 – 55
Withdrawal time (min), unadjusted (in patients without polypectomy)	14	10 – 22
Mayo Endoscopic Score	1	0 – 2

BBPs, Boston bowel preparation scale

tent detachment occurred. No patient reported abdominal pain. One patient experienced self-limiting small volume post-polypectomy bleeding on Day 2 with no haemodynamic compromise, decline in hemoglobin or requirement for hospitalization. Endocuff Vision was deemed not to have contributed to this event. No other post-procedural bleeding was reported.

Lesion detection

Sixty-three polypoid lesions were removed in 17 patients (▶ **Table 4**, ▶ **Fig. 1**). Six patients (24 %) had 12 dysplastic lesions (tubular adenomas with low-grade dysplasia), giving a dysplastic lesion per colonoscopy rate of 0.48. Three patients (12 %) had sessile serrated polyps.

All identified lesions were successfully resected at time of colonoscopy apart from one laterally spreading, 100-mm flat

▶ **Table 4** Resected polypoid lesions.

Pathology	Number
Tubular adenoma with LGD	12
▪ Cecum and ascending colon	6
▪ Transverse colon	3
▪ Descending and sigmoid colon	3
▪ Rectum	0
▪ Median Size (range)	4 mm (3 – 100)
Tubulo-villous adenoma	0
Sessile serrated polyp	4
▪ Cecum and ascending colon	3
▪ Transverse colon	1
▪ Descending and sigmoid colon	0
▪ Rectum	0
▪ Median size (range)	6.5 mm (4 – 20)
Hyperplastic polyp	20
▪ Median size (range)	4 mm (2 – 14)
Inflammatory pseudopolyp	1
Inflammatory tissue	3
Normal tissue	20
Polyp not retrieved	3
TOTAL	63

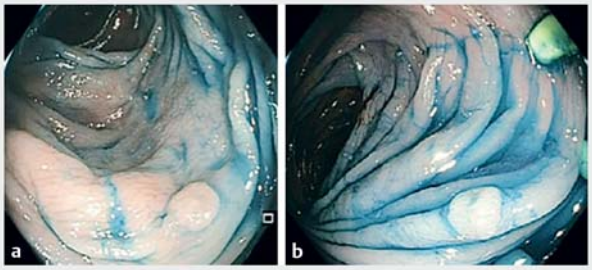
LGD, low-grade dysplasia

dysplastic lesion in the sigmoid colon, which was histologically confirmed as low-grade dysplasia on biopsy. The patient elected to undergo endoscopic resection followed by surveillance at a later date.

Discussion

Dysplastic lesions in patients with UC are typically flat and difficult to detect [7, 8]. Modern HDWLE and dye-spray chromoendoscopy have increased detection rates [9 – 11, 24], but lesions are still missed, and surveillance intervals and cost-effectiveness remain poorly defined. This pilot study demonstrates that a distal attachment improving ADR in a non-IBD population, Endocuff Vision, is safe and feasible for use in patients with UC.

Endocuff Vision has not previously been investigated in patients with IBD, and is relatively contraindicated in severe colitis due to theoretical concerns about mucosal trauma. In this study of patients with clinically inactive UC, withdrawal of the scope and removal of Endocuff Vision if severe colitis was unexpectedly encountered was planned but not required in any of 25 patients. Endocuff Vision-assisted colonoscopy was completed in all patients. One patient with Mayo endoscopic 1 disease in the rectum was noted to have self-limited mucosal bleeding (last-



▶ **Fig. 1** Endocuff Vision exposing sessile polypoid lesions. **a** Endocuff Vision flexible arms pulling mucosa down on the right, exposing a sigmoid polyp. **b** Endocuff Vision flexible arms interrogating adjacent mucosa to expose a sigmoid polyp.

ing less than 5 seconds) resulting from mild linear trauma, of no clinical consequence. However, eight other patients with Mayo 1 disease and five patients with Mayo 2 disease underwent the procedure without incident. Although these numbers are small, the suggestion from this cohort is that endoscopic inflammation up to Mayo 1, and probably Mayo 2, is compatible with safe use of Endocuff Vision.

Regarding other salient colonoscopic endpoints, a CIR of 100 % was achieved, with a TIR of 88 %. Deep TI intubation was achieved in 12 of 26 patients; one of whom was excluded from analyses upon detection of Crohn's ileitis. A brief view of 2 to 3 cm of the TI was achieved in 11 patients, with no clear view in three, due to the flexible arms of the device. This may represent a potential limitation to use of Endocuff Vision in patients with IBD, especially those with colonic Crohn's disease, in whom assessment of the TI may be clinically important. Nonetheless, in patients with confirmed UC, the primary aim of surveillance colonoscopy is to detect dysplasia and early CRC, both of which are unaffected by lack of visualization of the TI. Insertion and withdrawal times (including pancolonic dye-spray, biopsies and polypectomy) using the device were also within the range expected with non-Endocuff Vision-assisted chromoendoscopy, meaning total colonoscopy time did not appear to be prolonged [25]. Conversely, studies in Endocuff Vision-assisted colonoscopy in patients without IBD have demonstrated similar insertion times to the current study [26 – 28], and thus UC per se was not associated with slower insertion using Endocuff Vision.

It must be acknowledged that this was a relatively small feasibility study, with most colonoscopies performed by a single operator. To be applicable for use by all endoscopists, larger studies with multiple operators are required. This study was not designed to assess superiority of Endocuff Vision-assisted HDWLE over conventional colonoscopy for detection of dysplastic lesions. However, dysplasia was detected in six of 25 patients, with a further three patients having sessile serrated polyps. These rates are similar or higher than previously documented for chromoendoscopy surveillance in patients with UC [11, 29, 30]. Given that dysplasia in IBD is typically flat [7, 8] and may be hidden behind colonic folds, and the improved ADR using Endocuff Vision in the non-IBD population [13 – 16, 28], this device may improve detection of dysplasia in patients with IBD. To answer this question, an adequately powered controlled trial is required.

The potential value of Endocuff Vision-assisted chromoendoscopy in this population may lie in reduction in healthcare expense if future studies show improved sensitivity for detection of dysplastic lesions, and surveillance intervals can be increased through an improved negative predictive value of examinations. Sporadic adenoma detection in the same group of patients may also be enhanced. Though features that may differentiate colitis-associated dysplasia and sporadic adenomas have been described, none have been validated, and these lesions can appear similar histologically [31]. Previous histological activity predisposing to colitis-associated dysplasia may also assist, but can be difficult to determine accurately [11, 31, 32]. In this study, dysplastic lesions were not subclassified, but this may be considered on the basis of molecular markers in a future controlled comparative study. This device is far less expensive than other approaches that have been shown to confer additional efficacy such as the Endochoice Full Spectrum Endoscopy (FUSE) [33].

Conclusion

In conclusion, Endocuff Vision-assisted HDWLE with chromoendoscopy is feasible and safe in patients with UC undergoing surveillance colonoscopy, including in patients with up to mild to moderate disease activity. Further studies are required to confirm superiority of Endocuff Vision-assisted HDWLE with chromoendoscopy for detection of dysplastic lesions in patients with IBD compared with routine HDWLE with chromoendoscopy.

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Competing interests

Dr. Saunders has previously received an educational grant and equipment support from Arc Medical and is a paid speaker for Norgine Pty Ltd. The funding for this study was provided by Norgine Pty Ltd. The funding source had no role in the design, practice or analysis of this study.

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