



To chromo or not to chromo: That is the question!

Marion JF, Waye JD, Israel Y, et al. Chromoendoscopy Is More Effective Than Standard Colonoscopy in Detecting Dysplasia During Long-term Surveillance of Patients With Colitis. *Clin Gastroenterol Hepatol* 2016; 14: 713-9.

Ulcerative colitis and Crohn's disease increase the risk of colon cancer by two fold over the lifetime of the patient compared to the general North American population (1). Other factors that compound this elevated risk in our Inflammatory bowel disease (IBD) patients include the extent of disease, duration of disease, a family history of colon cancer and concomitant diagnosis of primary sclerosing cholangitis (PSC). Most society guidelines have endorsed IBD surveillance in the form of 4 quadrant biopsies every 10 cm with a total of 32 biopsy specimens. This technique is far from being ideal as random biopsies lack sensitivity at detecting dysplasia with dysplasia detection confidence being in only 5% of the colon surface area and 80% of the time with this technique (2). Most recently the SCENIC consensus statement favored the use of dye-spray chromoendoscopy (CE) as the ideal surveillance modality for our IBD patients. A large retrospective study published in 2015 showed that using dye-spray CE did not increase dysplasia yield when compared to standard white light or random biopsies (3). Clinical practice continues to be heterogeneous between gastroenterologists pertaining to surveillance methods used and even on the number of random biopsies obtained (4). With high definition white light colonoscopies and the ability to evaluate the mucosa with enhanced image resolution (5); are these random biopsies truly necessary and whether dye spray CE only needs to be performed in high risk patients?

Chromoendoscopy has been the proposed gold standard for surveillance in IBD which utilizes indigo carmine or methylene blue as a contrast agent to identify subtle or flat lesions throughout the colon. These lesions can then be biopsied specifically to increase the yield of dysplasia. A meta-analysis of six studies and 1277 patients by Subramanian et al in 2011 showed that CE was associated with a 7% greater yield in dys-

plasia detection. Four out of the six studies with a total of 1075 patients looked at miss rates of dysplasia with a cumulative 40% lower miss rate with CE when compared with white light endoscopy.

In the May 2016 issue of Clinical Gastroenterology and Hepatology, Marion and colleagues try to answer the ever elusive question- what is the optimal colon cancer surveillance method for our inflammatory bowel disease patients? They studied 68 IBD patients prospectively at Mount Sinai Hospital in New York from June 2006- October 2011 from their Index study that included 102 patients. All these patients were >18 years of age, had a confirmed diagnosis of extensive ulcerative colitis (at least left sided disease) or Crohn's colitis (>1/3rd of colonic involvement). Exclusion criteria for the study was having an inadequate bowel preparation, allergy to methylene blue dye, a glucose-6-phosphate deficiency, coagulation disorder, renal disease or a personal history of colon cancer. They followed the current surveillance timelines as set forth by the American Gastroenterological Association guidelines. They trained all the endoscopists at their institution with the correct method for CE. The patients in the study underwent all three methods of surveillance (standard white light endoscopy, dye-spray CE and random biopsies) at the same appointment. The endoscopist took 4 quadrants random biopsies from each segment, identified lesions on white light and biopsied or removed them with the aid of biopsy forceps or snare polypectomy and the methylene blue (0.1%) was applied to the mucosa starting from the cecum. The colonic mucosa was then examined for any visible lesions. The median follow up time for these patients was 27.8 Months. These 102 patients had a median disease duration of 21 years. Results showed that after three colonoscopies per patient only 6 dysplastic lesions were detected by random biopsy as opposed to targeted white light biopsies detecting 11 dysplastic lesions and CE detecting 27 respectively. A total of 4 patients were referred for colectomy for high-grade and low grade dysplasia. The dysplasia in these 4 patients was identified with methylene blue CE. Dysplasia detection with methylene blue

CE (odds ratio (OR), 5.4; 95% CI, 2.9-9.9; $p < 0.001$) and standard colonoscopy targeted white light biopsies (OR, 2.3; 95% CI, 1.0-5.3; $p = 0.054$) was higher than random biopsy sampling. Those having significant dysplasia who were referred for colectomy the pathology in the colectomy specimen was in agreement with pre-operative colonoscopy findings of dysplasia with dye-spray CE 80% of the time. White light targeted biopsies correctly identified dysplasia 10% of the time in the colectomy specimen whereas random biopsies were 20%.

Similar to other studies in the past, this study also supports the use of CE for dysplasia surveillance in IBD patients. This has also been recommended by the British Gastroenterology Society guidelines (6), consensus statements by the European Crohn's and Colitis organization (7) and the most recent Surveillance for Colorectal Endoscopic Neoplasia Detection and Management of Inflammatory Bowel Disease (SCENIC) consensus statement (8) advocating CE for optimal dysplasia surveillance in IBD patients. Despite the presence of this evidence, a vast majority of gastroenterologists chooses to continue with random biopsies for dysplasia surveillance in IBD. There are a number of reasons for this clinical inertia and slow adaptation of widespread CE.

Firstly, the Marion study and most other prior studies utilized standard definition colonoscopies in their comparison to dye-spray CE. The studies (3,9) above comparing High definition colonoscopy and targeted biopsies versus dye-spray CE did not find a difference in dysplasia detection among the two comparison groups. With these conflicting results more studies need to be done to definitively show that dye-spray CE is indeed superior to high definition white light colonoscopy.

Secondly, most endoscopists would want to know with longer procedural time spent doing dye-spray CE along with the increased cost, is this surveillance of any additional benefit? Can it increase the surveillance intervals with an exam negative for dysplasia when compared to high definition white light endoscopy?

The third factor limiting this uptake of CE could be trained of the gastroenterologists and nursing staff in dye-spray CE in community practices where patient volume for IBD surveillance is limited. Is it really feasible for them to spend all those resources to undergo training the staff for a few cases every month with limited proficiency or is it better to refer to an IBD center where superior expertise is available? The expertise at a large IBD center will provide a superior CE when compared with an endoscopist with inadequate training and not aware of what to really look for. Another reason is that patient bowel preparation needs to be excellent and there should be no visible inflammation.

As there are no studies that have evaluated the reduction in incidence of colon cancer in our IBD patients with the use of dye-spray CE and high definition white light colonoscopy, there will still be debate as to what will be the ideal. Till a lot of these questions are answered the majority of IBD patients without dysplasia can safely undergo either high definition white light colonoscopy with targeted biopsies or dye-spray CE depending on the expertise of the endoscopist and the individual risk to the patient of developing colonic neoplasia.

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