Chromoendoscopy in Community Practice


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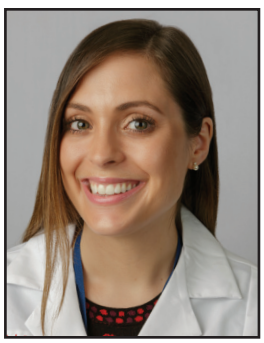
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Background: Patients with inflammatory bowel disease (IBD) have increased risk of developing colorectal neoplasia associated with chronic inflammation. Surveillance colonoscopy for longstanding disease is the standard of care. Typically, conventional white light endoscopy (WLE) is used with random biopsies; however, studies from several academic centers have demonstrated chromoendoscopy increases diagnostic yield for intraepithelial neoplasia in (IBD) compared with (WLE).

Aims:

Compare the feasibility and yield of chromoendoscopy vs WLE surveillance colonoscopy in a community based practice.

Methods:

A retrospective review of surveillance colonoscopies performed by one physician in a community based private practice with and without chromoendoscopy in patients with IBD between January 2005 & August 2012. Demographic data, time for procedure, number of biopsies, number of jars, and yield of dysplastic lesions were obtained.

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Results:
25 dysplastic lesions were found in 64 procedures with chromoendoscopy (39.1%) versus only 8 in 120 procedures (6.9%) with WLE (p<0.001).

Conclusions:
Chromoendoscopy is feasible in community private practice. Compared to WLE, chromoendoscopy yields a higher rate of dysplastic lesions, similar to the increased yield reported from academic centers.

INTRODUCTION

Early detection of dysplastic tissue during colonoscopy allows early intervention and may decrease colon cancer and improve survival.[1] Studies from several academic centers have demonstrated chromoendoscopy increases diagnostic yield for intraepithelial neoplasia in inflammatory bowel disease (IBD) compared with white-light colonoscopy (WLE).[2,3,4] The feasibility of this technique, however, has not been adequately studied in the community setting. Our study evaluates a single physician's experience with chromoendoscopy in patients with IBD.

Background

Patients with Crohn's and ulcerative colitis have increased risk of developing colorectal neoplasia associated with chronic colonic inflammation. This risk rises with duration and extent of disease and other factors including primary sclerosing cholangitis (PSC), family history of colon cancer, and histologic disease activity. Current ASGE guidelines recommend surveillance colonoscopy every 1 to 3 years starting approximately 8 years after onset of left sided colitis and Crohn's disease involving at least 1/3 of the colon, and annually in cases of PSC with IBD (starting at time of PSC diagnosis).[5,6] Most endoscopists will take random four quadrant biopsies from every 10 cm of the colon with the aim of collecting at least 32 biopsies to maximize sensitivity in detecting dysplastic lesions. This approach relies on sampling luck and may overlook early neoplasia. In addition, previous studies have shown poor adherence in obtaining 32 biopsies. Furthermore, the yield of random biopsies is exceedingly low.[7,8] Dysplastic lesions often have flat or subtle borders and early lesions may not be detected by conventional standard definition or even high definition white light endoscopy (WLE).

Over the past decade, numerous studies from tertiary academic centers have established the advantage of chromoendoscopy over WLE.[9,10,11] The use of chromatographic dyes to better visualize colonic mucosa allows for easier detection of subtle dysplastic tissue. Contrast dyes, such as indigo carmine, coat the surface of gastrointestinal mucosa highlighting pit pattern of normal mucosa.[12] Absorptive dyes, such as methylene blue, are taken up by normal mucosa, leaving dysplastic tissue unstained.[13,2] Irrespective of the dye utilized, chromoendoscopy facilitates targeted biopsy or lesion removal by highlighting the borders of flat or subtle neoplastic tissue. Previous studies have reported a 3 to 6 fold increase in number of lesions detected using chromoendoscopy with increase in sensitivity and specificity of detecting dysplastic tissue.[14,15]

The feasibility and practicality of this technique in the community setting has not been adequately studied. There is a significant increase in length of procedure which some argue may make chromoendoscopy prohibitive in a private practice setting. However, if targeted biopsies have higher efficiency in detecting dysplasia, random biopsies may be avoided which would result in greater savings from pathology costs as well as keep procedure time comparable to conventional colonoscopy. Other barriers may include lack of exposure to chromoendoscopy during GI fellowship or afterwards, unfamiliarity with the Kudo pit classification, cost and availability of dyes for chromoendoscopy, lack of additional compensation for performing chromoendoscopy lack of specific billing code for chromoendoscopy, and finally lack of data showing reduction of incidence and death from colorectal cancer as a result of utilizing chromoendoscopy.

Methods

We performed a retrospective review of surveillance colonoscopies with and without chromoendoscopy in patients with IBD between January 2005 &

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August 2012. The choice of using chromoendoscopy (indigo carmine 0.1 to 0.4%) for a surveillance exam was at the discretion of the endoscopist (SAS) and was not randomized. Procedure reports and pathology were reviewed. On the procedure reports, a detailed description of the polyp detection before or after chromoendoscopy was specifically noted by the physician (SAS) performing all the surveillance colonoscopies. This was done with the anticipation of analyzing whether the extra time spent in doing chromoendoscopy would be justified by an increased yield. The scopes used transitioned from standard definition to high definition during the study period (2010 in the outpatient ambulatory center and 2006 at the hospital). Demographic data (age, gender), diagnosis (Crohn's, ulcerative colitis, inflammatory bowel disease unspecified), smoking and family history, history of polyps, length of time for colonoscopy (defined as scope insertion to scope removal), complications from procedure, location & number of biopsies, and final tissue diagnosis from pathology were collected. The Lifespan/Rhode Island Hospital Institutional Review Board reviewed and approved the study protocol.

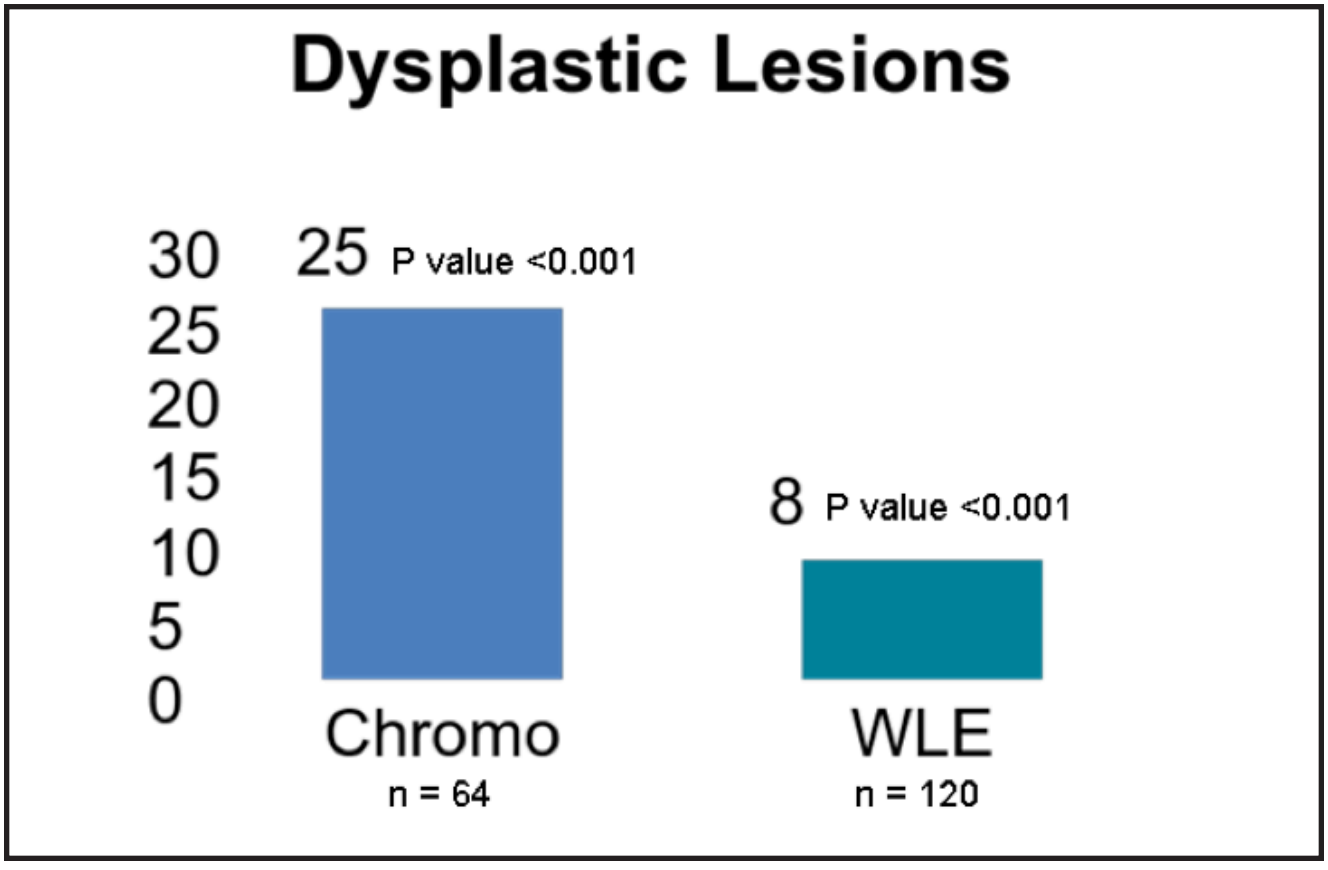
Results

A total of 184 colonoscopies were evaluated. Of these, 64 were performed using chromoendoscopy with indigo carmine dye. Cases comprised 118 individual patients, 64 males and 54 females, with a mean age of 51.6 years. There were no adverse events associated with colonoscopy with or without chromoendoscopy in the study population. These demographics are outlined in Table 1.

The average length of procedure was 38.8 [34.1, 43.4] minutes for chromoendoscopy, and 20.5 [18.1, 22.9] minutes without ($p<0.001$). Chromoendoscopy yielded an average of 42.0 [38.0, 46.0] biopsies in 13.1 [12.4, 13.86] jars per case, while white-light averaged 34.9 [32.4, 37.3] biopsies in 10.0 [9.68, 10.44] jars ($p<0.001$) per case.

White light colonoscopy found 87 polyps and chromoendoscopy found 157 polyps. An average of

Figure 1. Study Design Showing Patient Selection



2.4 [1.9, 3.0] polyps were resected per case during chromoendoscopy while white-light yielded 0.7 [0.5, 1.0] polyps per case on average ($p<0.001$). Chromoendoscopy led to discovery of 25 dysplastic lesions in 64 colonoscopies at a rate of 0.39 [0.23, 0.55] per case compared to 8 dysplastic lesions in 120 colonoscopies at a rate of 0.07 [0.02, 0.11] per case with WLE ($p<0.001$), (Figure 1). Of all polyps discovered via chromoendoscopy, 31% were dysplastic lesions. With white light, 7% ($p=0.002$) of all polyps resected were dysplastic. In our study, there was only one case, which found low grade dysplasia on a random biopsy; otherwise all remaining dysplastic lesions were resected polyps.

We divided our study population based on extent of disease, into left sided colitis, ileocolitis, and pancolitis. On analyzing different groups, percentages of dysplastic lesions found were 16.2%, 6.5%, and 77.3% respectively. We looked at the following variables, extent of disease, age, gender, family history, and, smoking in relation to total number of dysplastic lesions, using t test; P values, were 0.71, 0.74, 0.41, 0.75, 0.26, respectively. A previous personal history of polyps was significantly associated with subsequent dysplastic polyp detection ($p = 0.001$). These results are presented in Table 2.

Discussion

Chromoendoscopy allows for increased recognition of dysplastic polyps especially in higher risk populations such as patients with IBD.[16,17] Our analysis is consistent with published data from tertiary academic centers and demonstrates that chromoendoscopy can be done safely in a community private practice setting and with increased yield for dysplastic lesions.

In our study colonoscopy time was prolonged by an average of 18 minutes per procedure with chromoendoscopy, which is higher than the 11 minute average reported by Subramanian.[17] This is at least in part due to the endoscopist still doing random biopsies with chromoendoscopy. Since early 2014, the endoscopist has given up random biopsies with chromoendoscopy and switched to chromoendoscopy for all surveillance in IBD with only targeted biopsies. For the few patients with co-existing PSC, a previous history of dysplasia on random biopsies, or multiple pseudopolyps, random biopsies in addition to chromoendoscopy is still employed. A review of the last 20 cases with chromoendoscopy from October 2017 to February 2018 showed an average time of 29.6 minutes per case and 5.7 jars per case and included several patients with multiple pseudopolyps in

Table 1. Baseline Demographics and Clinical Characteristics

Total number of colonoscopies	184
Total number of patients	118
Sex (male/Female)	64/54
Age (mean in years ± standard deviation)	51.6±13.893
Age range	21 - 80
Final Diagnosis: **UC** **CD** **IBDU**	 64(118) 47(118) 7(118)
Colonoscopies with Chromoendoscopy (Indigo carmine dye)	64
Complications from colonoscopy	0
Smoking status at the time of colonoscopy (None/ Current/Former/Unknown)	101/22/56/5
Family history of colon cancer (None/first degree/ second degree)	81/29/8
Personal history of dysplastic polyps at time of colonoscopy (No/Yes/Unknown)	98/84/2
Patients with Primary Sclerosing Cholangitis	3
Left sided disease	23
Ileocolitis	27
Pancolitis	68

Table 2. Chromoendoscopy vs. White Light Colonoscopy

	With Chromoendoscopy n=64	Without Chromoendoscopy n=120	P Value
Average length (minutes)	38.8 [34.1, 43.4]	20.5 [18.1, 22.9]	<0.001
Number of biopsies per case	42.0 [38.0, 46.0]	34.9 [32.4, 37.3]	<0.001
Number of jars per case	13.1 [12.4, 13.86]	10.0 [9.68, 10.44]	<0.001
Number of Polyps	157	87	<0.001
Average of polyps resected per case	2.4 [1.9, 3.0]	0.7 [0.5, 1.0]	<0.001
Number of dysplastic lesions/rate of detection	25/0.39 [0.23, 0.55]	8/ 0.07 [0.02, 0.11]	<0.001
Percentage of dysplastic lesions detected	31%	7%	0.002
Dysplastic lesions in left sided disease n/%	6/16.2 %		0.72
Dysplastic lesions in ileocolitis n/%	2/6.5 %		0.91
Dysplastic lesions in pancolitis n/%	25/77.3 %		0.58
Dysplastic lesions in smokers (current and former) n/%	16/20%		0.28
Dysplastic lesions in males n/%	17/52%		0.2
Dysplastic lesions in females n/%	16/48%		0.4
Dysplastic lesions with first degree history of colon cancer %	5/18%		0.38
Dysplastic lesions with personal history of polyps n/%	21/75%		0.001

whom multiple random biopsies were taken. Thus with this approach most cases are done under 30 minutes making it practical from a scheduling and community practice perspective. In addition, all colleagues within the same community practice have adopted chromoendoscopy into their practice for selective cases without difficulty.

The technique allowed for a five-fold higher rate of detection of dysplastic lesions compared to white light colonoscopy. This correlates with published data citing a 3 to 5 fold difference.[10,18] Our experience is consistent from the "real world" experience from a multicenter study in Spain with 350 IBD patients from 2012-2014 who underwent WLE followed by chromoendoscopy

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with indigo carmine. In this study, 41.5% of the procedures were with standard definition scopes and 58.5% were with high definition. A total of 94 dysplastic (1 Cancer, 5 HGD, 88 LGD) lesions were found with a dysplasia miss rate 40/94 (57.4% incremental yield with chromoendoscopy). No significant learning curve was observed, no difference was noted between experts and non-experts in chromoendoscopy and increased yield with chromoendoscopy was seen regardless of whether standard or high definition scopes used. The authors concluded that any endoscopist can do chromoendoscopy and it works better than WLE high definition or standard definition. In contrast, a recent single center, prospective study in Calgary Canada randomized 270 patients with longstanding IBD 1:1:1 to surveillance dye spray chromoendoscopy, high definition WLE and "virtual chromoendoscopy" using the Pentax iScan technology. All of the procedures were performed by a single highly experienced endoscopist with only targeted biopsies for all cases. Initially for dye spray chromoendoscopy 0.4% indigo carmine was used and later .03% methylene blue due to shortage of indigo carmine. No difference in dysplastic lesion detection between the three techniques arguing against chromoendoscopy.

In our population, random biopsy yielded low grade dysplasia in only one patient. This patient has chosen to not have colectomy and remains under surveillance with annual chromoendoscopy without further dysplasia detected with the exception of a few visible dysplastic polyps seen with chromoendoscopy. Thus, the yield of random biopsies finding dysplasia was approximately 1 in 6,600. This is consistent with other studies[19,7] that the utility and cost effectiveness of random biopsies is exceedingly low. Furthermore, the 32 random biopsies are estimated to sample only 0.03% of the mucosal surface. Two studies concluded that even with standard white light endoscopy, most dysplastic lesions found were endoscopically visible.[8,20] These studies reported that 73–77% of dysplastic lesions and 89–100% of invasive cancers in UC patients were detectable endoscopically with white light colonoscopy.

The expense from random biopsy must also be taken into account. The most recent Medicare fee-schedule lists an average pathology cost of $73 per specimen jar submitted for gross and microscopic examination (laboratory processing and pathologist reading). As for private insurance, one commercial insurer in our region pays $150 per specimen jar (personal communication, James Carlsted, MD). As chromoendoscopy yielded 13.1 jars per case the average pathology cost was $956.3 for patients who had Medicare and $1,965 for private insurers. On the other hand, WLE yielded 10 jars per case resulting in $750 for Medicare and $1,500 for private insurance. However, chromoendoscopy cases in our analysis averaged a higher number of biopsy jars compared to WLE, but these included both targeted as well as random biopsies. While it was outside the scope of our study, abandoning the practice of random biopsy and performing targeted biopsies alone would significantly reduce the pathology cost associated with surveillance over the lifetime of a patient with IBD. We estimate that the number of jars with targeted biopsies with chromoendoscopy would average 4 (sampling for disease activity and removal of visualized lesions). The estimated cost saving in terms of pathology costs would be $438 for Medicare patients and $900 for commercially insured patients per case. This is particularly important in showing value in the current MACRA/MIPS view of physician services. Furthermore, since a negative chromoendoscopy colonoscopy is associated with a lower risk of colectomy for dysplasia/cancer the interval between surveillance may be increased based on other risk factors leading to further cost savings.[18] In line with this, the British Society guidelines[21] suggest 5 year intervals for low risk IBD patients.

There are several limitations to the generalizability of our study. All procedures were performed by a single endoscopist. Patient selection toward chromoendoscopy was not random and patients with longer duration of disease, history of dysplastic findings or other risk factors may have generated a higher index of suspicion to select use of chromoendoscopy and hence yield of dysplastic polyps. Over the time period of our analysis, newer generation high-definition endoscopes were introduced which was not factored into our study design. The absence of statistically significant relation between variables known to be associated

with risk such as FH, smoking, gender, and number of dysplastic polyps detected is not surprising given the sample size, and retrospective non-randomized design.

Our data adds to growing body of literature supporting the practice of chromoendoscopy as an effective tool in detecting dysplastic lesions and thereby preventing colorectal cancer. It should be utilized more frequently in patients with IBD undergoing surveillance colonoscopy. Our experience shows it can be performed successfully and safely in the community practice setting. ■

All authors contributed substantially to the manuscript and approved the final manuscript. The study was conceived by SAS. NJ and SAS wrote the protocol for IRB approval with input from MR. NJ did the initial chart reviews and collection of data. JF and MAA performed a critical review of the previous data and focusing on risk factors for colon cancer and filling in gaps in missing data. SR performed all the statistical analysis with input from SAS, NJ and MAA. The bulk of the manuscript was written by NJ, MAA and SAS with critical input from all the authors. Each author read and approved the final, submitted manuscript.

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