ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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Insights Into Colonoscopic Surveillance for Dysplasia in Inflammatory Bowel Disease

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G&H How has colonoscopic imaging evolved?

JL The major change that has occurred is improvement in the optics of colonoscopes. Providers used to be accustomed to viewing standard-definition images. Once we experienced high-definition images, there was no going back. Moving from standard-definition to high-definition white-light endoscopy has enabled a major improvement in the ability to identify changes in the mucosa. In the era of standard-definition colonoscopes, chromoendoscopy was particularly valuable for dysplasia surveillance of patients with ulcerative colitis or Crohn's disease. Chromoendoscopy helped bring out subtle changes that were not evident with standard-definition scopes. Progress is continuing to be made in the world of colonoscopic imaging with the addition of what some people refer to as virtual chromoendoscopy, using light-filtering techniques such as narrow-band imaging, which allows for even better visualization of the mucosal surface and vascular patterns.

G&H Who should undergo chromoendoscopy nowadays?

JL The answer to this question is partly dependent on the skill set of the endoscopist. Endoscopists should use the technique with which they are best able to detect dysplasia. In routine clinical practice, most patients undergoing surveillance colonoscopy for ulcerative colitis or Crohn's disease are not having the procedure performed with chromoendoscopy. Most dysplasia surveillance is being performed using high-definition white-light imaging with the ability to turn on a virtual chromoendoscopy tool as needed. Most providers limit dye-spray chromoendoscopy to subgroups of their patients where it seems particularly valuable. One of these subgroups includes patients in whom dysplasia was detected in a nontargeted random biopsy. In this case, the endoscopist, by definition, did not see the lesion, so using chromoendoscopy to try to bring out a subtle lesion is indicated. Many providers will also use chromoendoscopy in patients with primary sclerosing cholangitis or other patients at particularly high risk of developing colon cancer. Lastly, if the procedure is being performed with a standard-definition colonoscope, dye-spray chromoendoscopy is recommended.

G&H Are there differences between surveillance for ulcerative colitis vs Crohn's disease?

JL The general principles of dysplasia surveillance in ulcerative colitis and Crohn's disease are the same since the risk of cancer is proportional to the amount of colon that has been involved with inflammatory bowel disease. The approach to dysplasia surveillance should be tailored to the amount of the colon that has been diseased. Many patients with Crohn's disease have very limited, if any, colonic involvement, and those patients do not require accelerated dysplasia surveillance. Similarly, patients with ulcerative proctitis do not require accelerated dysplasia surveillance because so little of their colon has been involved.

G&H How have the concepts of endoscopic improvement and histologic remission impacted surveillance recommendations?

JL The evolving dysplasia surveillance recommendations reflect both the improved ability to control mucosal inflammation with medications and improved ability to identify and remove dysplastic lesions at colonoscopy. Together, this has allowed for surveillance intervals to be extended. In the era of standard-definition white-light colonoscopy, the 2005 consensus conference recommended surveillance every 1 to 3 years. Now, with better treatments to reduce intestinal inflammation, presumably reducing the risk of cancer, coupled with better imaging, some patients may only need surveillance approximately once every 5 years. The data supporting these longer surveillance intervals mainly come from observational studies. I doubt there will ever be a randomized trial comparing a 2- or 3-year surveillance interval with a 5-year surveillance interval. As such, we need to come to our best recommendations based on the observational data.

Relatively few people still qualify for annual surveillance. These might be people who have a history of invisible or high-risk dysplasia in the recent past, people with dense pseudopolyps throughout their colon, and people with primary sclerosing cholangitis. A 1-year interval might also be considered in people who have had extensive colitis with severe active inflammation and people with a family history of colorectal cancer in a first-degree relative under the age of 50 years.

On the other end of the spectrum, 5-year intervals would apply to people whose disease has been very well controlled who do not have any history of invisible or visible dysplasia in the past 5 years. The people who have never had high-risk dysplasia could potentially move to a 5-year interval, particularly if their last 2 colonoscopies have had complete healing, both endoscopic and histologic. Although longer surveillance intervals are more convenient for patients, systems need to be in place to ensure that surveillance is not forgotten as part of health maintenance for patients with inflammatory bowel disease.

G&H Should biopsies be targeted or random?

JL This is a controversial issue for which there is not a definitive answer yet. Providers should biopsy anything that looks abnormal. What is less clear is whether there is any added value to taking biopsies of mucosa where the provider does not have a strong belief that dysplasia is likely to be present. To date, I am aware of one completed clinical trial and two ongoing clinical trials (one in the United States and one in Canada) that have looked into this issue. The completed trial was conducted quite some time ago in Japan and was a relatively small study of approximately 220 patients. Interestingly, the number of dysplastic lesions and the number of patients with 1 or more dysplastic lesion was numerically higher in the group undergoing targeted biopsies as opposed to the group undergoing random and targeted biopsies. However, looking at the data from the group having both random and targeted biopsies, quite a bit of dysplasia was found in the random biopsies. The explanation for this is not completely worked out. I hypothesize that the potential downside of random biopsies is that they are distracting to the endoscopist. Because the endoscopist is so busy obtaining random biopsies, they miss lesions they should have picked up in a targeted biopsy, and sometimes they accidentally biopsy the same lesion.

The URBI study, the aforementioned ongoing trial in the United States, is being conducted at approximately 20 sites throughout the country and is being led by our group. This noninferiority study is looking at the role of random biopsies when using high-definition white-light colonoscopy. The hypothesis is that taking a limited number of random biopsies is noninferior to the previously recommended protocol of taking 4 random biopsies every 10 cm throughout the colon. In both of these strategies, providers biopsy and remove any lesions seen using targeted biopsies. Within the next few years, this study and the ongoing clinical trial in Canada should provide strong evidence to establish best practice guidelines for the use of random biopsies.

G&H Aside from targeted vs random biopsies, are there any other controversial issues regarding colonoscopic surveillance in inflammatory bowel disease?

JL There is a controversy as to whether high-definition white-light imaging is inferior to high-definition white-light imaging with dye-spray or virtual chromoendoscopy. In the most experienced hands, I suspect that dye-spray chromoendoscopy is superior to high-definition white-light endoscopy alone, as has been supported by a recent meta-analysis. For endoscopists who are not using dye-spray chromoendoscopy on a very regular basis, I am not sure that it is superior to high-definition white-light colonoscopy with or without advanced imaging.

Another controversy is whether virtual chromoendoscopy modalities are better than high-definition white-light endoscopy. This has not been proven, nor has it been definitively proven that dye-spray chromoendoscopy is better than virtual chromoendoscopy. If virtual chromoendoscopy is just as good as dye-spray chromoendoscopy, it is certainly much easier to perform.

As noted earlier, we do not have strong evidence to guide surveillance intervals after dysplasia is found. The general principles are that patients with a high-risk lesion—meaning that the lesion is larger than 2 cm, has high-grade dysplasia, irregular borders, or could not be completely

removed easily (even after multiple attempts)—should be brought for repeat colonoscopy in 3 to 6 months. Additionally, patients with an intermediate-risk lesion (1-2 cm lesions with low-grade dysplasia) should probably come back at approximately 12 months, and patients with a low-risk lesion (a dysplastic lesion removed completely that was less than 1 cm in diameter or was pedunculated) should come back at 24 months. What is not included in this guidance is how to follow up patients with invisible dysplasia detected on random biopsies. These are lesions that typically have not been completely removed. Should colectomy be recommended for patients in whom low-grade dysplasia is being picked up repeatedly on random biopsies, and who else should be recommended for colectomy to try to prevent colon cancer?

Finally, it is not known whether any surveillance is needed in patients who have undergone total proctocolectomy with creation of a J-pouch. These patients have had approximately 98% of their colon and rectal mucosa removed, which likely reduced their risk of colorectal cancer by about 98%. No special dysplasia surveillance is recommended for patients with ulcerative proctitis since very little of the colon mucosa has been diseased. Should the same principle apply to patients with a J-pouch? Better data are needed on the incidence of cancer of the rectal cuff and J-pouch after colectomy overall and among those who had colectomy to treat dysplasia.

G&H What other questions remain in this field?

JL I think the role of artificial intelligence will be figured out over the next decade, maybe sooner. It is easy to imagine how artificial intelligence can play a part in identifying dysplasia, helping us know whether it is completely removed, and interpreting biopsies to better identify patients who are at high risk for having additional dysplasia or colon cancer, as well as those who are at low risk and can have longer surveillance intervals. I think we will get these answers in the not-too-distant future.

G&H Is there anything else you would like to discuss about surveillance in inflammatory bowel disease?

JL Any cancer screening and surveillance program is better than none. The highest-risk patients, in some ways, are those who slip through the cracks and fall out of a surveillance program. This is something we should all be keeping on our radar. Even though the risk of colon cancer is declining in patients with inflammatory bowel disease, it is still appreciably elevated compared with the general population. Fortunately, good techniques are available in terms of both medical and endoscopic approaches that have contributed to the declining risk of colon cancer, which hopefully will continue to fall in the decades ahead.

I would also like to acknowledge the passing of Professor Anders Ekbom on July 29, 2024. He was a surgeon in Stockholm, Sweden, who spent much of his career at the Karolinska Institute and the Karolinska University Hospital. In 1990, he published what I consider to be the seminal article on the risk of colon cancer in patients with ulcerative colitis using data from Sweden to clearly show for the first time that the major risk factors were the extent of disease and how long the patient had the disease. This led to the creation of the modern practice of performing dysplasia surveillance. He was a giant in our field whose work continues to impact the practice of medicine.

Disclosures

Dr Lewis has consulted or served on an advisory board or data monitoring committee for Amgen, Crohn's & Colitis Foundation, Eli Lilly and Company, Galapagos, Janssen Pharmaceuticals (Johnson & Johnson), Merck, Odyssey Therapeutics, Pfizer, Protagonist Therapeutics, Sanofi, and Spyre Pharmaceuticals. He has had research funding or in-kind support from Nestle Health Science, Takeda, Janssen Pharmaceuticals, AbbVie, and Eli Lilly and Company. He has had educational grants from Janssen Pharmaceuticals. He has performed legal work on behalf of manufacturers of generic ranitidine and 3M. He is an advisor to Chylometis in exchange for stock options and to Dark Canyon Labs in exchange for stock.

Suggested Reading

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