ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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Surveillance of Inflammatory Bowel Disease

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G&H What is the risk of colorectal cancer in patients with inflammatory bowel disease?

TU Patients with long-standing Crohn's colitis and ulcerative colitis have been demonstrated to have an increased risk for colorectal cancer relative to the general population. A recent meta-analysis by Jess and colleagues, which was limited to population-based studies, demonstrated a 2.4-fold increase in colorectal cancer in ulcerative colitis patients relative to the general population. A slightly older meta-analysis that included population-based studies and specialty center studies found a 4.5-fold increase in colorectal cancer in patients with Crohn's colitis relative to the general population. Therefore, inflammatory bowel disease (IBD) patients undergo screening and surveillance for colorectal cancer earlier and more frequently than people in the general population.

G&H Does the colorectal cancer risk differ between patients with ulcerative colitis and those with Crohn's disease?

TU Crohn's disease and ulcerative colitis are currently thought of as 2 distinct illnesses, although they are likely many more, each with its own genetic and environmental cues and, thus, each likely to have different associations with colorectal cancer. Nevertheless, the proposition of surveillance is currently considered similarly in these diseases (although that may change in the future). Currently, it is commonly believed that, square centimeter per square centimeter, patients with Crohn's disease of the colon and patients with ulcerative colitis have approximately the same risk for colorectal cancer, which is why surveillance is performed in the same fashion for both groups.

G&H Has the risk of colorectal cancer remained the same over the past decade?

TU Over the past few years, we have seen reports demonstrating a diminution in the risk of colorectal cancer in long-standing IBD. It appears that the risk is less than that estimated by previous generations, which has been encouraging. Many clinician-scientists have attributed this change to the improved and more common use of anti-inflammatory medicines, although I find the chemoprevention studies to be limited at best, with modest risk reductions and no mortality benefit demonstrated. Nevertheless, this is the leading theory for explaining the reduction of risk over time.

G&H What are the specific risk factors for colorectal cancer in patients with IBD?

TU There are a number of known risk factors for colorectal cancer in patients with IBD. One of the most important is a longer duration of disease; the risk of colorectal cancer does not appear to accrue above that of the general population until approximately 8 years of disease. Patients with more anatomically extensive disease are also at greater risk for colorectal cancer. The risk is substantially increased in patients who harbor concomitant primary sclerosing cholangitis (PSC); in fact, physicians do not even wait for 8 years to pass before initiating surveillance of these patients (beginning at the time of the PSC diagnosis). Not surprisingly, patients with a family history of colorectal cancer also

have an increased risk, as do patients with a greater degree of histologic inflammation over time. Likewise, patients with pseudopolyps in their colon as a function of the healing process from an inflammatory burden during some point of their history have a greater risk of the development of colorectal cancer, as do patients in whom dysplasia has been found during a colonoscopic surveillance examination.

G&H What is the pathogenesis of colorectal cancer in patients with IBD?

TU Colorectal cancer often occurs as a result of the inheritance or acquisition of a series of mutations in colonic epithelium along the chromosomal instability pathway. It is commonly believed that in IBD, a greater inflammatory burden results in an increased risk for these mutations in the colonic tissue, which accelerates the risk of colorectal cancer. We are fairly certain that the pathogenesis of colorectal cancer in these patients involves the inflammatory burden, but we do not fully understand the many mechanisms at play.

G&H According to published guidelines and consensus statements, is surveillance required in all IBD patients or just those with the risk factors mentioned above?

TU Surveillance is required only in IBD patients who also have other risk factors. For example, patients who have ileal Crohn's disease alone and patients who have Crohn's and ulcerative colitis with disease limited to the rectum and sigmoid are in the general surveillance pool, with colonoscopy recommended at age 50 years and subsequent examinations every 10 years in a dysplasia-free colon. It is not until a third or more of a person's colon is involved that the person has an increased risk for colorectal cancer and that surveillance should be performed more frequently (every 1 to 2 years in a dysplasia-free colon). The detection of dysplasia warrants either more frequent examinations or referral for colectomy, depending on the ability of the endoscopist to fully identify and completely resect all detected dysplasia. PSC patients with IBD should have annual examinations.

G&H How effective is traditional surveillance for colorectal cancer in IBD patients?

TU We have not yet been able to demonstrate in multiple studies that traditional surveillance is effective at reducing colorectal cancer morbidity or mortality in IBD patients, but there is certainly enough circumstantial evidence, including several case-control studies, to support its effectiveness.

As discussed above, IBD patients with the aforementioned risk factors for colorectal cancer have traditionally undergone routine white-light colonoscopy every 1 to 2 years. The recommendation used to be colonoscopy every year, but it has been relaxed to every 1 to 2 years in US-based guidelines, and is longer still in British Society of Gastroenterology guidelines, with 5 years between examinations in well-prepped, dysplasia-free colons with little inflammation. The colonoscopy should consist of good preparation and 4-quadrant, nontargeted biopsies of the colonic mucosa every 10 cm from the cecum to the rectum—with the specimens then preferably placed in separate jars—as well as the biopsy or removal of any identified or suspicious-looking lesions. With dye-aided chromoendoscopy, the need for nontargeted biopsies is uncertain.

G&H Based on the studies conducted thus far, how effective is chromoendoscopy for the surveillance of IBD?

TU Chromoendoscopy involves the application of dye spray to the lining of the colorectum to visually augment the colorectal lining, with enhanced appearance of the pattern of colorectal crypts and other aspects of the colorectal architecture. This allows for better appreciation of abnormalities of the colonic mucosa and better identification of dysplastic abnormalities. Chromoendoscopy has been shown to improve the detection of dysplastic polyps but is yet to be shown to be superior to conventional white-light colonoscopy. No longitudinal studies exist, so we really have no idea what the true benefits, if any, are for chromoendoscopy over standard white-light colonoscopy. When we start measuring real outcomes, such as the development of cancer or the need for colectomy, we will be able to retool surveillance strategies that will reduce cost and inconvenience as well as reduce morbidity, mortality, and worry for patients. Despite the promise of this technique, we are not there yet.

G&H Are there any other advantages to using chromoendoscopy compared with conventional white-light colonoscopy?

TU There are a number of theoretic advantages. As mentioned above, chromoendoscopy is likely more accurate than standard colonoscopy at identifying and removing dysplasia. Finding and removing small lesions may reduce the subsequent risk of the development of cancer at a subsequent colonoscopy. Theoretically, being able to clear the colon more effectively with a chromoendoscopic examination would not only enable the patient to be at less risk of having cancer at his or her next examination, but also increase the possibility that subsequent examinations could be spread out further over time. However, this theoretic advantage has yet to be demonstrated in a prospective or even a retrospective study.

Another theoretic advantage is that with better identification and better understanding of what is happening at the mucosal crypt level, it may not be necessary to

perform the laborious, tedious, and expensive process of biopsying the mucosa in a nontargeted fashion; all of the extra biopsies that have been obtained over the years may not be needed. The promise of chromoendoscopy is that surveillance colonoscopy will begin to approach practices similar to those of sporadic colorectal cancer screening and surveillance, with endoscopists identifying dysplastic polyps, removing them, and bringing patients back in a few years, depending on what was identified and removed.

G&H Should chromoendoscopy be used alone or in combination with other modalities for surveillance?

TU With chromoendoscopy, endoscopists do not spray the colorectal surface until they are on their way out, so good entrance white-light examinations are always part of the process. High-definition equipment (scopes, processors, and screens) aid in the detection of dysplasia in IBD and can be used when available.

G&H Is chromoendoscopy generally confined to specialized centers, or has it achieved widespread use among doctors?

TU Chromoendoscopy is mainly performed in specialized centers. It is quite easy to learn, but to my knowledge, there have not been any studies to understand how prevalent it is in the community setting. Anecdotally, whenever I give a lecture on chromoendoscopy, I always ask for a show of hands of physicians who use it, and that number seems to be increasing, even though it never seems to be more than approximately a quarter or a third of the room.

G&H Should chromoendoscopy be considered the standard of care for IBD surveillance?

TU This is the million-dollar question. I think that chromoendoscopy can be considered the best care for dysplasia surveillance of IBD, but I do not think that conventional white-light colonoscopy has been shown to be inferior in terms of real outcomes. Chromoendoscopy is a standard, but the older standard of IBD surveillance is still an acceptable standard. No one has demonstrated superiority in a longitudinal study thus far, so the old standard still lives.

G&H Is narrow-band imaging an effective option for IBD surveillance?

TU Narrow-band imaging (NBI) has been studied by Dekker and colleagues, among others, using yields or incremental detection of polyps and dysplasia as the metric of success and has not been shown to be superior. This is unfortunate, as NBI is a push-button technique and does not require sprays or dyes. However, without the ability to better detect dysplasia, NBI has no immediate future in IBD surveillance. Other push-button technologies with computer-aided manipulation of optics and depth of light penetration are being investigated, but studies demonstrating superiority over conventional white-light techniques or chromoendoscopy are lacking.

G&H Are any other modalities being examined for IBD surveillance?

TU There are several other adjunctive surveillance modalities being investigated, but although several clever spectroscopy techniques have shown some promise, there are no meaningful, wide-scale results as of yet. This includes an interesting, ongoing examination of a virtual chromoendoscopic system similar to NBI that uses different manufacturers' scopes, some of which are proprietary to the endoscopic equipment makers.

G&H What are the next steps in research?

TU It is important to further define the value of chromoendoscopy and to obtain a better understanding of the strengths and limitations of the other adjunctive techniques to truly determine whether there is a superiority in real outcomes (mortality, morbidity, cost, convenience, and patient satisfaction, among other outcomes). Further evaluations of training outside of specialty centers are also important. In addition, there is a need for the development of more novel tools, whether they are stool or blood tests or simple sigmoidoscopy and biopsy with other tissue-based biomarker testing, to better determine which patients are at greatest risk of colorectal cancer, instead of using a one-size-fits-all paradigm.

Dr Ullman has no relevant conflicts of interest to disclose.

Suggested Reading

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