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Postoperative Recurrence of Crohn's Disease: Reviewing Monitoring and Treatment Strategies

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm your host Dr. Peter Buch, and joining us today to discuss postoperative Crohn's disease therapy is returning guest Dr. Miguel Regueiro. Dr. Regueiro is the Chief of Cleveland Clinic's Digestive Disease Institute and is a leader in Crohn's disease research.

Dr. Regueiro, welcome back to the program.

Dr. Regueiro:
Thank you. Thanks for having me again.

Dr. Buch:
Dr. Regueiro, let's start at the beginning. What are the factors leading up to post-op Crohn's disease in patients, and what are the post-op recurrence rates nationally?

Dr. Regueiro:
So I think I'll start by answering the second question first. To put everything into context, the patient who undergoes, most commonly what we call an ileocecal or ileocolonic resection with the primary anastomosis between the ileum and the colon, the rates of recurrence that are not clinically evident—but what I mean by that is if you do a colonoscopy on the patient, you see Crohn's disease recur, and it's usually in the ileal side or the ilium small bowel side of the anastomosis—has been reported to be as high as 80 to 90 percent within the first year or two, so pretty high rates of recurrence. Now clinical recurrence, meaning when a patient feels that Crohn's disease, they get symptoms from that Crohn's disease recurrence, the national rates are estimated about 50 to 60 percent within the first three years in all-comers, and we'll get into that in a minute who gets treatment and not.

In terms of risk factors or factors that may predict those that are more likely to have postoperative recurrence versus not, the ones that are most likely are cigarette smoking, interestingly, as a high rate of recurrence of Crohn's disease. If the indication for surgery is what we call a penetrating complication, like a fistula, that's a high rate for recurrence as well. And then finally, if it's a patient who's on their second, third, fourth, fifth surgery, meaning this has been a pattern that they've had recurrence and required surgery, that also puts him at a higher rate for recurrence.

Dr. Buch:
And is there any relationship of extraintestinal manifestations and recurrence of Crohn's disease?

Dr. Regueiro:
It's a very interesting question. The simple answer is we don't entirely know. However, if we think about extraintestinal manifestations, joint inflammation, eye inflammation, skin inflammation, these consequences of immune-mediated inflammation that occur outside of the

bowel, our thought is that the more extraintestinal manifestations one has, the more likely they have more aggressive inflammatory bowel disease, Crohn's disease in this case. There has been some suggestion if you have a patient who has multiple extraintestinal manifestations, that may also factor into a higher rate of recurrence, probably just because the systemic inflammatory burden affecting the joints, the eyes, the skin, is also more likely to come back in the bowel.

Dr. Buch:
Thank you for that. So when and how do you monitor a patient for postoperative Crohn's disease?

Dr. Regueiro:
That's evolved over time, and the monitoring strategy has gotten much better. And the reason I say it's gotten much better—historically, meaning 10, 15 years ago and before—it wouldn't be uncommon for a patient to get surgery for their Crohn's, and then if they're feeling well, which a lot of patients after surgery fell very well, that they're more or less sent on their way and say, "Come back and tell us when you have symptoms." And what was found in the past were then these patients would come back with symptoms, the disease would have come back and progressed, and then they need another surgery. So now we're realizing that if we monitor earlier after surgery and more frequently, that we can pick up early Crohn's disease recurrence and prevent that progression and prevent that next surgery.

So the three modalities for monitoring that have been probably most established is fecal calprotectin, the other is a colonoscopy, and the other is ultrasound. And to be more specific about monitoring strategies—fecal calprotectin, which is a measurement of stool inflammation—if we check that three months after surgery, and now we know if the level's high, specifically over 150, that should prompt us to do an earlier colonoscopy, where if it's lower, lower than 150, we can probably wait six months, and I would now argue even a year before doing a colonoscopy, which colonoscopy is still the gold standard way to monitor for postoperative recurrence, meaning we look at the bowel, we see the anastomosis where the patients had surgery, and we see if there's recurrence of Crohn's disease, but it's an invasive test.

So intestinal ultrasound is now evolving, and there have been a number of good studies showing that intestinal ultrasound done by a gastroenterologist can actually pick up early recurrence of Crohn's, and I could see a day that comes when fecal calprotectin and an intestinal ultrasound may replace the frequency of colonoscopy. We're not there yet, primarily because in the United States most centers don't have intestinal ultrasound or don't have the expertise, but I do want to mention that.

Dr. Buch:
And you got me thinking, Dr. Regueiro, what is the accuracy of the noninvasive tests compared to our gold standard colonoscopy?

Dr. Regueiro:
Good question. The fecal calprotectin actually has a pretty high sensitivity and specificity for recurrent Crohn's disease, and the higher that number, the more likely that there's endoscopically active disease, meaning that if you do a colonoscopy, you see Crohn's disease. There's a gray zone, though, between 150 and 250 where the sensitivity and specificity may not be as high, so sometimes we need to use our intuition or our clinical judgment on those patients. Do we actually end up going ahead with a colonoscopy if then they're in that gray zone? But if it's very low, especially under 50, or very high in the high hundreds to thousands, those are pretty good at saying either you don't have Crohn's, very low Crohn's recurrence, or likely to have Crohn's recurrence, and we should probably undergo a colonoscopy.

Dr. Buch:
And once you've identified a patient with postoperative Crohn's disease, how do you work with that patient to choose the best medication?

Dr. Regueiro:
So taking a step back from even the active treatment of Crohn's is how do we prevent it, and I'll answer maybe both of those. So to answer your question first, if it's a patient who's not on any medication and they have recurrence of Crohn's disease that requires a medication, then we look at what they've been on before and maybe what's worked or not worked, and we come back to that. Now I will

tell you most of the patients who have surgery for Crohn's means they've had an aggressive disease, and if they have recurrence, we are favoring an advanced therapy, which means a biologic or a small molecule. And to simply put it this way, if a patient after surgery has recurrence of Crohn's disease and we're starting a treatment, it would be the same as starting a patient without having surgery who has moderate to severely active Crohn's on one of these advanced therapies, so that's if they have active Crohn's disease. If they have been on more of a preventative approach, which means we started medicine shortly after surgery to prevent recurrence, it used to be said that the only really good randomized controlled data we had, which are studies I was involved with, were looking at infliximab started within a month of surgery to prevent recurrence of Crohn's. Now a second study that came out recently looked at vedolizumab, so another biologic, to prevent postoperative recurrence. That's more of a prevention strategy. But the active treatment strategy really is like what we do with any Crohn's patient with moderate to severe disease.

Dr. Buch:
Thank you. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Miguel Regueiro about postoperative Crohn's disease.

So let's dive a little bit deeper into medications, Dr. Regueiro. Does a nonresponse to a preoperative medication mean that it should not be used post-op?

Dr. Regueiro:
Excellent, excellent question. This is something we kind of debate about all the time, we talk to about with our patients, and there have been a number of studies on this too. And just for transparency, I was involved in a number of these studies.

So let's put it this way. So patients on a medicine before surgery—and let's just say whatever the biologic is without even specifically picking up a medicine. There are really two ways that that patient came to surgery on the medicine. One is that they were on the medicines—say they were started on it two years ago before surgery—their disease was moderate, and on that medication they progressed over time; they had more severe disease; they developed a complication of their Crohn's, like a stricture of fistula despite being on that medicine. That would be a medicine that I would not reuse after surgery because that medicine did not successfully achieve remission of the Crohn's, and their disease progressed. So that's maybe easier to say not to use that, to pick a different class of medicine.

The more common scenario though is—and I use what I call the preoperative six-month rule—if it's a patient who was started on a medicine, a new biologic, for example, within six months of surgery, that is a patient that I will more likely recycle, meaning continue that same medicine after surgery. And the question is why? Why would you do that? Well, a lot of times patients who we start on a medicine prior to surgery, they're wanting and we're wanting to say, "Hey, can we use a medication to avoid surgery? Can we actually heal the Crohn's?" But sometimes the damage is too far gone. The Crohn's has a complication, and they're probably going to need surgery anyway. Starting that medicine is kind of a last ditch effort at healing their Crohn's disease and often doesn't work. It doesn't mean that the medicine has failed the patient. It may be that that medicine can be successfully continued. And in that scenario, new start of a medicine within six months of surgery, the studies that I've been involved with and others have shown that you can successfully continue that after surgery.

Dr. Buch:
And could intraoperative intestinal ultrasound change the post-op recurrence rates?

Dr. Regueiro:
So the intraoperative ultrasound is an interesting concept, and I would say that's probably more in the realm of still research to look at what we call the mesentery or some other factors in the wall of the bowel in the operating room as the surgeon is doing the surgery. However, I think you bring up a good point about the intestinal ultrasound to follow and monitor the patient after Crohn's surgery may actually be a very good noninvasive way of picking up early Crohn's by actually seeing it on an ultrasound without having the patient have to go under colonoscopy. But the intra-op findings of the mesentery, the blood vessels, vasculature, the margins of resection, there's been a lot of surgery research around these concepts, and we're still learning about them, so I think we still have some way to go.

Dr. Buch:
Now in the last few minutes of our discussion, Dr. Regueiro, are there any additional thoughts you'd like to leave with our audience today?

Dr. Regueiro:
I think the additional thoughts around postoperative Crohn's disease is that we should not look at surgery as a failure, meaning that there are patients with Crohn's that require surgery because of a complication. And I would say the good news is our postoperative monitoring strategies that we've outlined in this talk have actually improved, and our postoperative medication strategies have dramatically improved. And we can actually now have patients achieve long-term remission after surgery and continue to do well. And then very finally, lifestyle probably does play a role, and a healthy diet is always important, and we like to stress that, especially in somebody who's undergone surgery.

Dr. Buch:
What a superb review on postoperative Crohn's disease. I want to thank my guest, Dr. Regueiro, for sharing his insights. Thanks so much for joining us today.

Dr. Regueiro:
Thank you very much.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit *GI Insights* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.