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Perianal Crohn's Disease: The Importance of Multidisciplinary Management

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch, and joining us today to discuss perianal Crohn's disease are Drs. Ben Cohen and Stefan Holubar. Dr. Cohen is the Co-Section Head and Clinical Director for Inflammatory Bowel Disease at the Cleveland Clinic in Ohio.

Dr. Cohen, thanks so much for being back here today.

Dr. Cohen:
Thanks so much for having us. We loved our experience last time, and we're happy to connect again.

Dr. Buch:
And, Dr. Holubar, is IBD Surgery Section Chief and Director of Research, also at the Cleveland Clinic. Welcome back to the program, Dr. Holubar.

Dr. Holubar:
Thank you very much. It's a pleasure to be here and share our experience with this often difficult-to-manage patient population.

Dr. Buch:
We certainly appreciated your very important previous discussion on the safety of anti-TNFs in the perioperative period, which is also available at *GI Insights* on ReachMD.com.

Now let's just jump into our discussion today, starting with you, Dr. Cohen. Why is a multidisciplinary team so important in the management of perianal Crohn's disease?

Dr. Cohen:
Well, perianal disease and fistulas affect over a quarter of patients at some point in their disease course, and approximately 10 percent within the first year of diagnosis. And importantly, fistulas have an enormous impact on quality of life for the patient, whether it's intestinal function, behavioral health, sexual health. And this is then further complicated by the fact that perianal disease is very difficult to heal and persists over time. So I highlight this to get to your question to really emphasize the complexity of the problem, and that sets the stage for why multidisciplinary care is so important.

Our institute chair at the Cleveland Clinic, Miguel Regueiro, had done a study many years ago showing that combined medical and surgical management of perianal fistula results in more significant initial response, as well as significantly less recurrence than medical management alone. And when a patient is a setup for recurring abscess, it's very difficult to make headway with the fistula tract, so it really requires the surgeon to drain the infection and place a seton that will prevent abscess recurrence while we wait for the medical therapy to have an effect.

But beyond this, I think the multidisciplinary team is even greater than the GI and the surgeon. We routinely have these patients work with our psychologists or dieticians and even our IBD pharmacists to optimize the IBD care because it's really important to aggressively optimize their medical therapy to have the best chance at fistula healing. And we also frequently discuss these patients in a multidisciplinary conference with surgeons, radiologists, pathologists to figure out the right approach and complex patients and decide on strategies such as diversion, which we're also going to discuss.

Dr. Buch:
Thank you for that very important response. Now turning it over to you, Dr. Holubar, antibiotics have always been the mainstay of perianal Crohn's disease therapy. But what medication should we reach for when antibiotics are not effective?

Dr. Holubar:
Yeah, it's a great question. If someone has an abscess that really needs to be having surgery with an examination or under anesthesia an incision and drainage, and then thinking about placement of a seton to prevent that external opening from closing and the patient from getting a recurrent abscess, antibiotics do have a role in improving patient quality of life when they have a perianal fistula because they can decrease the amount of fluid that comes out of the fistula. So it does help dry them up a little bit, and that does make the patient feel better and gives them a little bit of symptomatic control, but it's really more of a palliative type medical therapy rather than something that's really going to address the underlying fistula. And I would say in terms of medications, I would defer what next medications the patients should be on to, to Dr. Cohen.

Dr. Buch:
Perfect. Dr. Cohen, it's up to you. Here we go.

Dr. Cohen:
One of the issues we've had is that it's really only one therapy that's had a dedicated clinical trial with a specific fistula healing endpoint, and that was infliximab in the ACCENT I and II trials published in *The New England Journal* years ago. So I would say that infliximab is the real go-to medication for patients who have a perianal fistula and hoping to heal that with medical therapy. There's also been some data, although not in a trial with specific endpoint, showing some effectiveness for adalimumab, so you can group that anti-TNF class together as the most effective therapy for treating perianal fistulas.

And we've learned from some retrospective analyses that you really need to optimize the anti-TNF medications ideally by using combination therapy with a thiopurine or methotrexate. The benefit of that may come from improving the serum drug levels of the anti-TNF medication.

So my general approach when I have these patients is if they haven't been on an anti-TNF medication to put them on infliximab, usually in combination with azathioprine, and I try to achieve a trough drug level of 20. And ideally for healing, you want a prolonged treatment, more in the range of probably six to 12 months to hopefully see the effects.

Dr. Buch:
Dr. Cohen, are there any studies comparing the effectiveness of anti-TNF agents compared with the newer small molecules for perianal Crohn's disease?

Dr. Cohen:
So at this point there are no studies comparing anti-TNF drugs with newer small molecules or other biologic drugs for that matter. There was some early data presented from a subpopulation of Crohn's patients enrolled in the upadacitinib phase 3 clinical trials who had perianal fistulas that was presented at Digestive Disease Week in 2023 that suggested that upadacitinib is effective for perianal disease. However, this was a small group of patients, and the study wasn't powered to detect the signal there. However, I do think there's promise.

Hopefully, we'll learn a little bit about the new drug risankizumab from subpopulations of those clinical trials. Again, we won't have specific fistula and radiology endpoints, which I think are also going to be important when looking at fistula healing. And there was data presented that hasn't reached manuscript form that suggested there was benefit of ustekinumab in perianal fistula healing. But we need better trials with fistula endpoints and classifications to really prove that in a prospective manner.

Dr. Buch:
For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Drs. Benjamin Cohen and Stefan Holubar about perianal Crohn's disease.

Dr. Cohen, do you have any comments on the use of hyperbaric oxygen?

Dr. Cohen:
Generally, hyperbaric oxygen is well tolerated, though there are some risks related to sinus barotrauma, claustrophobia, oxygen toxicity, among other

things. There have been some case series in Crohn's disease suggesting that hyperbaric oxygen in combination with medical therapy can have positive results in fistula healing. But beyond the lack of high-quality data, some of the barriers to more widespread use are access, insurance coverage the frequency of treatments needed, so I think this is definitely an option I would consider particularly for the very severe patient, but I'm curious what Dr. Holubar thinks about the promise of hyperbaric oxygen.

Dr. Holubar:
Yeah, there's a lot of talk about hyperbarics, but in reality, it can be very difficult to get insurance approval. And usually, we use that as a last-ditch kitchen sink approach to rectal preservation in patients with really severe perianal fistulous Crohn's disease. It's not something we use routinely for the average perianal Crohn's disease fistula patient.

Dr. Buch:
Now, Dr. Holubar, what helps you decide whether to perform a fistulotomy versus ligation of intersphincteric fistula tract versus endorectal advancement?

Dr. Holubar:
It's a great question. So fistulotomies are used widely for cryptoglandular fistulas outside of the Crohn's population, and they're associated with a very high, probably over 95 percent success rate. And these are for low transsphincteric or intersphincteric fistulas, but they're really not used for Crohn's for a couple of reasons. Namely, there's concern over Crohn's patients being at risk of having lifelong diarrhea, and they certainly need every millimeter of anal sphincter, so we're really reticent to divide any sphincter with a fistulotomy and Crohn's patients.

That being said, we do have a research study looking at its use, and there's certainly a role for subcutaneous fistulotomy where you're not really taking any internal or external muscle fibers in the fistulotomy, but that still leaves a little bit of an anatomic divot or defect in the anus that can lead to a little bit of seepage through that divot there. When we talk about trying to get rid of the fistula for the patient, as mentioned, the two most common options are the LIFT procedure and the endorectal advancement flap. And the LIFT procedure is not often used for Crohn's disease, and that's when we make a little incision in the intersphincteric group between the internal and external sphincter, and then ligate the fistula on either side. And then it has about a 50 percent success rate. With the 50 percent that fail, they develop an intersphincteric fistula for which you can then do a fistulotomy.

Usually, Crohn's fistulas are too complex for a LIFT procedure, so we really don't use that many LIFTs in Crohn's, but the endorectal advancement flap is probably the go-to procedure for getting rid of the internal opening. So what we do is we curettage out the tract from the external opening, and then we lift up a partial thickness flap of the rectal wall, and in the process, we excise the tip of that flap, which is the internal opening, and then suture close the internal opening in the submuscular layer, and then close the flap over that. There's a new procedure that's come out of the Takeda stem cell trial, and we call that curettage enclosure, and that was shown to have a 50 percent success rate for Crohn's fistulas, and it's a variation on the endorectal advancement flap that's less invasive. And similarly, we aggressively curettage out the external track or possibly even do a fistulectomy of the external opening down to the muscle and leave that wound open. And then instead of doing a flap on for the internal opening, we just put a couple stitches there to close it and that is a very new procedure that is less invasive than the flap, and it probably has a 50 percent success rate. But the good news is, is that unlike a flat, if you have a recurrence, you just basically have to put a seton back in, and then you could move on to something different, for example, a flap because you really haven't burned any bridges with the curettage enclosure technique, which again is very new.

Dr. Buch:
Thank you for that. So, Dr. Holubar, when is a fecal diversion appropriate?

Dr. Holubar:
Yeah, that's another great question that causes patients to have a lot of concern. And unfortunately, the data is pretty clear that overall 25 percent of patients with intestinal Crohn's disease will also have perianal disease, and then five percent will have isolated perianal Crohn's disease where they don't have any intestinal inflammation. And for the patients with Crohn's and perianal disease, unfortunately, about 20 percent of them will be refractory to all combined medical surgical therapy, harkening back to the importance of the multidisciplinary team approach that Dr. Cohen mentioned, but about 20 percent of patients will be refractory to that and actually wind up with a proctectomy.

So when a patient is really suffering and having an awful quality of life, I'm fond of saying that pain starts at the bottom and works its way up. If you have an unhappy bottom, you have an unhappy life, and a laparoscopic diverting loop ileostomy can take about half an hour and really dramatically and quickly improve a patient's quality of life because there's no longer stool going through the fistula, and it basically becomes quiescent most of the time. We say that this loop ileostomy is temporary, or we hope that it would be temporary, but unfortunately, the majority of the time those patients are not going to be able to have a permanent restoration of their intestinal continuity.

But the good news is that these patients are pretty miserable, they're often agoraphobic, incontinent with constant seepage, constantly requiring trips to the operating room for exams under anesthesia and incision and drainage, and the ileostomy really improves their quality of life, and that's the good news.

Dr. Buch:
So we're nearing the end of our time today. Sticking with you, Dr. Holubar, any final thoughts you'd like to leave with our audience today?

Dr. Holubar:
I think the perianal Crohn's disease patients are a special subgroup of Crohn's that are very difficult to manage, and you really have to have an expert team in terms of both the IBD gastroenterologists and IBD colorectal surgeons who see high volumes of these patients because even in the best of hands, the outcomes are suboptimal, as we just alluded to, with a significant proportion going on to permanent diversion and/or a proctectomy. So we really want to give these patients the best chance at avoiding a permanent stoma if possible.

Dr. Buch:
Thank you, Dr. Holubar. And, Dr. Cohen, you get the final word.

Dr. Cohen:
I would just echo what Dr. Holubar has said on the importance of the multidisciplinary management. And really, when it comes to those surgical treatments, those are really only possible if we can get the medical therapy to heal any proctitis that's present. I think that's a big key. So from the medical side, our goal is to heal the proctitis, set them up as best as possible to hopefully, respond to a surgical management, but at the end of the day, it's about improving quality of life, and sometimes we do have to have difficult conversations about patients, about the best way to do that.

But hopefully, in the future again, we're going to have dedicated clinical trials with clear endpoints. The top-class consortium was an international consortium really working to redefine classifications and hope push the field forward in that regard.

Dr. Buch:
This has been an excellent discussion on perianal Crohn's disease. And I want to thank my guests, Dr. Ben Cohen and Dr. Stefan Holubar, for joining me to share their expertise and insights. Dr. Cohen, Dr. Holubar, thanks so much for being here today.

Dr. Cohen:
Thanks again for having us.

Dr. Holubar:
Yes. Thanks so much for having us.

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.