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Understanding Surveillance Guidelines for Barrett's Esophagus

Dr. Nandi:
Preventing esophageal cancer in the context of Barrett's esophagus requires vigilance. Vigilance is key. Globally, there are greater than 50,000 cases of esophageal cancer reported, and more than 11,000 of those cases are right here in North America. At five years out, the survival rate approaches 15 to 20%, at best. We recognize that surveilling Barrett's is key.

On this episode, we will review with Dr. Gary Falk on how we can best maximize surveillance guidelines for Barrett's esophagus and even review some of the evolving technologies that are helping us do just that. Dr. Falk is a Professor of Medicine at the University of Pennsylvania in the Division of Gastroenterology and Hepatology. Dr. Falk is the Director of the Esophagology and Swallowing Center at the University of Pennsylvania and is known as one of the world's foremost authorities on Barrett's esophagus. Gary, welcome to *GI Insights*.

Dr. Falk:
Thank you very much. It's a pleasure to be here.

Dr. Nandi:
Absolutely. Now we did a program with you about who we should screen and when we should screen and how to avoid pitfalls in making the wrong diagnosis of Barrett's. But once we have that diagnosis at hand, we need to be careful about how we look for dysplasia and risk stratify the degree of dysplasia. I'm hoping you could briefly review the guidelines as they relate to non-dysplastic Barrett's and then degrees of low-grade versus high-grade dysplasia, and how we can start to think about our interval of aggressive endoscopy or not.

Dr. Falk:
You know, once someone has given a diagnosis of Barrett's esophagus, they are classified as non-dysplastic, indefinite low-grade, high-grade or intramucosal cancer. And our approach to each is very different.

In a setting of non-dysplastic Barrett's esophagus, individuals who have had adequate surveillance and biopsies, the current recommendations are endoscopy at three- to five-year intervals. That may change in the future, stratifying individuals by length of Barrett's by less than 3 centimeters or greater than 3 centimeters with less than 3 centimeters going for five-year intervals and greater than 3 centimeters going for three-year intervals. That is taking place in other parts of the world today and may start taking place in the United States in the future as well. But that remains to be seen.

Indefinite for dysplasia is a very common diagnosis, when a pathologist really cannot clearly sort out whether someone has inflammatory changes or dysplastic changes. And in a situation like this, and all aspects of dysplasia, a number of steps should take place. For indefinite, the first thing that should happen is have that diagnosis reviewed by someone with expertise in GI pathology. If there is going to be a problem with indefinite for dysplasia, that usually will take place early on within the first six months. And what's the reason for this? This and low-grade dysplasia may in fact be markers of more prevalent higher-level lesions. So for indefinite for dysplasia, the recommendation currently right now is to repeat an endoscopy within six months after maximizing acid suppression. And if that is normal after that time, people then revert to a non-dysplastic pathway. And if it's abnormal, they go to annual surveillance until it goes away.

Low-grade and high-grade dysplasia is a different story because confirmed low-grade dysplasia by an expert pathologist is a potential indication or endoscopic intervention. High-grade dysplasia, the same thing.

But your endoscopic intervention really is going to be based first on getting expert pathology review. And then if there is low-grade dysplasia confirmed, then it's really a discussion with a patient as to whether they wish to proceed with continued surveillance or

endoscopic intervention. There is level-one evidence that endoscopic intervention with radiofrequency ablation is very effective in decreasing cancer risk in individuals with low-grade dysplasia. But there's also evidence from that same trial that diagnosis of low-grade dysplasia is never confirmed again in about 25% of individuals. So there is the potential for one out of four people with low-grade dysplasia getting unnecessary treatment.

So a practical approach to low-grade dysplasia is first to have a discussion with the patient. It's really shared decision-making, going through pros and cons of continued surveillance versus intervention. Part of it will be based on an age, comorbidities, and the overall health of the patient. Part of it is based on risk tolerance, and part of it is based on expertise.

There is important information that the finding of low-grade dysplasia, in addition to being downgraded, may, in fact, be upgraded. This concept of prevalent disease may be present. So I typically will recommend a repeat examination within three to six months when maximal acid suppression to exclude a prevalent higher level lesion. And you're really on high alert to be able to remove anything with endoscopic resection.

High-grade dysplasia when you look at data from Europe, almost 90% of individuals in the EURO-II trial with high-grade dysplasia or intramucosal cancer had a visible lesion. So in the setting of high-grade dysplasia, endoscopic intervention is the recommended approach, but it should be based on first making sure you have a flat Barrett's segment. Any mucosal abnormality, lump, bump, or irregularity should be removed with endoscopic resection to maximize staging. But intramucosal cancer, again, endoscopic therapy is the preferred approach, starting with endoscopic resection and then completion eradication therapy.

Dr. Nandi:
So let's say we visualize a nodularity in an area of Barrett's. Should we be biopsying that? Should we be referring that for EMR? What should be that next step?

Dr. Falk:
Now, that's a great question. – And I'm going to give you a somewhat hedged answer. So in a setting of a mucosal abnormality, if it looks like a lump or a bump, all guidelines say to biopsy any abnormality no matter how subtle. On the other hand, if you biopsy, that can interfere with endoscopic resection, and most of us are not going to consent an individual for routine surveillance for Barrett's for endoscopic resection. And it's really the exception for that ever happened. So one could approach it one of two ways. One could say let's biopsy and see where we stand or one could say, 'Listen, I'm concerned about how this looks, I'm going to refer.' I'm going to either bring the patient back and do an endoscopic resection myself, or refer to somebody in my group or in a center of excellence where endoscopic resection is done routinely.

Dr. Nandi:
I think that's important, and I think it depends on that experience of that endoscopist, which decision they make. But to be wary that there are some great specialists who do have the time and skill set and tools to go ahead and resect some of these completely and to contact your local tertiary care center for that expertise.

We talked about ablative therapies for some of these dysplastic lesions. Again, this is something that most endoscopists are going to refer to a high-volume center and specialist such as yourself. But just to walk us through, when we counsel our patients, how does one decide to use RFA versus cryo, for instance, or some other ablative therapy?

Dr. Falk:
So when you talk about endoscopic eradication therapy, the most important tool in the toolbox is endoscopic mucosal resection because all other techniques are really not to be applied until you've removed any visible lesions. Once visible lesions are removed, then the highest-level evidence continues to be radiofrequency ablation; there are multiple randomized control trials to show the efficacy and there's now experience of over 10 years with excellent outcomes with endoscopic eradications therapy with radiofrequency ablation.

There is also evidence that cryotherapy works. Cryotherapy until now, is not quite as easy to administer. There's a little bit of soup-making within in terms of the spray devices that have been used. And now there is a balloon-based device that is just come out for mass market use. That is an excellent tool with very promising evidence for myself that's really held and reserved for non-responders to conventional endoscopic eradication therapy.

Another thing that has been used in Europe that one can consider after endoscopic eradication therapy for little punctate islands is to apply argon plasma coagulation, but certainly not as a first-line therapy.

So really EMR is the cornerstone of it. ESD is a potential in select centers for more advanced lesions, and then radiofrequency ablation as probably the preferred choice based on level-one evidence and cryotherapy is also available, not right now with level-one evidence.

Dr. Nandi:

All points well taken. We definitely don't want to bury tissue and ablate, we want to resect first before we apply those types of ablative therapies. That's good news.

For those just tuning in, you're listening to *GI Insights* on ReachMD. And I've been speaking with Dr. Gary Falk, where we have been reviewing surveillance guidelines for Barrett's esophagus and a brief overview of how we apply EMR and ablative technologies.

Now, Gary, I want to shift a little bit I want to talk about gadgets and some of the technology that are being developed. One that I read with interest from afar as an IBDologist is the development of WATS technology. Can you describe to our listeners what that is and what its role may be in Barrett's dysplasia surveillance?

Dr. Falk:
So WATS stands for wide area transepithelial sampling. And it's a combination technique of sampling with an abrasive brush so that you get more than a cytology specimen, and almost a histology specimen. And the other part of this is that it then uses neural networks, really an early form of artificial intelligence to try to sort out all these cells to find abnormal cells. And the beauty of the technique is that allows you to sample a given area of Barrett's much more rapidly and potentially get more tissue to sample from. That's the concept in a nutshell.

Has it been put to the test yet completely? Not really. So there are lots of case series about this. The yield of this technology seems to be for lower-level lesions, mostly low-grade dysplasia, because high-grade and cancer are more visible.

And really the key question that's unanswered that I'd like to see answered with this is that can we use this technology and technique and avoid doing the Seattle protocol? Given the reluctance of the GI community to embrace the Seattle protocol, what's happening is that perhaps a less than optimal biopsy protocol is used. And this is then used as an adjunct. So the question is, how does it compare to the Seattle protocol? And can you replace the Seattle protocol with this? And if you can, that would be a game changer because it would make surveillance tissue sampling so much easier.

So there's promise. It's being used a lot, but it's unclear what the gain is of this compared to well-done surveillance with the Seattle protocol biopsies.

Dr. Nandi:
I think it's a fascinating platform, but like you said, we still have a ways to go to prove where it's going to be most high yield in the high-grade dysplasia or obvious advanced lesions, we may not need this technology to pick up what our eyes can.

Let me step back and just kind of look at the big picture. We've talked a lot about how to screen and how to surveil. But I can't shake this again, you noted that even with non-dysplastic Barrett's, the risk doesn't go to zero with regular surveillance? Should we ever stop surveilling somebody? Or what would be the right scenario to stop?

Dr. Falk:
So that's a great question. And one should not survey people that don't have Barrett's, number one. Number two there's a recent beautiful study done by Joel Rubenstein and colleagues looking at ways to determine one should stop surveillance. And it's really based on life expectancy, which most of us can't calculate in our head. And in talking to Dr. Rubenstein, one of the aspects of that study, which is how can we utilize their data to make a simple determination as to when we should stop?

Simplistically, I think that surveillance really has no role in individuals who can't survive or can't tolerate an intervention and frequent endoscopies. So if someone has multiple comorbidities that are going to preclude them from tolerating endoscopic interventions, chemo, radiation therapy, or surgery, it makes no sense to keep doing it because those other problems are going to probably do them in. It's not black and white. There's many shades of gray here. But there's no clear guidance like there is for colon cancer screening once stopped, and that interval between 75 and 85; things are individualized.

So there's no clear guidance here. But there is emerging data that you can have some prediction of how long someone is going to live. And if once reaches a certain threshold, it probably makes sense to stop.

If you're going to continue doing surveillance, you really need to adhere to intervals and not go too high. But clearly individuals who can't tolerate the risk of endoscopy is greater than the risk of not doing endoscopy, it makes sense to think about it very carefully. And I will typically stop surveillance in individuals who are not going to tolerate endoscopy or an intervention.

Dr. Nandi:
No, absolutely. That makes sense. I tell my patients that if we all live long enough, something's gonna break, right? We're all going to develop something. But if you see a pattern we have to balance that against the risks and your longevity individually. So lots of gray, as you mentioned.

Dr. Falk, thank you so much. I learned a lot from listening to you. I really appreciate you taking the time to share your insights on our program today. Any closing remarks before we go?

Dr. Falk:
I think we covered the high points. I think when it comes to surveillance and treatment, one has to be meticulous. Decisions about what to do are not automatically share decision-making with a patient. No one is ever flying solo. It's reasonable to get second opinion from pathologists or people who have high-volume Barrett's type practices because outcomes for any surgery or any intervention are better in high volume. It's okay to ask for help. And again, the key story with Barrett's is that even though it's associated with esophageal cancer and is a risk factor for esophageal cancer, most people with Barrett's esophagus are going to live just fine with this condition and are going to never develop cancer. That's a message that I give to all my patients.

Dr. Nandi:
And that's a message that we should be sharing more with our patients to alleviate any anxiety as well. Thank you very much, Dr. Falk.

For ReachMD, I'm Dr. Neil Nandi. To access this episode and others from GI Insights, please visit Reachmd.com/GIInsights, where you can Be Part of the Knowledge. Thanks for listening.