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## Bringing Barrett's Esophagus into Focus: A Look at Controversies & Unanswered Questions

Dr. Buch:

This is *GI Insights* on ReachMD, and I'm Dr. Peter Buch. The evaluation and treatment of Barrett's esophagus has been evolving over the last several years, yet there are many controversies and unanswered questions. Today we are privileged to have the expert guidance of Dr. Prateek Sharma, who helped author the AGA Clinical Practice Update on Endoscopic Treatment of Barrett's Esophagus with Dysplasia and/or Early Cancer Expert Review, published in *Gastroenterology* 2020. Dr. Sharma is a global expert on Barrett's esophagus, esophageal cancer, and novel imaging techniques. If I continued with all of Dr. Sharma's credentials and accolades, we would not have time for our session. Dr. Sharma, it's great to have you join us, today.

Dr. Sharma:

Thanks, Dr. Buch. It's my pleasure to be here and thank you also for that kind introduction.

Dr. Buch:

Let's get right into it, Dr. Sharma. As you are well aware, by using current criteria to evaluate for Barrett's esophagus, we are missing an important portion of the at-risk population. Can you review those criteria for our audience and share how we may improve surveillance in the future?

Dr. Sharma:

Yes. Thanks. Happy to do that, and I think there are two areas where we are missing out on the at-risk population. The first comes to screening, which is what's the population that is at high-risk to harbor Barrett's esophagus or esophageal neoplasia or cancer? And we struggle with the risk factors. We know that chronic gastroesophageal reflux disease, male gender, a history of smoking, obesity, family history of esophageal adenocarcinoma, those are risk factors for harboring that, and so our current screening guidelines tell us that if patients have a number of these risk factors, they should be considered for an upper endoscopy to rule that out. But that's the first issue is who has the Barrett's disease.

The second is that once you've diagnosed a patient with Barrett's esophagus, how do we know who's going to progress to cancer in the future? And right now, the surveillance programs are pretty generic, that they say that you should survey these patients every three to five years. We need to get into the issue of personalized medicine and a risk stratification score so that you can then treat these patients differently.

One such score that's been proposed is called the PIB, or the Progression in Barrett's score, which then assigns a number or a numerical score to each one of those risk factors and then shows that as the length of Barrett's esophagus increases, if a patient has a hiatal hernia, male gender, and if they're smoking, they're at a high risk for progression. So in the future, I'm hopeful we can tailor surveillance based on these risk factors.

Dr. Buch:

Excellent. How will we be able to sub-stratify low-grade dysplasia in the future to reduce surveillance load?

Dr. Sharma:

Yeah, again, another excellent point, Dr. Buch, and this relates to the heterogeneity that we see with low-grade dysplasia that the majority of the patients with low-grade dysplasia have a very benign outcome. And so we just struggle with who's at a high-risk for progression. A number of markers have been used, such as immunohistochemical staining, such as looking at concordance between two, three, four pathologists reading it and calling it as low-grade dysplasia.

In clinical practice, I look at some of the risk factors within low-grade dysplasia, such as, is the low-grade dysplasia at different levels within the Barrett's segment? If you see it in more than one biopsy, you are more likely to know that this is low-grade, rather than a sampling error.

Is it persistent over time? So I usually bring these patients back for repeat endoscopy and biopsy within three to six months. If low-grade dysplasia disappears, I actually think that's a very low risk patient. On the other hand, if persists, I'm more able to assign a high-risk to that patient along with those other risk factors and then survey them on an annual basis.

Dr. Buch:

How would you follow a young, asymptomatic patient who has a diagnosis of Barrett's esophagus made by an overly anxious endoscopist?

Dr. Sharma:

OK. So, now, Dr. Buch, you're starting to ask me those difficult questions, I see. So this is a very common clinical scenario and one of my take-home messages, when I teach about diagnosing Barrett's to the fellows and to the trainees, is that it's as important to know what is not Barrett's esophagus as it is to know what is Barrett's esophagus. And this goes to exactly your question is that it's a pre-cancerous condition. As soon as you assign a diagnosis of Barrett's to a patient, their anxiety hits the roof. Their insurance changes as well, the premium increases. So there are a lot of unintended consequences that sometimes as physicians and gastroenterologists, perhaps we don't think about those issues.

So the guidelines are now very clear about the diagnosis, which is that if you see columnar mucosa in the distal esophagus, which is usually lined by squamous and if it starts getting lined by columnar mucosa and that length is 1.0 cm or greater, and you biopsy that and it shows intestinal metaplasia, that's the patient that you should assign the diagnosis of Barrett's esophagus. If the length is less than the centimeter or you're not sure if it's even a few millimeters, that's best ignored. Don't try to biopsy that because that's usually not going to be very helpful.

So be very clear about what those diagnosis should entail and your point's very well taken is that this does lead to overt anxiety, so be very careful in making that diagnosis.

Dr. Buch:

For those just joining us, this is *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today I'm discussing Barrett's esophagus with Dr. Prateek Sharma.

Getting back to our discussion, Dr. Sharma, how do you explain esophageal adenocarcinoma not arising from Barrett's?

Dr. Sharma:

Yeah, so the majority of the esophageal adenocarcinomas are linked to Barrett's, and in fact, if you look at the precursor lesion, this is the only precursor lesion that we know about. Having said that, I'd say that in well-done studies, they're able to assign close to 90 to 95% of patients with esophageal adenocarcinomas to Barrett's esophagus. The remainder of those patients may arise de novo or from another lesion that we may not be aware of. But that I think is the minority.

The major issue is that not that whether it's coming from Barrett's or not, but studies have shown that very few patients with esophageal adenocarcinoma have a previous known history of Barrett's esophagus, which tells us that we have very poor screening guidelines in place and very poor screening programs. And part of it goes to your first question about who's at risk? Who should we screen? And that's the million-dollar question that we are struggling with, is trying to identify that patient population at risk. So if we can find those patients at risk, we will increase that substrate of esophageal adenocarcinomas, which are linked with Barrett's esophagus and therefore be able to diagnosis them very early on so that it's early stage cancer, which can be cured, rather than late stage cancer, in which the five-year survival is very poor, close to 10%.

Dr. Buch:

Thank you. If you have a patient with Barrett's and low-grade dysplasia, how do you decide whether to continue surveillance or to offer therapeutics?

Dr. Sharma:

It again goes back to the risk stratification point. I do ensure that the diagnosis of low-grade dysplasia is accurate and by accurate, I mean have you actually missed out on high-grade dysplasia or cancer? So I'm more concerned about missing out on high-grade dysplasia or cancer rather than a diagnosis of low-grade dysplasia. So I will typically repeat my endoscopy in those patients and make sure that I do a careful inspection of the Barrett's and the esophagus that there is no nodule, no lesion, which may harbor cancer, so that's my first step.

The second is re-biopsy. So I'll make sure that I take more biopsies this time during the second endoscopy. The third is review with your pathologist. Pathologists, unfortunately, cannot distinguish, or I'd say have a hard time distinguishing, low-grade dysplasia from inflammatory changes or from reactive changes within the biopsy that is submitted to them. And so I try to make sure I look at it with the pathologist, make sure that he or she knows what am I asking for here.

The fourth thing is I ensure that the patient is on adequate acid suppression therapy because if there's acid coming into the esophagus, that can lead to inflammation that can lead to reactive changes, which can make the diagnosis of low-grade dysplasia very difficult. So those are all the initial steps that I go to before deciding whether this patient truly has low-grade dysplasia or not.

Then I sit down with the patient; this is one of those in which you truly need to have shared decision-making. You tell the patient the risks and benefits of either surveillance or endoscopic therapy because both of them have some risks and benefits going along with it. And so going back to the document you were referring to, the practice guideline update, is very sort of open in that statement about management of low-grade dysplasia, seeing that both of these are very reasonable treatment approaches to the patient. And so having an open discussion goes a long way.

Dr. Buch:

So Dr. Sharma, what is your thought about artificial intelligence for evaluating Barrett's esophagus?

Dr. Sharma:

AI, as we know it, is gradually taking over our lives, right? I mean, we have voice commands for Siri, for Alexa, we have smart phones, a number of them are AI-driven and so it's just a matter of time that it will creep into the management of a number of diseases, which it already has. In Barrett's esophagus, AI will help us detect these lesions, these dysplastic areas with which I've already highlighted may sometimes be difficult to find.

So it's a branch of artificial intelligence called Computer Vision, which deals with algorithms, which depends and is based on what you're seeing with the endoscope and that is then fed into computers, which are able to then tell us where the abnormal areas are in real time, during endoscopy, highlight those areas for us and telling us that "well, this area looks abnormal," that's the area perhaps to biopsy. Now this is already being started to use in mammography, for example, as you well know, Dr. Buch, and in radiology, where these AI algorithms are helping radiologists identify small areas of breast cancer, small lung nodules, which may be very difficult to discern with the naked eye. So very soon in Barrett's also, we will be to a point and studies are currently ongoing, which will help diagnose these areas and these areas of early cancer. All in all, I think it will help improve patient care and improve patient outcomes.

Dr. Buch:

Before we wrap up, is there anything else you would like to share with our audience?

Dr. Sharma:

No, I just want to highlight just a few things that make an appropriate diagnosis of Barrett's; don't over-call it, don't under-call it, enroll the patients in appropriate surveillance intervals, make sure you're examining the Barrett's carefully and then doing your targeted biopsy, and then for those patients with high-grade dysplasia and cancer, they can be treated endoscopically with minimally non-invasive therapies. The future's really exciting in this field and I urge all of you who are interested in this field to go and do some searches on our GI journals and get more information about it.

Dr. Buch:

Thank you. That's all the time we have for today. So, I want to thank Dr. Prateek Sharma for helping clarify these very important points regarding Barrett's esophagus. Dr. Sharma, thanks so very much for joining us here today.

Dr. Sharma:

Thank you.

Dr. Buch:

For ReachMD, I'm Dr. Peter Buch. To access this episode and others from our series, visit [ReachMD.com/GIInsights](https://ReachMD.com/GIInsights), where you can Be Part of the Knowledge. Thanks for joining us today.