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Reviewing Management Strategies for Barrett's Esophagus & EAC

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch, and today we are joined by Dr. Joel Rubenstein. Dr. Rubenstein is the author of, "Gastroesophageal Reflux Disease Is Not a Great Screening Criterion: Time to Move on to Other Strategies for Controlling the Burden of Esophageal Adenocarcinoma," published in the *American Journal of Gastroenterology* November 2022. Dr. Rubenstein is a research scientist at the Kettles VA in Ann Arbor, Michigan, and a Professor of internal medicine in the Department of Gastroenterology and Hepatology at the University of Michigan School of Medicine. His research focuses on management strategies of Barrett's esophagus.

Dr. Rubenstein, welcome to the program.

Dr. Rubenstein:
Thank you very much, Dr. Buch. I'm delighted to be here talking with you.

Dr. Buch:
Let's dive right in, Dr. Rubenstein. Why have only 20 percent of patients with esophageal adenocarcinoma undergone endoscopy?

Dr. Rubenstein:
Well, first off, we've been relying on GERD symptoms to identify people at risk for esophageal adenocarcinoma, EAC, but only 50 percent of patients with EAC report having had significant prior GERD symptoms, so right off the bat we miss about half of those patients; but even of the remaining half, only a minority have had an EGD before they are diagnosed with cancer. The reason for that isn't entirely clear, Dr. Buch, but there are a number of possible explanations. It seems to me the most likely one is that people are much more likely to undergo an endoscopy for GERD symptoms if those symptoms are not responding to medications, like PPIs.

Swathi Eluri at University of North Carolina performed a study of a large multi-practice network and found that only 39 percent of GERD patients who met the stringent criteria for screening had undergone EGD, and even among those the great majority were referred for refractory symptoms rather than just for screening purposes. But patients with refractory symptoms are not really at increased risk for Barrett's esophagus compared to people whose symptoms are easily managed. And patients whose GERD symptoms are under good control, either with prescription or over-the-counter medications, are at just as increased risk for Barrett's as those who are not controlled, and yet they don't complain to their provider, and they are very unlikely to get screened.

Dr. Buch:
Thank you very much for that. And are patients with GERD who are refractory to therapy at an increased risk for Barrett's esophagus?

Dr. Rubenstein:
If their refractory symptom is heartburn, they are at increased risk for erosive esophagitis, though in a previous study, we did not find any evidence of increased risk of Barrett's esophagus. And if their symptoms are atypical, like cough or throat clearing, or even if their

symptom is regurgitation, and that's not responding to PPI, they're not at increased risk of erosive esophagitis or Barrett's esophagus. The reason that those patients have refractory symptoms is probably because most of them don't actually have GERD causing those symptoms in the first place, as gastroenterologists listening to us, they know that these are the patients who are most commonly referred to us for "GERD" and are most likely going to get an endoscopy, but the patients who are sitting at home managing their GERD symptoms totally fine, don't get referred to us.

Dr. Buch:
And what should we know about the role of patient's gender and race in endoscopic screening?

Dr. Rubenstein:
Thanks for asking about that. GERD is an important risk factor for Barrett's esophagus and EAC, but there are other important risk factors, like gender and race. Male sex is a very important risk factor for EAC. Men are about 2.5 times as likely as women to have Barrett's esophagus and five times as likely to develop EAC, and black individuals tend to be much less likely to develop EAC than white individuals for reasons that we don't entirely understand. Hispanic individuals have an intermediate filerisk. Native Americans have at least as great a risk as white individuals.

We recently conducted analyses of endoscopic screening and concluded that screening is cost-effective in white and black men with GERD symptoms but not quite so in white women and even less cost-effective in black women. In fact, in some of the scenarios in black women, screening could actually cause net harm. Although we didn't study this directly, if other risk factors are present, such as obesity or smoking or family history, that might push screening to be cost-effective in white women.

Dr. Buch:
So from your vantage point, Dr. Rubenstein, what needs to change when it comes to screening patients for Barrett's esophagus?

Dr. Rubenstein:
I believe we need to deemphasize GERD. GERD is indeed an important risk factor for EAC, but it's not the only one, and EAC may be really the only cancer where screening criteria are based on symptoms, and that causes providers a lot of confusion, confused screening, which in all other context, for like colon cancer screening or breast cancer screening, it's in the context of asymptomatic people, and they confuse that with diagnostic testing. We've tried now for 20 years to peg screening for EAC with GERD symptoms, and that's not working, clearly.

There are a number of validated tools out there to take into account not just GERD symptoms, but they also include other factors, such as age, sex, obesity, and smoking in order to predict risk, and there's even online calculators available for helping providers estimate and communicate that risk to their patients; but unfortunately, they don't get used, and I think it's a lot to expect of a busy primary care provider to recognize all these nuances that we've talked about today.

So while EAC is an important cause of death, it's still relatively uncommon, and primary care providers have a lot of important issues seeking their attention. So ultimately, I think what we need to do is build some automated symptoms for using electronic health records to predict that risk of EAC and communicate that to providers for their patients who are at elevated risk so the providers could offer a screening.

Dr. Buch:
And that's what we're going to talk about in the second half. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Joel Rubenstein about strategies to improve the detection of Barrett's esophagus.

Now switching gears a bit, Dr. Rubenstein, can you tell us about Houston-BEST?

Dr. Rubenstein:
Sure. The Houston-BEST—BEST stands for Barrett's Esophagus Screening Tool—was developed by Theresa Wenker at the Houston VA, using known risk factors for Barrett's and EAC, and those include GERD symptoms and age, sex, race, smoking, body mass index,

and a family history of esophageal cancer. She developed that intentionally for use with electronic health records, and it was internally validated at the Houston VA in a separate cohort, and then externally validated using data from a cohort we had previously enrolled at the University of Michigan and the Kettles VA in Ann Arbor. This shows that the prediction tools that are currently available can be adapted for use with electronic health records, and I really think that's where the future of this lies.

Dr. Buch:
And how successful are other modalities in detecting Barrett's esophagus?

Dr. Rubenstein:
That's a great question. Aside from traditional sedated endoscopy and biopsy, there's a number of other screening modalities, unsedated transnasal endoscopy, which uses a scope that's much smaller than a regular endoscope. That's been around for a few decades, and multiple studies have demonstrated its accuracy, including using a mobile screening van to go to the patients rather than having the patients come to us, but it hasn't taken off, and my impression is that's because we have this huge infrastructure built around endoscopy units, and we just don't have that infrastructure built up for doing transnasal office-based endoscopy or mobile vans.

There are a number of other newer technologies that are a bit less invasive, and all of which, essentially use tissue sampling devices that patients swallow and then are retracted using some sort of tether. The furthest one along is called Cytosponge, which is an abrasive sponge condensed in a gelatin capsule. The patient swallows that capsule, and it's attached to a string. The capsule dissolves in the stomach, and then the nurse or technician retracts the string and the sponge back out through the mouth. In the United Kingdom, where this was invented, they performed very large studies with tens of thousands of patients with this demonstrating its accuracy for identifying Barrett's esophagus of at least two centimeters in length, and they found it's well tolerated, at least there in the UK.

Dr. Buch:
And before we conclude, Dr. Rubenstein, are there any other thoughts you'd like to share with our audience today?

Dr. Rubenstein:
First off, a lot of people confuse dyspepsia with reflux symptoms. Just to be clear, dyspepsia is discomfort that's in the abdomen, and it can be epigastric, it can be periumbilical, whereas heartburn should be located in the chest or retroxiphoid. And when patients have dyspepsia, that is not an increased risk for esophageal adenocarcinoma and not really something that we consider as a risk factor for screening.

I do want to be very clear that we've been talking about screening today. Patients who have alarming symptoms, such as dysphagia, bleeding obviously, anemia, those are things that require endoscopy regardless of whether their symptoms are under control or refractory or any of that sort of thing. Those patients should get an endoscopy.

Dr. Buch:
These were some wonderful insights into screening our patients for Barrett's esophagus. I want to thank my guest, Dr. Joel Rubenstein, for a great discussion.

Dr. Rubenstein, thanks so much for joining us today.

Dr. Rubenstein:
Thank you very much.

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