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### Expert Perspectives on Guideline Updates for NASH

#### Announcer:

You're listening to *GI Insights* on ReachMD, and this episode is sponsored by Siemens Healthineers. Here's your host, Dr. Charles Turck.

#### Dr. Turck:

The American Association of Clinical Endocrinology, or the AACE for short, recently released updated clinical practice guidelines on nonalcoholic fatty liver disease in partnership with the American Association for the Study of Liver Diseases, also known as the AASLD. So, what do these guideline updates recommend for the diagnosis and management of nonalcoholic steatohepatitis, or NASH?

Welcome to *GI Insights* on ReachMD. I'm Dr. Charles Turck, and joining me are Drs. Scott Isaacs and Zobair M. Younossi. Dr. Isaacs is an endocrinologist in practice at Atlanta Endocrine Associates. Dr. Isaacs, welcome to the program.

#### Dr. Isaacs:

Thank you for having me.

#### Dr. Turck:

And Dr. Younossi is the Chairman of the Department of Medicine at the Inova Fairfax Medical Campus. He's also a Professor of Medicine at Virginia Commonwealth University Inova Campus and an Affiliate Professor of Biomedical Sciences at George Mason University. Dr. Younossi, it's great to have you with us.

#### Dr. Turck:

Starting with you, Dr. Isaacs, can you give us a high-level overview of the guideline updates on NASH from the AASLD and AACE?

#### Dr. Isaacs:

Well, we're proud to have published the first NAFLD guidelines for endocrinology and primary care, and this is so important because endocrinologists and primary care physicians are seeing patients with NAFLD every day. About one in three patients have NAFLD, and of those, about a third have NASH with advanced fibrosis. But the prevalence is double in those with type 2 diabetes or metabolic risk factors, such as obesity, especially central obesity, as well as dyslipidemia and hypertension.

#### Dr. Turck:

Moving to you, Dr. Younossi, what do the updated guidelines tell us about the role of liver biopsy to diagnose NASH?

#### Dr. Younossi:

So, the guideline helps in terms of providing some, a decent pathway where we can use a liver biopsy. You know, historically, liver biopsy has been an invasive procedure. It is really the only good way to get a piece of liver tissue to make the diagnosis of steatohepatitis, which is a pathologic diagnosis, and that has been the gold standard for diagnosing steatohepatitis. Now, over the years, as we have developed better and better noninvasive tests the role of liver biopsy, the use of liver biopsy has fallen dramatically. Currently, we still use liver biopsy when a patient is a candidate for a clinical trial because that still is a requirement for enrollment in clinical trials. Also, you can use liver biopsy when there is a discrepancy between noninvasive tests. For example, you know one test suggests a patient's at high risk, another one would suggest that a patient's at low risk. You can find out if the patient, you know, what is the stage of liver disease in that patient with a liver biopsy, of course, and that is occasionally used. And finally, probably the most important, is that liver biopsy can be used in the context of superimposed other liver diseases, such as the patient that comes in with fatty liver disease but also has very high autoimmune antibodies or autoimmune markers, and you want to make sure that the patient doesn't have superimposed autoimmune hepatitis in the context of nonalcoholic fatty liver disease. So, this is really currently the role of

liver biopsy, that the guideline document provides some, you know, advice to providers in terms of how to use it and when to use it.

**Dr. Turck:**

Now if we focus on high-risk patients with diabetes for just a moment, Dr. Isaacs, why is the early detection of NASH so important in this patient population?

**Dr. Isaacs:**

Well, endocrinologists and PCPs need to pay attention to liver because NAFLD is the hepatic manifestation of metabolic syndrome, and by diagnosing patients early, we can prevent cirrhosis and address risk factors for cardiovascular disease, which is the number one cause of mortality, and the patients that tend to progress to NASH with advanced fibrosis are those who have type 2 diabetes, obesity, or other metabolic risk factors. And type 2 diabetes and NAFLD are mutually detrimental, meaning that having NAFLD increases the risk for type 2 diabetes, and for patients that already have diabetes, it makes it more difficult to manage, primarily due to hepatic insulin resistance. And NAFLD also increases atherogenic dyslipidemia, increasing the risk for cardiovascular disease, and so, having type 2 diabetes makes NAFLD worse, increasing the risk for NASH, fibrosis, cirrhosis, and liver cancer.

**Dr. Turck:**

And staying with you, Dr. Isaacs, what do the guidelines tell us about the role of noninvasive exams, like the ELF test, to assess disease progression?

**Dr. Isaacs:**

Well, from my perspective as an endocrinologist practicing in Atlanta, an imaging test to measure liver stiffness like transient elastography is very helpful, but it can be difficult to do if you don't have access to the test. And another way is using a blood test like the ELF test, which is helpful to use as a prognostic test for patients with NASH with advanced fibrosis, and it's simple to order a blood test just like any other lab test, and the results are straightforward to interpret and explain to patients.

**Dr. Turck:**

For those just joining us, this is *GI Insights* on ReachMD. I'm Dr. Charles Turck. I'm speaking with Dr. Scott Isaacs and Zobair Younossi about the latest guidelines on nonalcoholic steatohepatitis.

So, Dr. Younossi, if we switch gears and take a look at therapeutic updates, can you give us an overview of what the guidelines recommend for the treatment of NASH?

**Dr. Younossi:**

Well, those patients with nonalcoholic fat liver disease, all patient require a lifestyle intervention, and especially if they are considered to be high-risk NASH through the noninvasive test algorithm that the guideline provides. Now, it's important that lifestyle intervention is not a passive thing where you can actually tell the patient, well, just go lose weight, you know, with exercise and diet, and come back and see them in six months. That never works. You have to actually consider a lifestyle intervention as really a prescription that requires a multidiscipline team of not only hepatologists or laboratologists but also primary care physicians and exercise specialists, nutritionists, and even behavioral health expert. In that context, you have to not only provide tools for the patient to be successful with their diet and exercise, but also you have to monitor them closely, the same way that you monitor a blood count or a liver enzyme when you start new medication for patients. So, it has to be really very regimented the lifestyle intervention for patient with nonalcoholic steatohepatitis. Now, in the United States, we recommend a Mediterranean diet for patients who have NASH, and what that has to be at least accompanied in some context with moderate physical activity, the two seem to work better, and the guideline would provide even more in-depth sort of detail of how to use lifestyle intervention in the context of treatment of NASH.

**Dr. Turck:**

And before we close, I'd like to hear from both of you on how these guideline updates may improve the diagnosis and treatment of patients with NASH. Dr. Isaacs, let's start with you.

**Dr. Isaacs:**

The key point for endocrinologists and primary care physicians is knowing that the prevalence of NASH in the population that we are seeing in our offices is very high. In patients with diabetes, one in five have NASH with clinically significant liver fibrosis. So, it's important and helpful to have a prognostic test for NASH patients who have advanced fibrosis and having a prognostic test like the ELF test is helpful because many can have normal liver enzymes, and there are currently no other noninvasive tools available to prognosticate patients with NASH. So, getting the diagnosis of liver disease can be difficult for patients to hear, but it's also incredibly motivating for patients to make lifestyle changes needed to lose weight and halt or reverse disease progression.

**Dr. Turck:**

Thanks, Dr. Isaacs. And Dr. Younossi, I'll turn to you for the final word.

**Dr. Younossi:**

I think that the most important part of the guideline that provides a pathway of how to identify patients with high-risk NAFLD. Those are the patients that have evidence that they would probably will have more of a progressive course, and as context, you know, looking at those patients with type 2 diabetes or other metabolic risk factors and using a noninvasive test, such as FIB-4, and really re-stratifying those patients with other noninvasive tests, such as an ELF test, which is enhanced liver fibrosis test, or a trans elastography will find most of our patients who are not at risk for advanced fibrosis or for adverse outcome, but it also could help identify those patient that we can consider at high risk. This is the group, the high risk patients with nonalcoholic fat liver disease that we need to focus on in terms of managing their risk factors, diet and lifestyle intervention, and then ultimately, drugs and clinical trials, of course, initially, but then the drugs that will be approved for nonalcoholic steatohepatitis. So, this guideline provides a clear pathway that will then provide the pathologists, primary care physicians and other providers a pathway of how to actually focus on finding the most at-risk patients with nonalcoholic fat liver disease.

**Dr. Turck:**

Well, with those final thoughts in mind, I want to thank my guests, Drs. Scott Isaacs and Zobair M. Younossi, for sharing their insights on the updated AASLD and AACE guidelines for nonalcoholic steatohepatitis. Dr. Isaacs and Dr. Younossi, it was great having you both on the program.

**Dr. Isaacs:**

Thank you.

**Announcer:**

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