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Managing MASLD in Patients with Obesity

Dr. Buch:
This is *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today I'm joined by Dr. David Tendler to explore the connection between obesity and metabolic dysfunction-associated steatotic liver disease, or MASLD for short. Dr. Tendler is part of the clinical faculty at the Duke University Department of Medicine in Durham, North Carolina.

Welcome to the program, Dr. Tendler. I'm looking forward to our discussion.

Dr. Tendler:
I look forward to speaking with you as well.

Dr. Buch:
Dr. Tendler, let's start with the big picture. What should we know about the pathogenesis of MASLD and its relationship with obesity?

Dr. Tendler:
MASLD, which I'm sure your listeners understand stands for metabolic dysfunction-associated steatotic liver disease, in yesteryear was referred to as NAFLD or non-alcoholic fatty liver disease. But the nomenclature has changed to reflect the pathophysiology. And because of the pathophysiology, it's gotten this name which ties back to the term metabolic, and that's where it ties into obesity and other conditions that relate to metabolic disease.

In this case, the pathophysiology largely stems in most cases from insulin resistance, which underlies most causes of the metabolic syndrome. And as it ties to obesity, that's one of the pillars of the metabolic syndrome along with hypertension, dyslipidemia, and in some cases, glucose issues such as diabetes.

Dr. Buch:
Thank you. And as a follow-up to that, what should we know about lean MASLD? And does the treatment approach for these patients differ from those with obesity?

Dr. Tendler:
There is a percentage of patients—relatively small but not insignificant, probably in the 10 percent range—who have what's called lean MASLD, meaning that they don't meet obesity criteria. And the main issue in that patient population is that the treatments may differ depending on whether or not their disease stage warrants treatment considerations of medicines like GLP-1s or other medications which might impact weight loss if weight loss is not appropriate in that situation. But otherwise, most of the treatments that we advocate for obese patients or overweight patients with MASLD are the same, and I'm sure we'll touch on some of those measures.

Dr. Buch:
So the bottom line here is that even though these are lean individuals, we should still recommend weight loss for them?

Dr. Tendler:
Weight loss when appropriate, but in these situations, we're really trying to address other cardiovascular risk factors like dyslipidemia, hypertension, diabetes if pertinent, alcohol consumption, and then consideration depending on their disease stage for medications, which may include GLP-1s if weight loss is not a contraindication. But there are other pharmacological treatments that we have available to us as well for the non-obese patients where weight loss is not a desirable outcome.

Dr. Buch:
So when evaluating a patient for MASLD, what testing do you recommend?

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Dr. Tendler:
So in addition to the non-invasive fibrosis testing to try to get an assessment of the stage of disease, we have to keep in mind that patients who present with abnormal liver enzymes, even if they're found to have fatty liver on an ultrasound or conclusively by other means, can have other liver diseases. So it's still important in that population that presents with an abnormal liver enzyme test to make sure that we get a good history that includes their alcohol consumption and medication use and also make sure that risk factors for viral hepatitis, like hepatitis B and C, are explored and that those tests are appropriately done to exclude other liver diseases like hepatitis B, hepatitis C, as well as common metabolic diseases like hemochromatosis and autoimmune hepatitis when pertinent.

So we want to make sure that even in this population when they present with abnormal liver enzymes, while we want to address the fatty liver and ultimately that's always going to be an important aspect of their care, we also want to make sure that we're not missing other common liver diseases.

Dr. Buch:
For those just joining us, you're listening to GI Insights on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. David Tendler about how obesity and MASLD are related.

How does your treatment approach differ between MASLD and MASH?

Dr. Tendler:
So this is where it becomes really important to risk stratify patients, whether or not they have simple steatosis. And in those cases, we're just trying to address management non-pharmacologically in most patients, because those treatment options are generally reserved for patients with more fibrosis, usually stage two or three fibrosis.

So in the patients who have just simple steatosis or very low-stage or non-fibrotic MASLD, what we're doing is making sure that they're trying to take off about 5 percent of their total body weight, increasing their activity levels, avoiding excess alcohol, and keeping up on their vaccinations, and then addressing other cardiovascular risk factors, treating hypertension, treating dyslipidemia, and treating abnormal glucose levels.

For patients who have been found after doing fibrosis assessments to have stage two or three disease, those are the patients we then need to be a little bit more aggressive with in terms of both monitoring and treatment, and that's when we start to have discussions about pharmacological measures.

Dr. Buch:
And a further follow-up question with regard to therapy: how do we decide whether we're going to be doing a GLP-1 agonist versus resmetirom?

Dr. Tendler:
In reality, it comes down often unfortunately to insurance coverage, and GLP-1 access has become very difficult and usually unaffordable in most patients. But it is an ideal treatment option for patients that have obesity because what we're trying to treat is the patient, not just their liver. So there's a lot of obesity-related issues that would be great to address if we could, which obviously includes not only heart disease risk factors, but even simple things aside from that, which might include chronic lower back pain or knee pain or other obesity-related conditions. So in that patient population who has had a hard time losing weight and has obesity-related conditions and even sleep apnea or other things like that, that's ideal. In patients where it's not practical or affordable to get GLP-1s, then if we're able to get resmetirom, that's a very viable option. Both have been shown to improve liver histology and reduce the rate of progression. So they're both reasonable options.

Dr. Buch:
Thank you. We're in the last few moments of our conversation, Dr. Tendler. Do you have any additional thoughts you'd like to share with clinicians treating patients with MASLD, particularly when we think about obesity and other metabolic risk factors?

Dr. Tendler:
I think one of the most important things is to understand that MASLD is part of the obesity spectrum. Not talking about the lean patients, but in the obese population, it's part of the disease spectrum which includes so many other conditions. And because of the majority of patients we'll evaluate in this realm will be found to have simple steatosis just statistically, it doesn't really mean that they should be ignored.

In addition to just monitoring to make sure there's not progression of liver disease, we want to keep in mind that this should be viewed in those patients as a warning shot across the bow that this is a group of patients that might have an increased risk for dying from

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cardiovascular disease rather than their liver disease. So we still have to address that population aggressively and make sure that we take advantage of the knowledge of having a metabolic condition to try to address the risk factors that put them at greatest risk for mortality and morbidity.

Dr. Buch:
Dr. Tendler, thanks so much for sharing these very important insights on obesity and MASLD. It was great having you on the program.

Dr. Tendler:
I enjoyed speaking with you, Dr. Buch, and I appreciate the invitation.

Dr. Buch:
Thank you so much. 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 and looking forward to learning with you again very soon.

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