**Transcript Details**
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/gi-insights/learning-about-the-new-definition-of-masld/15976/

**ReachMD**
www.reachmd.com
info@reachmd.com
(866) 423-7849

---

Learning About the New Definition of MASLD

**Dr. Buch:**
Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch, and joining me today to discuss cardiovascular disease and metabolic dysfunction-associated steatotic liver disease, which was formerly known as non-alcoholic fatty liver disease, is our returning guest, Dr. Paul Kwo. Dr. Kwo is a Professor of Medicine and the Director of Hepatology at Stanford University located in Stanford, California.

Dr. Kwo, welcome back to the program.

**Dr. Kwo:**
Thanks so much for having me.

**Dr. Buch:**
It's a true pleasure. Dr. Kwo, to give our audience a little clarity, can you explain why non-alcoholic fatty liver disease is now called metabolic dysfunction-associated steatotic liver disease, or MASLD for short, and how it's categorized?

**Dr. Kwo:**
Yes. So this was the new nomenclature. It had came about because of the need to try to reach consensus on an overarching term that can encompass all of the various causes of fatty liver disease. So just epidemiologically, if you will, what has been called non-alcoholic fatty liver disease, is the most common liver disease worldwide. In some parts of the world, the prevalence is actually quite high, approaching 30 to 40 percent. And so for that reason, this disease, which had been called non-alcoholic fatty liver disease, which, of course, connoted that there's no alcohol contribution to the fat, was thought to be in some ways stigmatizing, and then number two, didn't really accurately convey the interplay between metabolic-driven cytosis, which can come from insulin resistance and all of the other metabolic dysfunction-associated inflammatory patterns, as well as the contributions of alcohol. And so because this steatotic liver disease, or which is fatty liver, it just contributes so much to the liver disease that we see, it was felt that this term steatosis or steatohepatitis needed to be the underlying foundation for the liver disease. And then the other two dominant contributions to steatotic liver disease, or fatty liver disease, are non-alcoholic fatty liver disease, or the metabolic dysfunction or metabolic syndrome, contribution to this would be accounted for by calling this now metabolic dysfunction-associated steatotic liver disease, or MASLD. And this is now defined as somebody who has hepatic steatosis and at least one of the five traditional cardiometabolic risk factors that we typically contribute to metabolic syndrome. So that was the metabolic component.

And then they wanted to also account for the amount of alcohol contribution, which also occurs for people who have steatotic liver disease, and this is also something that's also extremely important as well because we want to be sure that people recognize that there is a contribution for alcohol-associated liver disease, which needs to be accounted for, and that is important for us to be able to quantify. And so there is now a category outside of pure metabolic-associated steatotic, or metabolic dysfunction-associated steatotic liver disease, called Met-ALD, which really is trying to describe metabolic alcohol-associated liver disease, and these are individuals who consume greater amounts of alcohol, which has been defined empirically as 140 grams a week for females and 210 grams a week for males, respectively. And then if you have fatty liver disease with inflammation, and then this is now, which we used to call non-

alcoholic steatohepatitis, this is now called metabolic dysfunction-associated steatohepatitis, so it's not NASH but rather MASH. And of course, there is still alcohol-associated liver disease, which contributes substantially to our disease burden. It's now the number one indication for liver transplant worldwide.

**Dr. Buch:**
Lots of information, but I got a couple of questions here for you. What do we know about the patients who have MASLD and also consume alcohol? Do we have a lot of information on those patients yet, or are we gathering information for future use?

**Dr. Kwo:**
Yes. So this is an important overlap that we are going to have to continue to study because there is no question that alcohol use, even a small amount, may contribute to steatotic liver disease, and ultimately, lead to progressive fibrosis and liver damage. And we empirically now try to quantify the amount of alcohol that's consumed such that if you are drinking less than two drinks per day or 140 grams per week for women or three drinks per day or 210 grams per week for men, then the predominant steatotic liver disease you have is MASLD. If you have higher amounts than this, then it's alcohol-associated liver disease predominant, and so this is the continuum now that's being defined.

And as we move forward and learn more about this, we're going to probably recognize that the amount of alcohol that is being consumed is clearly not healthy, particularly in the setting of alcohol plus metabolic dysfunction-associated liver disease, that the amount of safe alcohol to consume is going to fall considerably. And in fact, you should not be drinking if you have metabolic dysfunction-associated static liver disease regularly.

**Dr. Buch:**
Great. My other question here is first a definition for the audience. If you can just define what a PEth test is, and then describe whether you use a PEth test to determine whether your patients are consuming excessive alcohol.

**Dr. Kwo:**
Yes. So PEth is a biomarker phosphatidylethanol, and it reflects relatively recent alcohol use. As I was saying, the number one reason that we're transplanting in the United States is for alcohol-associated liver disease now, and one of the challenges we have is identifying individuals who have sufficient sobriety skills to maintain their sobriety, and we try and work with them for purposes of harm reduction. However, we do try to also verify that they've been able to stop their harmful consumption of alcohol, and we do this by looking for the metabolite phosphatidylethanol, or as it called PEth. And so PEth is very accurate, and it allows us to identify drinking that's occurred within the past few weeks, and compared to other prior biomarkers, doesn't have as many challenges, so it's used widely in the transplant arena. With regard to steatotic liver disease and those who have metabolic dysfunction, usually we're not so routinely using PEth here except if we're trying to, if you will, ascertain maybe that how much alcohol is being consumed is maybe not being accurately reported by the patients that we're evaluating.

**Dr. Buch:**
For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Paul Kwo about metabolic dysfunction-associated steatotic liver disease.

So, Dr. Kwo, should patients with MASLD also be concerned about cardiovascular disease?

**Dr. Kwo:**
So yes. In fact, your question about whether or not cardiovascular disease is a concern for MASLD is a very important one because the majority of people with MASLD, or stereotactic liver disease, actually don't develop progressive liver disease. Probably just 20 to 25 percent of individuals who have MASLD actually develop inflammation in the liver, called MASH or progressive fibrotic disease, that has the potential to progress to cirrhosis or even hepatocellular carcinoma. So what drives the mortality then for people who have MASLD is actually cardiovascular events, and so that is why we counsel all of our patients who have metabolic liver disease, that they are at increased risk for future cardiovascular outcomes.

And so when we see our patients with metabolic dysfunction-associated steatotic liver disease, we're evaluating them and just counseling them that they need to pay attention to their cardiovascular health because they are at risk for things, such as heart attacks, strokes, peripheral vascular disease, congestive heart failure. All of these are sequelae of atherosclerotic cardiovascular disease, and so these areas must also be carefully followed by their patients and their family physicians.

**Dr. Buch:**
It's a perfect segue. And what modifications could address cardiovascular risks in patients with MASLD?

**Dr. Kwo:**
So they are the traditional good health. So they should have things, like their hypertension, managed well. Many people with MASLD have dyslipidemia. This means they'll have high cholesterol and high triglycerides, and these need to be managed as well. The presence of the metabolic syndrome with hypertension, obesity, and all of those risk factors also need to be addressed as well. In addition to aggressively addressing blood pressure management, diabetes optimization, there are certain classes of medicines that are probably underutilized, and we need to be more aggressive in utilizing these. For instance, the statin therapies are considered a first-line therapy for primary prevention, and many physicians are actually hesitant to use them in patients with liver disease because it turns out they have a tremendous safety record, and they are a class of medicines that we should be using if appropriate in patients who have MASLD and cardiovascular risk factors.

In addition, the sodium-glucose cotransporter 2, SGLT-2, inhibitors and then the glucagon-like receptor GLP-1, these are medicines, such as semaglutide, which are all the rage for losing weight, but they also have beneficial effects in those with fatty liver disease and cardiovascular outcomes. And there's good preliminary data in early phase trials that some of these medicines can improve metabolic dysfunction-associated steatotic liver disease that has resolved the inflammation and damage.

So all of these need to be combined with a healthier lifestyle that would include things like avoiding alcohol. I tell my patients who have MASLD it's not that they can't drink, but they should really limit their amount of alcohol, and that can be sometimes a very unpopular recommendation, but with MASLD I think will be beneficial.

**Dr. Buch:**
Thank you. And in the last few moments of our discussion, Dr. Kwo, is there anything else you'd like to share about MASLD and cardiovascular disease with our audience?

**Dr. Kwo:**
A couple of important things. So number one, with the worldwide prevalence of MASLD, it's important that we just recognize and intervene in those who have metabolic syndrome, and we screen appropriately for MASLD. Some of the more sobering statistics that are emerging are that between MASLD and alcohol, these are going to be the dominant liver diseases over the next 20 years or 30 years, and these diseases, while difficult to address, actually are diseases that we can identify early. And we're really trying to emphasize screening for these diseases at the earliest stages and catching these disorders before you develop significant complications of fibrosis, cirrhosis, or you develop significant cardiovascular outcomes. And so we have relatively good noninvasive testing to identify people with early-stage metabolic dysfunction-associated stenotic liver disease, and there aren't enough liver doctors, endocrinologists, and cardiologists to take care of all of these patients, so we're going to really rely on a partnership with our primary care providers who can help us identify these people and appropriately risk stratify them so that those with liver problems can come to the liver doctors; those with cardiovascular issues can come to the cardiologists. And in my opinion, as we move forward to successfully address this challenge, it really will be a team effort and take a village to make sure that we appropriately identify and risk stratify this population.

**Dr. Buch:**
I want to thank my guest, Dr. Paul Kwo, for educating us about this extremely important topic. Dr. Kwo, I really enjoyed our conversation today, and thanks for being here.

**Dr. Kwo:**

Thank you for having me.

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