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M3: Managing the Cardiometabolic Risk in MASH

Announcer:
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Dr. Eckel:
Hello. This is CME on ReachMD, and I'm Dr. Robert Eckel, and joining me today is Dr. Naim Alkhouri. And the task before us is discuss this whole evolving element of cardiometabolic risk in patients with MASLD and MASH. Naim, welcome to the podium this morning.

Dr. Alkhouri:
Thank you for having me.

Dr. Eckel:
So I think we think about the various options in treating people with fatty liver disease; renamed, of course, most recently, a complicated name [metabolic dysfunction-associated steatotic liver disease]. But why don't you review with this kind of a stepwise approach to modifying this cardiometabolic risk in patients with these forms of fatty liver disease.

Dr. Alkhouri:

Happy to do so. Of course, MASLD can be a progressive liver disease, and we need to target the liver disease and, hopefully achieve MASH resolution, fibrosis regression. But we cannot be so myopic and just focus on the liver. This is a systemic disease, and I think we need to manage the cardiometabolic risk factors. So weight loss is a key component of any approach to managing MASLD, and this can be achieved with the lifestyle intervention, antiobesity medications, or bariatric procedures. We should also look at the effects of any intervention, including medications, on each component of the metabolic syndrome. So the ideal drug should also lead to better glycemic control improvement in dyslipidemia, and potentially also improvement in hypertension. in addition to all of this the ideal approach also should achieve reduction in cardiovascular outcomes so major adverse cardiac events, for example, and we do have some medications now indicated for diabetes and obesity that can do that. And then we also need to reduce liver outcomes, what we call major adverse liver outcomes, such as progression to cirrhosis and decompensation. So this is a holistic approach to treating MASLD and MASH.

Dr. Eckel:
Well, Naim, this whole independent relationship between various forms of fatty liver disease, particularly MASH and more extensive disease, such as cirrhosis diseases we hope to prevent by these interventions; ultimately, is that an independent relationship? Or is it entirely due to the dependency on what we know as cardiovascular disease risk factors?

Dr. Alkhouri:
So MASLD and MASH are independent risk factors for cardiovascular disease. This has been shown, after adjusting for obesity and type 2 diabetes. And actually managing cardiovascular risk is a big important step in everything we do for these patients. And unfortunately, because patients with MASLD sometimes they have mildly elevated liver enzymes, there are several studies showing that

they are actually undertreated with statin medications that can be very beneficial for them and this is a point I wanted to make today that, you know, statins are safe in patients with chronic liver diseases, including MASLD and MASH, and we need to utilize them as indicated to decrease cardiovascular risk.

Dr. Eckel:
Because weight reduction is so important, do we give up on lifestyle alone? Should we be going to these medications first or upfront? Or should the patient have an opportunity to lose, say, up to 10% or greater weight loss on their own without pharmacotherapy?

Dr. Alkhouri:
Yeah, a comprehensive lifestyle intervention should always be a component of any intervention we do for patients with MASLD and MASH. Unfortunately, the success rate of achieving that 10% total body weight loss is limited, even in the context of clinical trials, only about 10-15% of patients are able to achieve this, threshold and maintain it. And that leads us to using antiobesity medications, with medications like semaglutide, tirzepatide, up to 75% of patients are able to achieve that 10% threshold of weight loss, which has been associated with MASH resolution and fibrosis regression.

Furthermore, with bariatric surgery such as Roux-en-Y gastric bypass, the weight loss can be, between 25 to 30%, and this has been associated also with MASH resolution, fibrosis regression, but more importantly, recently, with reduction in MACE and major adverse liver outcomes.

Dr. Eckel:
Alright, importantly in patients with type 2 diabetes, there's some literature to indicate that pioglitazone may be additionally useful. Can you comment briefly on the use of a TZD in these patients to create benefit in terms of their liver disease?

Dr. Alkhouri:
Of course. Pioglitazone has proven benefit in patients with, MASH. However, it's been associated with weight gain and potentially other adverse events. But I do utilize it in my clinic in selected patients with MASH and significant fibrosis.

Dr. Eckel:
Alright, to summarize, we've dealt with the issue of how important weight loss is in managing patients with MASH and MAFLD, and we're hopeful that this has been useful to you And I thank Dr. Alkhouri for being part of this. He's the expert in this space. I'm simply the moderator. Thank you very much.

Announcer:
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