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Navigating ASCVD and Pancreatitis Risk in Severe Hypertriglyceridemia

Announcer:
You're listening to *Heart Matters* on ReachMD. This program titled "Navigating ASCVD and Pancreatitis Risk in Severe Hypertriglyceridemia," is sponsored by Ionis Pharmaceuticals Medical Affairs. And now, here's your host, Dr. Charles Turck.

Dr. Turck:
Welcome to *Heart Matters* on ReachMD. I'm Dr. Charles Turck. Today, we're taking a case-based look at severe hypertriglyceridemia and exploring how the 2026 American College of Cardiology/American Heart Association, or ACC/AHA, Multisociety guideline on dyslipidemia management can help inform clinical decision-making.

Throughout today's discussion, we'll follow a hypothetical patient over time, exploring how treatment priorities may evolve and explaining which tools clinicians can use along the way.

Joining me for this conversation is Dr. Andrew Freeman. He's a board-certified cardiologist and Director of Cardiovascular Prevention and Wellness, and Clinical Cardiology and Operations at National Jewish Health in Denver, Colorado.

Dr. Freeman, it's great to have you here today.

Dr. Freeman:
Thank you. It's a pleasure to be here.

Dr. Turck:
So, Dr. Freeman, let's jump right into our case. Would you walk us through an example of a patient with severe hypertriglyceridemia and highlight what stands out in the initial presentation?

Dr. Freeman:
Absolutely. So let's imagine our patient is a 55-year-old man named Dean.

His systolic blood pressure is 140 mmHg, his BMI is 35, and he has type 2 diabetes with an A1c of 7.1 percent. His estimated glomerular filtration rate, or GFR, is 60.

Dean's fasting lipid panel, with all values measured in milligrams per deciliter, shows a total cholesterol of 130, HDL-C of 38, LDL-C of 95, and triglycerides of 910.

He doesn't smoke, and he has no history of acute pancreatitis. He's currently being treated with a moderate-intensity statin, a maximally tolerated angiotensin receptor blocker, and metformin 500 milligrams twice per day. He's minimally physically active and eats the standard American diet.

So right away, we can see that Dean meets the criteria for a patient at risk for atherosclerotic cardiovascular disease, or ASCVD. And to better understand his risk profile, we can leverage the PREVENT-ASCVD calculator recommended in the 2026 ACC/AHA Multisociety guideline. And this tool helps estimate 10-year ASCVD risk, which, in Dean's case, is about 6.1 percent, placing him in an intermediate-risk category.[1]

But what also stands out is that, despite having no symptoms or prior history of acute pancreatitis, his fasting triglycerides are 910 milligrams per deciliter. For reference, fasting triglycerides below 150 milligrams per deciliter are generally considered normal, and for

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most patients I aim even lower. The 2026 ACC/AHA Multisociety guideline defines severe hypertriglyceridemia, or sHTG, as fasting triglycerides of greater than or equal to 500 milligrams per deciliter, so Dean clearly meets that threshold.[1]

Dr. Turck:
That's a great introduction to the case. So once you've identified both intermediate ASCVD risk and sHTG, how does the 2026 ACC/AHA Multisociety guideline help frame your initial management priorities?

Dr. Freeman:
So for a patient like Dean, ASCVD risk reduction is a high priority, and management starts with lifestyle intervention and optimization of underlying cardiometabolic disease. We'd want to intensify statin therapy while optimizing glycemic control. At this time, we should also assess for secondary causes of hypertriglyceridemia.[1]

In terms of lifestyle management for patients with sHTG, the guideline recommends referring the patient to a registered dietitian nutritionist.[1] Because these dietary changes can be difficult to sustain, dietitian support can help patients implement triglyceride-lowering approaches, including limiting added sugars, refined carbohydrates, saturated fat, and avoiding alcohol.[1,2] And with Dean's triglyceride levels approaching 1000 milligrams per deciliter, a more intensive low-fat or very-low-fat dietary strategy could be considered.[1] That said, I think it's also important for clinicians to be familiar with the dietary factors that contribute to elevated triglyceride levels so they can reinforce the guidance provided by a dietitian.

Beyond nutrition, weight reduction and physical activity are also key components of treatment, particularly in patients with obesity and type 2 diabetes.[1]

But this is also where management becomes more nuanced, because when triglycerides remain persistently elevated above 500 milligrams per deciliter despite statin therapy, we're thinking not only about ASCVD risk reduction. We also need to consider acute pancreatitis risk and residual atherogenic burden.[1]

Dr. Turck:
So, Dr. Freeman, how do you think about the competing risks of ASCVD and acute pancreatitis in a patient with sHTG, and how does that impact ongoing risk assessment?

Dr. Freeman:
This is where sHTG becomes more complex clinically, because we're managing two overlapping but distinct concerns. On the one hand, Dean has elevated ASCVD risk driven by diabetes, obesity, hypertension, and atherogenic triglyceride-rich lipoproteins. But at the same time, the 2026 ACC/AHA Multisociety guideline calls attention to the risk of acute pancreatitis in patients with sHTG, especially as fasting triglyceride levels move closer to 1000 milligrams per deciliter.[1]

It's also important to note that in patients with sHTG, LDL-C alone may not fully reflect residual atherogenic burden. LDL-C measures cholesterol mass per LDL particle, but in patients with elevated triglycerides, diabetes, or broader cardiovascular-kidney-metabolic syndrome, it can actually underestimate the total number of circulating atherogenic particles.[1] In fact, in these patients, elevated triglyceride levels are associated with increased small, cholesterol-depleted LDL particles, which have been shown to be more atherogenic than large LDL particles.[1,3]

That's where evaluating non-HDL-C and apolipoprotein B, or apoB, can be especially helpful in guiding our decision-making. Non-HDL-C captures all atherogenic lipoproteins, including triglyceride-rich remnant particles, while apoB provides a more direct measure of atherogenic particle number. So ultimately, when LDL-C levels appear controlled but apoB or non-HDL-C remain elevated, these markers can provide a more accurate estimate of ASCVD risk than LDL-C alone.[1]

And so the 2026 ACC/AHA Multisociety guideline includes treatment goals for both LDL-C and non-HDL-C. In a patient like Dean with intermediate ASCVD risk, the LDL-C goal would generally be less than 100 milligrams per deciliter, while the recommended non-HDL-C goal is less than 130 milligrams per deciliter.[1] So even though he's already met those targets based on his current lipid profile, ongoing monitoring is important in the setting of sHTG. Personally, for patients like Dean, I often push for LDL-C goals even lower than the guideline targets.

Dr. Turck:
For those just tuning in, you're listening to *Heart Matters* on ReachMD. I'm Dr. Charles Turck, and today I'm joined by Dr. Andrew Freeman to explore guideline-based severe hypertriglyceridemia management through a patient case.

So, Dr. Freeman, let's look ahead to our patient's follow-up visit three months later. How's Dean doing?

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Dr. Freeman:
This is where the case becomes especially informative. Dean returns after following the treatment plan, and in many ways, he appears to be making meaningful progress.

His systolic blood pressure is now down to 125 mmHg, his BMI has decreased from 35 to 34, and his hemoglobin A1c has improved from 7.1 percent to 6.5 percent. His estimated glomerular filtration rate remains stable at 60.

On Dean's repeat lipid panel—again, measured in milligrams per deciliter—total cholesterol has decreased from 130 to 125, HDL-C has increased slightly from 38 to 39, and LDL-C has improved from 95 to 80. His current medications now include high-intensity statin therapy, an angiotensin receptor blocker, hydrochlorothiazide, and metformin 1000 milligrams twice daily.

But despite all those improvements, Dean's fasting triglycerides have increased from 910 to 1100 milligrams per deciliter, and that really becomes the key turning point in this case. It tells us that even when a patient is doing many of the right things and several of their cardiometabolic parameters are improving, sHTG can continue to worsen in certain cases.[1]

And we'll come back to some of the potential reasons why that can happen later in the discussion.

But first, that turning point is so important because once a patient's triglycerides exceed 1000 milligrams per deciliter, the risk of acute pancreatitis becomes even more of a major clinical concern and the 2026 ACC/AHA Multisociety guideline makes a critical distinction here. For any patient with a fasting triglyceride level of 1000 milligrams per deciliter or greater, the immediate management priority shifts to preventing acute pancreatitis.[1]

Dr. Turck:
With that in mind, could you walk through the risks and burden of sHTG-associated acute pancreatitis?

Dr. Freeman:
Of course. There are a few reasons why preventing acute pancreatitis in patients with persistent sHTG becomes a priority.

Hypertriglyceridemia is the third most common cause of acute pancreatitis, accounting for approximately five to 22 percent of all cases.[4] One analysis found that patients with triglyceride levels above 1000 milligrams per deciliter—like Dean—had over a 17-fold higher risk of acute pancreatitis compared with patients whose triglyceride levels were below 200 milligrams per deciliter.[5]

Once a patient with sHTG has experienced an episode of acute pancreatitis, their risk of recurrence within one year can be as high as 24 percent.[5]

What's more, the burden on patients can also be substantial. In my experience, acute pancreatitis can mean more than a week of abdominal pain, an inability to tolerate oral intake, and hospitalization. Compared with acute pancreatitis from other causes, sHTG-associated pancreatitis has been associated with higher rates of ICU admission, persistent organ failure, pancreatic necrosis, and mortality. Hospital stays also tend to be significantly longer, with one study reporting a median hospital stay of 17 days in these patients compared to seven days in patients with acute pancreatitis from other causes who had normal triglyceride levels.[6]

From a healthcare-system standpoint, recurrent episodes, prolonged hospitalizations, and the need for intensive care can add substantially to the overall burden of disease.[7-9]

Dr. Turck:
Thank you for walking us through that, Dr. Freeman. If we turn now to intervention strategies, what can clinicians do to manage patients with persistent sHTG—particularly those with fasting triglycerides above 1000 milligrams per deciliter?

Dr. Freeman:
So treatment starts with reinforcing intensive lifestyle intervention—particularly a diet that eliminates added sugars and alcohol, limits refined carbohydrates, and reduces fat intake to about 10 to 15 percent of total calories.[1] I usually tell my patients the lower, the better.

The guideline also recommends initiating first-line triglyceride-lowering medications, including fibric acid derivatives or prescription omega-3 fatty acids—not over-the-counter products—to reduce the risk of acute pancreatitis. Fibric acid derivatives can lower triglyceride levels by approximately 30 to 50 percent, although treatment response can vary among patients.[1]

I also want to mention that for pregnant individuals with sHTG, high-dose omega-3 ethyl esters may be used throughout pregnancy, while fibric acid derivatives may be considered after the first trimester. These therapies may be used along with lifestyle intervention to help reduce triglyceride levels and pancreatitis risk.[1]

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Now, going back to Dean's case, this is also the stage where clinicians should consider whether an underlying genetic chylomicronemia syndrome may be contributing to the presentation, especially in patients with persistent or treatment-refractory sHTG.[1]

Panel-based genetic testing can help differentiate multifactorial chylomicronemia syndrome, or MCS, from familial chylomicronemia syndrome, or FCS. And tools like the North American Familial Chylomicronemia Syndrome scoring system can help estimate how likely FCS may be and whether additional genetic evaluation should be considered.[1]

That distinction is clinically relevant as dietary management may differ between MCS and FCS. Patients with FCS often require more restrictive, very-low-fat dietary intervention because of impaired chylomicron clearance, along with strict avoidance of alcohol and added sugars. But for patients with MCS, a low-carbohydrate and low-fat diet can help reduce triglyceride levels.[1]

Dr. Turck:
So, Dr. Freeman, before we wrap up, what are the biggest lessons from Dean's case that clinicians can apply in practice?

Dr. Freeman:
I think one of the biggest takeaways is that sHTG requires clinicians to think beyond LDL-C alone when assessing ASCVD risk. Tools like PREVENT-ASCVD can help estimate overall cardiovascular risk, but in patients with sHTG, non-HDL-C and apoB can provide more accurate insight into residual ASCVD risk, particularly when apoB and LDL-C are discordant. It's also a reminder to ensure patients with sHTG are receiving guideline-directed statin therapy.[1]

Another key point is that management priorities shift in sHTG as triglyceride levels rise. When fasting triglycerides are between 500 and 999 milligrams per deciliter, management is focused on reducing risk of ASCVD and acute pancreatitis. But once fasting triglycerides exceed 1000 milligrams per deciliter, preventing acute pancreatitis becomes the immediate clinical priority.[1]

And finally, persistent sHTG should prompt clinicians to think carefully about underlying genetic chylomicronemia syndromes, since identifying conditions like MCS or FCS can have important implications for long-term management and dietary intervention. All of this to say, caring for our patients with sHTG requires a personalized approach.[1]

Dr. Turck:
That's a great way to round out our discussion. And I want to thank my guest, Dr. Andrew Freeman for helping us better understand how a guideline-driven approach can help us navigate severe hypertriglyceridemia management.

Dr. Freeman, thank you for joining me today.

Dr. Freeman:
Thanks so much for having me.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. Thanks for listening.

Announcer:
This program was sponsored by Ionis Pharmaceuticals Medical Affairs. If you missed any part of this discussion or to find others in this series, visit *Heart Matters* on ReachMD.com, where you can Be Part of the Knowledge.

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