Lipid Tests and Risk Assessment for Patients with Dyslipidemia

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CHRISTIE M. BALLANTYNE, M.D.: Welcome back to these foundations of the cardiometabolic health certification course. Well, now that you have covered the pathophysiology of lipid metabolism, I would like to move to something pragmatic. This is the lipid test. How do we interpret them and combine them with risk assessment for patients with dyslipidemia?

I am Christie Ballantyne. I am the chief of Cardiology and Cardiovascular research at Baylor College of Medicine and Director of the Center for Cardiometabolic Disease Prevention at Baylor College of Medicine in Houston, Texas.

DR. BALLANTYNE: Well, guidelines change over time, and sometimes it is a little bit confusing to remember all the nuances of all the different guidelines. But very importantly there is a fundamental concept that has been at the center of all of the lipid guidelines. And this is because the CVD risk is the guide to the intensity of lipid-lowering therapy.

ASCVD Risk Assessment – Patient Case #1

. BALLANTYNE: Well, let us illustrate how we match the intensity of therapy to the risk of the patients, and use or lipid profiles and step through some cases. So, let us start off with our first case.

DR. BALLANTYNE: This is a forty-seven-year-old African American male. He is seen in follow-up two months after recent non-STEMI. His risk factors were significant for hypertension for ten years, and lifelong high cholesterol, along with a family history of both premature heart disease and high cholesterol. And he has taken numerous statins. He was on eighty milligrams of atorvastatin, and ten milligrams of ezetimibe, until he developed terrible muscle pains and weakness four months ago. Stopped his statin, and unfortunately came in with a non-STEMI. Now appropriately, he was discharged on a different statin because he had a problem with the atorvastatin eighty milligrams, he was placed on rosuvastatin ten milligrams, also a high-intensity statin but at a lower dosage. Ezetimibe was continued at ten milligrams.

He is seen now in follow-up. He says he still has some sore muscles, but he denies any weakness and he is continuing to take the medication since it is tolerable.

On a physical examination, his blood pressure is 135 over 85. He is six foot two. He weighs 180 pounds. His BMI is 23. He has corneal arcus. There is no xanthomas or xanthelasmas. He has got a normal cardiac and vascular examination.

DR. BALLANTYNE: In regards to his medication, he is taking chlorthalidone, amlodipine, and carvedilol. So, he is on three medications related to blood pressure. Rosuvastatin and ezetimibe for his lipids. He is on aspirin eighty-one milligrams daily in terms of antiplatelet therapy.

His lipid profile is a total cholesterol of 198. Triglycerides 100. HDL cholesterol, 60. And KDL cholesterol, 118 milligrams per deciliter. His glucose is 98. He has normal renal function in the liver function test. His creatinine kinase is 320. The upper limit of normal is 170. Hs-CRP is 2.2 milligrams per liter.

DR. BALLANTYNE: Well, let us startup with a few questions. What kind of lipid disorder does he have? And do you think he has a genetic disorder? And if so, how do you make the diagnosis?

DR. BALLANTYNE: First of all, let us review his lipids. His total cholesterol is 198. His triglycerides are 100. His HDL is 60, and his LDL cholesterol is 118 milligrams per deciliter. Now that is while he is taking rosuvastatin 10 milligrams and ezetimibe 10 milligrams. And that combination will lower your LDL cholesterol more than fifty percent, and he is still at 118. So, it is important if you do not have the records, we can calculate backwards, his baseline almost likely was well over two hundred, and it is very important to ask him, for example, what was your highest cholesterol in his face, it was over three hundred. And a lot of people rem - remember their cholesterol and not their LDL cholesterol. But you can see that this is someone who has had lifelong high cholesterol, and he also had a family history of high cholesterol and heart disease.

So, this goes to the diagnosis. And I like to keep things simple. Uh, if you have a family history, of early cardiac events or of a very high cholesterol, and you have a documented high LDL cholesterol in the past. If we look at the number over 190, that is sufficient for the diagnosis of familial hypercholesterinemia. And these really, we have talked about it, there is lots of different types, there is the Dutch Lipid Clinic and Simon Broome. These are the American Heart Association guidelines. They are simple for clinicians to remember because we think of over 190 in our guidelines as being a - a very high level of LDL cholesterol, where you are supposed to start therapy.

It is easy to get information about family history, so you put those two together and you can make a diagnosis this would be someone who has heterozygous familial hypercholesterinemia.

DR. BALLANTYNE: There are four known FH genes. And these all make sense if we talk about the - the lecture recently on pathophysiology. We know that the LDL particles get removed by the LDL receptor. If you have mutations in the LDL receptor that - or loss of function mutations, you do not remove the particles well. If you have a mutation in APO B, so that it does not bind T the other receptors, you do not remove the particles well. And also, PSK9 is very important in regards to causing the degradation of LDL receptors. And if you have a gain of function mutation at PSK9, all of these can cause high LDL, and those are usually seen in what we would call them autosomal dominant pattern.

There is also another less common mutation in the – an LDLRAP1. This is autosomal recessive hypercholesterolemia. This mediates the positioning of the LDL receptor, the coated bits. So, uh when you order genetic testing very frequently, they will include these four genes looking for a molecular confirmation of familial hypercholesterolemia.

DR. BALLANTYNE: So, when we are talking about testing for lipids, let us also review the testing for genetic testing and in – in patients with familial hypercholesterolemia. It provides a definitive molecular diagnosis of FH and may end up being that somebody who has a bad family history and their LDL, might be a little under 190, they can still have familial hypercholesterolemia. We see this sometimes with people's LDL's are 170 or 180.

It gives some information in terms of prognostic and risk stratification because these individuals have fed lifelong high levels of LDL because they have a hereditary disorder which is raising LDL beginning really at birth.

It also facilitates family-based cascade testing, and this can help in regards to genetic counseling. Uh, you know, there has been looked at, there is minimal psychological impact about that. The testing has gone down, it is affordable and accessible now. And there is a nice review in JACC, in terms of the expert panel, I was a member of this, but looking at a lot of the issues and pros and cons of this.

DR. BALLANTYNE: There is also a very nice resource, provided by the FH Foundation. And this is guided towards patients to give them more information about the benefits and also some of the limitations of this.

And it is important is a negative test does not rule out that they have familial hypercholesterolemia. There are sometimes mutations that are not detected, and so that is something that as I said, can be a useful test, it is not mandatory to make the diagnosis. You can make it simply by clinical factors.

DR. BALLANTYNE: Now, this is another review by the National Lipid Association scientific statement on genetic testing. So, we have mentioned – and this one is broader, this is so we can get all lipid disorders. So, it can aid in the clinical diagnosis and target of treatment for specific disorders. It can increase patient adherence and motivation. It can help family members.

DR. BALLANTYNE: There are some considerations. Not all those genetic tests are created equally, and a lot of people get things like 23 and me, which are really not of being done for the same diagnostic purposes. Uh, there is the issue of what is called a pathogenic variant or likely pathogenic variant. And as time evolves, that information changes, and so it can also change over time and between laboratories, so this is another potential issue. I mention that directed consumer testing can give false pauses, false negatives. It is not the same as clinical genetic testing. Polygenic risk scores are very interesting. They are becoming more popular. We are getting more data. Unfortunately, they are not standardized for all, basically, if you take a look at uh racial background, some of the tests do not work as well in some populations. And there - I do not think quite ready for prime time in terms of routine clinical usage. Hopefully down the road we will get these so that they work better for everyone. And then the intensity of therapies are guided by the LDL cholesterol levels, not by the genetic mutation

DR. BALLANTYNE: Okay, now, let us come back to our case. So, remember these are his medications. His LDL is 118. Now the CK, one important thing about CK levels is the upper of normal are 170, but what we see is, for example, that it - Black individuals tend to have

higher levels of CK. They have not changed, that that was observed many years ago in a study done called the ERIE [phonetic] study by Keith Ferdinand. So, it is something that it is important to look at to CK. This, it turns out it is his baseline level of CK. It is not really elevated. But that is important because sometimes people will stop the drugs in someone because they are thinking that this is an adverse effect.

DR. BALLANTYNE: So, let us go back to the LDL cholesterol. And now we have, you will hear more about this when we talk about treatment. But it is such so important that I want to cover the issue when we are doing our lab testing, what is a high level? What is a normal level? So, what do you think is the most consistent with your view here?

The LDL target should be less than 70. The LDL target should be less than 100. There is no LDL target, he should be placed back on forty milligrams of rosuvastatin, with discontinuation of ezetimibe that the - his LDL is not an important issue, we should focus on lowering the CRP. The CRP in which you would increase the dose of aspirin to do that.

His LDL cholesterol is above the threshold. To consider additional LDL cholesterol lowering therapy for a high-risk individual with ASCVD.

DR. BALLANTYNE: And let us go to our question here of an LDL target or an LDL threshold.

DR. BALLANTYNE: Now, the target of therapy is to lower the levels of atherogenic lipoproteins, and what we usually measure is LDL cholesterol. So, our target is to lower LDL cholesterol. The concept of a threshold is when it has been uh espoused in our guidelines, the 2018 AHA, ACC cholesterol guidelines. And what we have is risk categories that this person has clinically ACVD. So, he is in the risk category of clinical ACVD. He has had a non STEMI. The question comes up, is he in the very high-risk group or not at a very high risk group?

If he is in the very high risk group - so both of these people get high intensity statins, but if they are in the very high risk group, we want to see is what happened to the lipids after you treated the person? Did you get the levels of LDL to what we would consider to be a reasonable level? You have had success insuring of the therapy in terms of reducing the concentration of atherogenic lipoproteins because if it is over 70, you have not. So, that is the concept of a threshold. It means you have got to do something more for someone like this. And you can measure, look at the level of LDL cholesterol, if it is greater than or equal to 70, you need to do more, or the non HDL greater than or equal to 100, and you will hear more about what else to do with this.

You know we have got other therapies besides statins, PSK9 inhibitors, ezetimibe. And you will hear more that bempedoic acid and a new sRNA. So, there are other options to lower that are non-statins to give thee further reductions in people where the number is above this threshold concept.

DR. BALLANTYNE: So very high-risk patients, what does that mean? So that includes a history of multiple major ASCVD events. Those at the top. A recent ACS, history of MI, history of ischemic stroke, symptomatic PAD. Or they had one major, ASCVD event and multiple high-risk conditions. The high-risk conditions are very common: age over sixty five, heterozygous FH, history of bypass surgery or PCI outside of the event, uh diabetes,

hypertension, CKD, smoking, persistently elevated LDL cholesterol, history of CHF. Well, what about this patient? So, this patient has had a recent ACS, and we already said has heterozygous familial hypercholesterolemia, hypertension, and has a persistently elevated LDL cholesterol of over 100. So, this person falls into the very high-risk category.

DR. BALLANTYNE: What is the next step for the treatment of his lipids? Well, he is in the very high-risk category.

DR. BALLANTYNE: So, what do the guidelines say? And this gets a little bit complicated because we have multiple sets of guidelines basically, but the ACC, AHA guidelines say, if they are over 70 uh for this patient in a very high-risk category, you need to add a nonstatin therapy.

The European guidelines take a little different focus, but this person - - high risk category if its less than 55. So, by either side of the guidelines you need to add something else for this patient. They have a target here. This is a goal - a goal of getting less than 55 uh with it. So, there – there is a little different approach here, but it turns out for most patient's they are quite similar.

The European guidelines also include Apo B levels uh for you to be looking at. And that is not in the American Heart Association guidelines at this time uh except as a risk enhancing factor. But we will talk a bit more about Apo B, along with non HDL cholesterol, looking at both of these parameters.

DR. BALLANTYNE: So, he started on a PCSK9 inhibitor. Very practical question, when should you obtain follow up lipid labs? That we start the therapy, when is an inappropriate time to look at the response of the response of therapy to this patient?

DR. BALLANTYNE: So, let us go through the uh NLA scientific statement, obtain lipid measurements four to twelve weeks after a change in lipid treatment. If some one's acutely ill, they were very sick in the hospital that may lower the lipid levels so as an inpatient, I think it is very reasonable to get them but you may require follow up outpatient testing. In terms of apheresis, you want to measure lipids immediately before the - the - the - the procedure, then you can get it afterwards. But the ones before will tell you, you know, how high did you go and how low did you go right after the procedure.

For PCSK9 inhibitors, if you are giving it every two weeks, you would like to measure this just before the - the next injection. So, that gives you some idea, because levels go down and they go up a little bit. And if you are measuring just before two weeks, or if you are doing it once a month, get it shortly before the next inject - injection.

DR. BALLANTYNE: What test should you order to evaluate this response to therapy? A lipid panel with calculated LDL cholesterol, direct LDL cholesterol, Apo B, LDL particle concentration by NMR, or LDL particle concentration by iron mobility?

DR. BALLANTYNE: Let us go to our NLA scientific statement, which was published fairly recently. So, in the absence of cost-effective, accurate, and widely available direct method of measuring LDL cholesterol, what we see based upon the LDL cholesterol in clinical trials and clinical practice is largely relied on the calculation of LDL cholesterol.

So, thus a lipid panel gives you a calculated LDL cholesterol. However, these are problematic when you have high triglycerides. And so, at that point, you should be using non-HDL cholesterol.

The advantage of non-HDL cholesterol, it can be fasting or non-fasting. And it is very effective for guiding ASCVD. Particularly we talked about in the response to treatment. It was an LDL cholesterol, of greater than or equal to 70, or a non-HDL cholesterol, greater than or equal to 100. In regards to the LDL calculation, it turns out there is more than one way to do this. The Friedewald equation is the old way of doing it. There is a Martin Hopkins equation and there is also a new NIH equation. So, you might want to take a look when your ordering labs, how do they calculate the LDL cholesterol. And we will talk a bit more about this.

Now, if you are getting non fasting lipids and they came - come back elevated, then it is very reasonable to - and the next time you see that you can still use that data, but to try to get some on the fasting state to see if the fasting lipids are elevated.

DR. BALLANTYNE: So here is a sample lab report that your lab reports should end up talking about usually what the desirable values in terms of the, you know, HDL for men and women desirable, we have different numbers. Non HDLD cholesterol, we talked about, should be less than 100 for a high-risk patient, LDL should be less than 70. And we think of triglycerides should be less than 150. These are some other numbers to keep in mind in regards to particularly after you have used statin therapy, what would you like to see in your patient in terms of a good response?

DR. BALLANTYNE: In regards to advanced lipoprotein testing, and these are considering select patients, so the measurement of Apo B may be beneficial in regard as initial evaluation of selected patients and people under the therapy, particularly with HC symptoms, elevations of triglycerides, metabolic syndrome. The LDL particle concentration may also be helpful, however, and we will talk a bit more as there are multiple ways to measure LDL particle concentration and unfortunately, they are not standardized very well.

So, you may get an LDL in one laboratory. Another one measured it by different methodology, and you really can correlate those two measurements. The measurement of LP(a is, I think, something very important to get in our patients in regards to risk assessment - assessment at least once in our adult patience. Because if they have very high levels, they have higher risk. And remember that statins do not lower LP(a).

So, and particularly uh for people with higher ASCVD risk, then sometimes even if the LDL is less than 70, they may have residual atherogenic lipoproteins that are going beyond LDL. Particularly when you see this elevation of triglycerides, metabolic syndrome, diabetes, and that is when you should be looking at non-HDL cholesterol that is available in everybody from the lipid panel, or things like Apo B and LDL C.

DR. BALLANTYNE: All right, so let us kind of go again and looking at your options as a clinician. Uh so you can get a - the calculated cholesterol, and this is basically from lipid profile, just different methods of calculation for this. There is also the remnant lipoprotein cholesterol. And this can either be measured specifically or calculated. If you calculate it,

I do not think it used too much more than a non HDL cholesterol, as part of the same equation. You are just taking total cholesterol and subtracting LDL and HDL, if that would be it you have a direct measurement of LDL, but um there are also assays where you can measure or RLP cholesterol.

We talked about non HDL cholesterol. This is, I think very useful for lots of patients to be looking at this. And one could argue in fact that we should be looking at non-HDL cholesterol instead of LDL cholesterol, as it works in everybody, and it works a little better than LDL cholesterol. But it is – it – it is hard to change the way uh historically our focus on LDL.

And then there is Apo B. And this is measured by usually either Immuno turbidometry or nephelometry, other Immunoassays and that there be - there are some issues in terms of which lab - which kits are they using. But in general, there is standards for this in that there is improvement in the measurement of Apo B, we can still do better.

DR. BALLANTYNE: Now, NMR is something that is nuclear magnetic resonance, where you can look at the lipoproteins by a different methodology and look at HDL, LDL, VLDL, subclasses. However, it turns out that a lot of was initially done by a - - with a specific magnet and also proprietary software.

Subsequently there are multiple other magnets used with different proprietary software's. And it turns out the correlation is imperfect. So, you're getting an LDL P, but they do not necessarily mean the same thing when done by different laboratories.

The same – even though it is the same sample, it would give different values into different labs. Now within the lab, if it is repeated in the same way uh I think it is a useful measurement, but that is another layer of confusion.

That turns out that there is also an iron mobility analysis, that can do LDL and HDL P that gives also an LDL particle concentration. But if - yet a different methodology and the norms are clearly different. Usually, the LDL P is less than a thousand, this is less than twelve hundred.

You can measure small density LDL cholesterol and there is a new automated assay for this which has been approved by the FDA and that can have benefit in some patients.

Uh, out of these tests, as I mentioned, LP A is the one I think that we should be getting at least once in all of our patients because this is primarily genetic and it is a very important part of a family history.

ASCVD Risk Assessment – Patient Case #2

DR. BALLANTYNE: Well, let us come back and look at patient case number two. And we are going to go to a different type of lipid disorder.

DR. BALLANTYNE: So, this is a fifty three year old, white male with a family history of cardiovascular disease and hyperlipidemia presents complaining of a rash on his abdomen

and back. He has a history of hypertension, high cholesterol, and triglycerides which has been treated for ten years. He has not been exercising, says he has had long hours and lots of stress and gained fifteen pounds since his last visit two years ago. That was pre Covid. Uh atenolol one hundred milligrams, hydrochlorothiazide at twenty five milligrams for blood pressure. And on atorvastatin ten milligrams, and historically been on aspirin, eighty one milligrams.

And there is some questions now about do we need - how much aspirin should we be using?

DR. BALLANTYNE: First question, according to the ACC, AHA guidelines, should you check his lipid profile? Yes, no, he is on appropriate treatment, he is in primary prevention, he is on ten milligrams of atorvastatin or unsure.

So, the correct answer is yes. And there was a lot of confusion unfortunately. When the 2013 guidelines came out and focused on statin therapy, because at that time we did not have that much information on statin therapy. Somehow people thought that just because you put someone on a statin, you do not need to check the lipids. Now that is not at all what they ever said.

DR. BALLANTYNE: They said that, in fact, the only way you are going to know if someone is adherent and if they are responding to the therapy of both your drug and their lifestyle would be to check lipids. You should get the four to twelve weeks after you start, or you change the dose for every three to twelve months thereafter.

So, this person should get at least once a year a lipid profile. And this is one of the most important aspects in regards to the management of lipoproteins. Can you imagine someone trying to treat blood pressure where you never check blood pressure? Or you are going to treat diabetes without checking hemoglobin A1c? So, this is something that is extremely important is that you should be routinely checking lipids in patients who are on therapy for their lipids. We have got to monitor adherence.

DR. BALLANTYNE: And the only way you can monitor adherence is in fact to measure lipids. All right on physical examination, he is obese, his blood pressure is up, 140 over 90. 220 pounds. BMI is 31.6. 42 inch waist. Liver is palpable below the coastal = costal margin. And we see this rash of which came up fairly recently, and uh, he does not understand why it came up.

DR. BALLANTYNE: We get the labs back, and the triglycerides are sky high, they are 1150, and this was after a twelve hour fast. HDL is 30. Cholesterol is 310, his glucose is elevated at 165. AST is up. ALT is up a little bit. Bilirubin, alk phosphatase, TSH are okay with it.

DR. BALLANTYNE: So, what is the most likely lipid diagnosis? A, a type one hyperlipidemia. B, a type two hyperlipidemia. C, type three hyperlipidemia. D, type four hyperlipidemia. Or E, type five hyperlipidemia?

Well, the correct answer is type five hyperlipidemia, and this is taking you back to remember the Fredrickson classification. But basically, we talk about the LDL particles. That is our main focus in regards to athero – atherogenic proteins. And that is because historically

well, that is – that is what is the driver now. We are in a world right now where we have so much more obesity and diabetes and we see many more patients with high triglycerides.

So, what are the particles that transport triglycerides? Well, these are the VLDL particles. Those are larger particles with more triglycerides. And then you have a particle that you get after you eat, called a chylomicron particle, at which, if you remember from our lecture on the lipid metabolism is - so this is a very large particle, has lots of triglyceride in it. In most individuals with severely elevated triglycerides have a mixture of the VLDL and the chylomicron particles. That is what we call type IV hyperlipidemia.

Type one is chylomicronemia. Pure chylomicronemia that is a rare disorder, it is usually by our old terminologies, autosomal recessive, or now biallelic, you have two defective mutations. And - and this is much less frequent. It is - this is, you know, somewhere between one and two hundred and fifty thousand, and one of a million individuals.

The other condition where you might see a pretty high triglyceride is type three. This is IDL, dysbetalipoproteinemia. Sometimes they will see a pattern of uh you may have cholesterol of four hundred, and a triglyceride of four hundred. In this case, if we go back and look at the numbers, the triglyceride was well over a thousand and the cholesterol was 310. So, they are not almost even. The triglyceride is much, much higher. And this is typically a type five hyperlipidemia. That is what most of you will see in practice when you see a patient with very high triglycerides.

DR. BALLANTYNE: The next question about this patient. Which of the following may be an important secondary cause of his hyperlipidemia? Alcohol intake, diabetes, the beta blocker, the diuretic, or all of the above?

Well, the correct answer is all the above. And one thing that is very important when we see the high triglycerides is to do a thorough history and look for secondary causes. Ah, you want to ask about alcohol, and then the concern is his diabetes. In this case, glucose was 165. Had not been known to be diabetic, but in the last couple of years has gained a lot of weight, been sedentary, taking a beta-blocker, and a diuretic that could also lead to some increases. So, you need of medication history. What is happening with lifestyle? What is happening with weight gain? And what is happening with the diet? These are all very important because they make a tremendous influence on the level of triglycerides.

Now, does this person have a genetic predisposition? Yes, almost certainly because what ends up happening is most people, even if they do all these things wrong. They are not going to get a triglyceride of 1100. So, it is a combination of genetic predisposition along with this gene by the environment, the lifestyle aspects.

DR. BALLANTYNE: Next question, which of the following agents would not be affected for reducing his triglycerides: statin, fibrate, niacin, bile acid-binding resin, omega 3 fatty acids? Well, you would not want to use a bile acid-binding resin in this patient because can raise triglyceride. It has a favorable effect on glucose, but with a triglyceride of 1100, you certainly do not want to raise it. When you see triglycerides in this zone, you are worried about the risk for pancreatitis.

Niacin, also is something that would raise - lower triglycerides, but it would raise glucose most likely if you use a high dose. So, that is not a first line option here.

Most of you will hear more about this, but the most effective agents available, are fibrate, omega three, statins though, particularly if we use a high-intensity statin a high dose, are also beneficial for lowering triglycerides.

DR. BALLANTYNE: Let us go back to the lab values. So, remember the triglycerides are 1150 here. Um, the glucose was elevated. We did not see other secondary causes other than the obesity, diabetes.

DR. BALLANTYNE: So, what is the approach to the patient with high triglyceride. We talked about evaluation of secondary causes. So, very important at this time, once you identified them, what are you going to do? Well, he needs to stop drinking. Um, consider the medications, uh and then the issue of the weight gain in the last two years, what is happening with the dietary habits and the exercise habits. So, you need to check a hemoglobin A1c. We - we already – he mentioned the renal function here, urinalysis is important to rule on the nephrotic syndrome. TSH and the liver function. The liver function tests and the exam, this person that has at the least NAFLD. They are going to have fatty liver with hepatomegaly.

DR. BALLANTYNE: Question. Next question, what is the initial goal of therapy recommended by the lipid guidelines for the patient with severe hypertriglyceridemia? A, reduced triglycerides of less than 150, B, less than 500, C, get the non HDL to less than 160, D, get the HDL to over 50, or E, all of the above?

Well, the correct answer is to reduce the triglycerides to less than 500, because we know that if you get triglyceride in that zone, you really take away, the risk of pancreatitis goes down to close to zero. The risk gets very high when you're over one thousand. But remember that is fasting, triglyceride. And so, if someone is bouncing around seven or eight hundred, they may be that there that day when you are seeing them, but all it takes is for that person to go out and have a big fatty meal with some alcohol, and they may be around two thousand or three thousand.

DR. BALLANTYNE: So, he was instructed to stop all the alcohol. He was scheduled for a dietary consult for a diet with reduced fat and reduced simple carbohydrates. And instructions to begin walking thirty minutes daily. I always find it useful to tell patients, listen, you - triglyceride that is how you transport energies the way we transport fatty acids. Your glucose is up, your triglyceride are up, you have got an increase abdominal fat and you have got a problem with your energy metabolism. So, what are we going to do?

Well, you know when you eat fat, it is got nine calories per gram. Carbohydrates, four. But those are your two energy substrates. You have got to reduce both of those. You have got to burn up more. You got to exercise. And we usually make a bet that if you get after this, we will see your numbers go down within days certainly, within four or five days. Within one week, you will see it at a very nice improvement.

In addition, the medications were changed to put him on a more favorable profile. well, he was on a high dose of beta-blocker, plus lisinopril. He was started on metformin. The A1c was checked. And he was started on omega 3 fatty acids.

Now, let me make one point. In this particular case, this is for lowering triglycerides. If there is an issue of heart disease with that, then you have to have a specific consideration and you will hear more about this in your lectures is the type of omega 3 fatty acid that is used. We only have data with the EPA there.

DR. BALLANTYNE: All right, so six weeks later shows up, he has lost some weight. He started exercising, blood pressure on the new medications is improved. He has lost a little bit of weight. His triglycerides have come down nicely, 350, we are no longer in the pancreatitis zone area. His HDL has come up nicely. Non-HDL is 162. His glucose is now 125. His A1c is 6.4 percent.

DR. BALLANTYNE: What is your recommendation at this time? Our next question, increase the atorvastatin to eighty milligrams, increase exercise and intensify diet to achieve further weight loss, increase metformin to 1000 milligrams BID, or all of the above? Well, let us start off first in regards to his lipids.

DR. BALLANTYNE: All right. So, in people with diabetes, especially those with multiple risk factors, or those aged fifty to seventy-five, it is reasonable to use high-intensity statins to reduce LDL by greater than or equal to 50 percent. Uh and we can look at consideration if you are not able to do that of the addition of ezetimibe. So, ten milligrams of atorvastatin is something that is - is it beneficial? Yes, but this is somebody who has still got hypertension. The non HLDL cholesterol is 160. So, this person needs further reduction.

DR. BALLANTYNE: And so, we have diabetes aged forty to seventy-five, you can look at moderate-intensity statin, but you can also if you feel they are in a higher risk category, could go to a high-intensity statin. So, I think it would be very reasonable to go to eighty milligrams of atorvastatin. Now, in addition, clearly, we talked about, you know, lifestyle.

DR. BALLANTYNE: This person should keep working on it. They are not all the way there yet. They had made some changes, things are better, but they need to lose more weight. Continue to exercise and diet for that. In terms of increasing the metformin, I do not know that we have quite as much data in that. The A1c is 6.4 percent, so that would be the least important of the three things that were mentioned there for this.

DR. BALLANTYNE: Now, one of the important things is when we are in this situation of primary prevention, and that is going to be very common in our practice. There is a lot of people who if someone is in the high-risk category, you know, we need to be very aggressive with those people and put them on a high-intensity statin. But what about the people who are in the borderline zone of 5 to 7.5 percent? That is using the pooled cohort equation. Or that somebody is an intermediate risk for this? So, at times we may be uncertain what to do with people, and this is where we have the concept of looking at risk enhancers, and also coronary artery calcium scoring. Because I think that this is a very powerful test for - for risk assessment. So, there are some other things that can go beyond the pooled cohort equation in regards to optimizing this.

DR. BALLANTYNE: What are the risk-enhancing factors? Well, family history of premature ASCVD, if someone has hypercholesterolemia, metabolic syndrome, this person has more than metabolic syndrome, they got diabetes. CKD, chronic inflammatory conditions, history of premature menopause, and then South Asian ancestry is, for example, higher. It is a high-risk group for cardiovascular disease.

DR. BALLANTYNE: What about lipid biomarkers? Persist in the elevated triglycerides over 175. That is what in these guidelines, I personally use over 150. Elevated CRP, high Lp(a) elevated Apo B, low AVI. These are other very important risks enhancing factors.

ASCVD Risk Assessment – Patient Case #3

DR. BALLANTYNE: Well, let us finish up, and we will just quickly go over patient case number three. And this one is really just to emphasize some points about where we have come.

DR. BALLANTYNE: Where are we now? Where do we use to be? So, this is a fifty-seven-year-old man with a recent acute myocardial infarction, hypercholesterinemia, diabetes, and hypertension. Total cholesterol was 250. Triglycerides 260. HDL, 45. On atorvastatin 80 and ezetimibe 10 milligrams daily.

Now this person is in the very high-risk category. We covered that earlier today by the US and the European guidelines. Here is the issue, the triglycerides are elevated and he is on a high-intensity statin and ezetimibe. By the Friedewald equation, the LDL ends up being 53.

Well, according to our guidelines, when we are talking about, you know, a threshold of greater than or equal to seventy. You would say well, this - this is a pretty good treatment. If you use the Martin Hopkins equation, the LDL is seventy-two. Or if you just look at the non-HDL cholesterol, it is a hundred and five. That is over a hundred. And then, if you are going to go with the European, his Apo B of 68 is over the desirable level.

So, it is important LDL cholesterol is a very useful measurement, but the Friedewald equation is suboptimal in people with elevated triglycerides, and sometimes when you see these lower levels, it is also suboptimal. Particularly if someone is on a PSCK9 inhibitor, and you get the number back and it is very low. Forget the Friedewald LDL, look at the non HDL cholesterol, or do the Martin Hopkins equation.

And Martin Hopkins, some labs or have changed that but not all of them. So, I would emphasize that non-HDL cholesterol is a very useful measurement in our patients, particularly the cardiometabolic patients since they have high triglyceride, clustering of risk factors.

The non-HDL over 105, this person still has atherogenic lipoproteins. They still have residual risk from atherogenic lipoproteins. They are not really where you want them to be. So, whether you call it a goal or above the threshold, this person you would like to lower the atherogenic lipoproteins further, and one could consider a PSCK9 inhibitor in this individual to further reduce their risk for having a recurrent atherosclerotic cardiovascular event.

So, it is important to check the lipid profile but use all the data. And when we see this elevated triglyceride, you have to be thinking of more than just the LDL cholesterol. So, look at the non-HDL cholesterol. Hopefully, they do Martin Hopkins. This is somebody you can consider an Apo B measurement in. If you have a labs that you are using on a regular basis and you understand what the LDL particle contract means, you could consider that.But this is somebody who actually still has a high level of atherogenic lipoproteins and could benefit from more intensive therapy. And you will hear more about what other ways to treat that.

DR. BALLANTYNE: So, this is a reminder. Most of the time we get a calculated level of LDL cholesterol. The Friedewald equation has some limitations. It should not be used at all if the triglycerides are over 400. But actually, whenever we see the higher triglycerides, for example in this case of 260, it does not work as well. So, either the Martin Hopkins or the NIH equations give a better performance. What is the easiest thing also for these people? Look at the level of non-HDL cholesterol.

DR. BALLANTYNE: So, Apo B is another consideration and LDL-C in these types of individuals. So, LDL cholesterol in people who have cardiometabolic disorders, when you see a high triglyceride and non-HDL cholesterol, that is your go-to that is already there and consideration of Apo B and also an LDL particle concentration.

However, the problem with the LDL particle concentrations is the lack of standardization from laboratory to laboratory within. And so, you have to be careful as to where did you order it? That they are not the same by the different methodologies.

DR. BALLANTYNE: Well, let us summarize what we have covered. CVD risk assessment is the guide to the intensity of lipid-lowering therapy. So, it is a very fundamental aspect to it, and so the interpretation of - of the lipid measurements has to be coupled with your risk assessment. Follow-up assessment of lipids is necessary in all patients to assess the efficacy adherence to both lifestyle and drug therapy.

You can't just start agents and just tell someone to diet and exercise. You need to also see what was the impact on their lipid profile.

Remember that reducing atherogenic lipoproteins, we are trying to reduce, our major target is LDL, but also these triglycerides proteins are problematic. So, the levels of LDL cholesterol, non-HDL cholesterol, Apo B, LDL P, LP(a), and triglycerides may all be useful to assist lipoprotein-related risk.

Follow-up testing with a calculated LDL cholesterol, non-HDL cholesterol, Apo B, and LDL P may be useful to assist response of therapy and the need to intensify therapy. Both pharmacological, and lifestyle therapy.

And it is important to understand the limitations of calculated LDL cholesterol and differences in methodology, remeasurement of LDL particle concentration if you are using some advanced lipoprotein testing.

Thank you very much for your attention.