NASH: Take Action! Podcast Series

EPISODE 4. Diagnosing NAFLD and NASH

TRANSCRIPT

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Fasiha Kanwal [FK] Welcome to the NASH Take Action Podcast. I am Dr. Fasiha Kanwal, Professor of Medicine, Chief of Gastroenterology and Hepatology at Baylor College of Medicine, Houston, Texas.

In this podcast, my colleagues Ken Cusi and Jay Shubrook and I will talk to global leaders in gastroenterology, hepatology, endocrinology, and primary care and about the real-world practical implications of screening, diagnosing, and managing people with NAFLD and NASH.

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In this episode, we are talking about diagnosing NAFLD and NASH, and here are the topics we will cover today: noninvasive diagnostic techniques for patients at high

risk for NASH; when to refer a patient to a hepatologist; and the role of liver biopsy in diagnosing NASH.

I am here with my co-hosts, Dr. Ken Cusi and Dr. Jay Shubrook. Ken?

Ken Cusi [KC]: Hi Fasiha. Yeah, I'm Ken Cusi, I'm the Chief of Endocrinology and Diabetes at the University of Florida at Gainesville in north Florida.

FK: Jay?

Jay Shubrook [JS]: Hi. Jay Shubrook, a family physician and primary care diabetologist at Touro University, California. Glad to be here.

0:01:45

FK: So Ken and Jay, as you know, we are talking about diagnosing NAFLD and NASH, and the challenges that, as clinicians, we face. What do you generally do as just with the first step, Jay, for diagnosing individuals at high risk for NASH? I'm sure you see a lot of patients.

JS: Sure. So I think first of all, I think we have to have an awareness of who's high risk. And sadly, there are more people who are high risk than not. But again, anyone who's got metabolic syndrome, anyone that's got type-2 diabetes, people who have insulin resistance and obesity are all going to be at higher risk for this condition. And I think that we have to have a plan for screening.

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And sadly, we didn't have a pathway before that was agreed upon by everyone. So I think that what we're recommending here, and what think should be really looked at, is doing some measurement of risk – you know, that could be done with a FIB-4

score – and some measure of elasticity of the liver. And so that may be done in primary care, it may not, but I think it all starts with knowing who to test. And that's an important thing that we haven't been able to do before.

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FK: Absolutely. Ken, how many patients do you send for liver biopsy?

KC: Let's put it this way. I did some research a little bit different, but on the clinical side, I don't send them for a biopsy. I send them to you guys, to the hepatologists, to make that decision after gathering, you know, additional information.

I think the problem starts earlier, in the sense that many of our endocrinologists still are not aware or thinking about NASH. They know about it, but did not make it operational, a little bit because we have this old school in mind that we worry about liver enzyme. If you look at liver enzymes just to make sure the statin is working. If it's high, they might send it to you.

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But as you know, Fasiha, most of our patients with NASH have liver enzymes in this bracket between 20 to 40. So as I like to say, the cutoff of 40 is like saying I want to diagnose diabetes with an A1C of 7-1/2. It's a high cutoff. And maybe, that's a homework that gastroenterologists should look at, I mean in terms of educating the rest of the players in what is a normal ALT.

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But getting back to what Jay said, I think that the cheap approach would be to stick in the mind a FIB-4 in the same way that we measure micro albumin or that we look for, you know, lipids in our daily practice. That would be a big step.

But the question is, how do you think we should be using the imaging, point-of-care imaging at this point? What is your gastroenterology field thinking about, Fasiha?

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FK: We also in our field are moving away from liver biopsy because we have so many other noninvasive ways to assess for fibrosis, which is the main lesion that we are looking for. For imaging, most of us use some sort of _____ elastography, the FibroScan, or vibration-controlled elastography is something which is commonly used. I would not say that it is available in all different practice settings, but most practice settings have a FibroScan, a FibroScan machine or something similar.

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In some institutions, we also have access to MR elastography that could be used. But across the board, the field is moving away from using liver biopsy. It is still used for patients, especially the ones that are enrolled in clinical trials, or when there is diagnostic dilemma, which is not that uncommon that if you do do different noninvasive tests and they are inconsistent, that is the group that we still go ahead and move towards liver biopsy, especially first when we change the management of pretest likelihood, or the suspicion is very high, for example, for cirrhosis or advanced fibrosis.

That's the group that we still lean towards liver biopsy, but overall we are relying on noninvasive diagnostic tests more and more.

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And I think that's the point. Jay, I remember in one of our earlier conversations that came up, their just thinking about it can make a difference, that we might think that we don't have access to these techniques or these tests in our practice settings, but you just have to pick up the phone and call someone and you realize that actually that resource is available. Sometimes the important part, I think, here is knowing about it, and thinking about it.

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JS: That's a great point. That's – one thing is that I think now, most endocrinolo-, in the past I had to convince endocrinologists that a lot of the patients with obesity or diabetes, type-2 diabetes, had NASH. How I think there is less resistance.

I think the next step will build this reflex, as we have for micro albumin, for sending somebody for an eye exam and talking about people with diabetes. And I think the next step would be, is action of measuring a FIB-4. Even in my own practice, some of my endocrinologists don't do that, particularly there are endocrinologists that don't like that much to take care of many patients with diabetes.

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And now, for our audience, FIB-4 is a diagnostic panel composed of age, AST, ALT and platelets. And in any web browser, you just put the FIB-4 calculator and it gives you a number. And the numbers to remember are if it's below 1.3, you are most likely at

low risk of advanced cirrhosis. If it's above – the double that 1.3 is 2.6 – bigger than 2.6, you're probably in trouble. You should schedule an appointment with your hepatologist. And in the middle - that's what happens in 30 or 40 percent of the patients – that's where we think imaging works.

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Now, when I give talks, I say, people say, "Oh, we don't have in primary care or endocrine clinics, an elastography machine, a FibroScan, or others." Say, "Well, just order it, the same way we order an x-ray or a bone density." If you have electronic medical records, it's nothing you need now, you can have it for the next visit, and hopefully with that, you'll be able to classify patients.

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Jay, you're in the trenches there, in the first – what do you do about that?

JS: Yeah, I want to highlight some things you both said that are so important. So first of all, don't rely on the transaminases to determine who has fatty liver. We know that well within the normal transaminases, you can have fatty liver all the way to NASH.

Two, you have very simple tools, like you mentioned, on a web browser. I have it on MedCalc. I can calculate a FIB-4 almost any time, very cheaply. And that helps to sort out who needs more.

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KC: Right.

JS: And then, to the point earlier, I thought I didn't have access to a FibroScan because I just assumed, oh, I never heard of it, I don't have access. But sure enough,

you do have it. All you have to do is ask either your hospital, or talk to your colleagues. I mean, if you have a gastroenterologist, they'll know where a FibroScan is.

And so this is why it's so important to be using a team-based approach, because we have more resources than we think we have, and this doesn't have to be complicated. And your patients are not all going to end up on a liver biopsy, which is what many people are worried about. So we've got quite a bit of simplification now, and I think quite honestly, better specificity.

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KC: So Jay, may I add something to you from the non-hepatology angle. I mean, this is really important, because one of the complaints I get from hepatologists is that either we don't send them, or we send them all. So I think that your hepatologists would be delighted that you did a FibroScan beforehand, and that you're sending them somebody that has a fibrosis level that's clinically significant in terms of risk.

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So, remember that we're not looking for just fat. So we know two-thirds of people with obesity or type-2 diabetes have fat; we just look at NAFLD in the liver, but we think about NAFLD just to identify those with fibrosis. And the FibroScan reports can be a little bit overwhelming for non-hepatologists. Just concentrate at least in that KPA, that number. If it's 8 or greater, I'm sure Fasiha wants to see them. What is your take on this, Fasiha?

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FK: I agree completely. Those are the individuals that we would like to see. The higher the KPA, the higher the risk of having suboptimal liver outcomes, and those are the patients that should be referred to a hepatologist.

So I talked to a hepatologist, Dr. Vincent Wong, head of the Division of Gastroenterology and Hepatology at the Chinese University of Hong Kong, and this is what he had to say.

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FK: Hi Vincent. It's a pleasure to have you here with us. Vincent, I wanted to get your opinion on what is your approach to noninvasive testing in patients who are at high risk for NASH.

VW: Okay. So, I think the context is really important. So, it depends on where we are, and what kind of patients we are looking at, because the pre-test probably of a advanced liver disease would really affect what kind of tests we should perform. And of course, the availability of the test would also be important.

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So recently, I have had the pleasure of working with different experts on preparing the AGA clinical care pathway. So the first step we really have to consider is what constitutes the high-risk group. After some discussion, we identified a number of individuals whom we would like to evaluate further.

Now, the most obvious one is for people who have already been diagnosed to have fatty liver. So, for example, under some imaging test or other investigations, those

patients were found to have fatty liver, and it would be our responsibility to work them up further to see whether the fatty liver is severe or not.

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But other high-risk groups would include patients with type-2 diabetes, and also patients with metabolic syndrome as defined by various metabolic factors, including not only diabetes but also the presence of hypertension, dyslipidemia, and obesity. And we also know that central obesity, as defined by the waist circumference, would be important.

Now, this is the first step, so we have to identify high-risk population, and then we have to talk about what tests to perform.

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Now, let's talk about the primary care setting, or non-specialist setting, first, because this is really where most of the patients are being seen. In those settings, although clinicians will see a lot of patients with fatty liver disease, but on the whole, the proportion of patients with really advanced disease, namely bridging fibrosis, cirrhosis, or even liver decompensation would be the minority. And therefore it would make sense to use some simple tests as initial screening.

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Now, according the clinical care pathway, the first test that clinicians may consider first would be a test called the FIB-4 index, which stands for fibrosis-4. It really incorporates four factors associated with advanced liver fibrosis. So, the four factors

would include older age, lower platelet count, and also two liver enzymes, the AST and ALT level.

Now, some of these factors are easy to understand because, like any chronic liver diseases, the longer the disease duration is, the more like the patient would have progressed to advanced stage, and therefore older age is important.

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Now, platelet count is obviously a useful biomarker for you to see patients with probable porto-hypertension and hypersplenism. So it is reflecting whether the patient may start to have advanced fibrosis, or even if it's cirrhosis. And then the AST and ALT would be more specific for the liver disease.

Now, with the FIB-4 index, the lower cutoff that we adopt would be 1.3, because we know that in multiple liver biopsy studies, that this is our cutoff with really high negative predictive value in excluding advanced liver fibrosis.

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More importantly, recent studies have also shown that in the general population setting, or in primary care setting, if a patient has no FIB-4 value of less than 1.3, really, in the next 15-20 years, the risk of the patient developing liver complications – cirrhosis, cirrhotic complications, and liver cancer – would be minimal, and therefore these tests, although very simple, has a very high negative predictive value, not only for histological fibrosis, but also for future liver-related outcomes. And therefore we believe that this would be a good initial test for screening.

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So, so far, if the test has a low value, we are pretty certain that the risk of liver disease and complication would be rather low. So, I think this would be a good start.

FK: Great, Vincent. I completely agree with that. And as you mentioned the AGA clinical care pathway describes it, and makes it quite explicit.

One thing that I think is worth mentioning is the effect of age on FIB-4 cutoffs, especially the lower cutoff. As you know, for patients who are older than 65, the cutoff is 2.0, based upon the studies that have looked at that, because age is an important component of FIB-4, and older age will pull the value higher. The recommendation in studies and in the clinical care pathway is to use the cutoff of 2.0 instead of 1.3 for patients who are older than 65. So that, I thought, was an important, I think, take-home message for primary care physicians who are taking care of patients. I had someone reach out to me about an older patient who had high FIB-4, and that context was important for that patient.

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So, Vincent, what do you recommend, or what do clinicians do if the FIB-4 is higher than the cutoff specified in the clinical care pathway? What is the next step that one can consider?

VW: Okay. Now, in the literature, there are a number of different cutoffs. But the one that we have adopted in the clinical care pathway would be 2.67. So, essentially, this would be the high cutoff with a higher probably of advanced liver disease. If a patient has a FIB-4 index of more than 2.67, we can basically refer the patient to a hepatologist for further evaluation.

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On the other hand, if the FIB-4 index is somewhere in between – so, higher than 1.3 in a younger patient, and higher than 2.0 in an older patient, and well less than 2.67, then we call that the intermediate-risk group. This is not to say that it must be somewhere in between; it just means that the value is not discriminating enough to tell us whether this is mild disease, severe disease, or somewhere in between. So this is where a second test would be helpful.

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Now, it depends on the availability of the second test, so if in settings where the second test may not be immediately available, then a referral to our hepatologists for further evaluation would make sense.

On the other hand, if our clinics have access to some second-line test, then they may also wish to have that first before making further decisions.

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Now, in the clinical care pathway, the recommended second test would be liver stiffness measurement by transient elastography. And the cutoff that we adopt would be 8 kilopascal for ruling out advanced liver disease, and 12 kilopascal for ruling in advance liver disease. And again, people in the middle ground between 8 to 12 kilopascal would have indeterminate risk and requires further testing, or even a liver biopsy for further characterization.

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FK: Great. And wasn't there another – I think you mentioned that the middle group, the indeterminate group. In clinical practice that's not a very small group. A third of patients, 30 to 40 percent of patients who undergo this testing would fall in that group, so it's not that uncommon that clinicians would encounter it. So, knowing that there is a second step that could be done even before patients are sent to a liver specialist is good to know.

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And I agree, I think it depends on local availability, so knowing what are the different resources that are available in a clinical practice setting is important. For example, some institutions would have a FibroScan or something similar for liver stiffness measurement available, so just knowing that is good for clinicians. Because then, really, for 30 percent of patients, they could refer their stratified into whether they really need to go see a specialist or not. And based upon different studies, a specialist referral can be avoided in a significant proportion of patients. So, I think that is also important to recognize.

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Any other tests, Vincent? Things are moving at such a fast pace with the new advancements in diagnostic modalities and testing. Do you think things are going to be very different with what we use in the next five years, or do you think the current recommendations in some form and shape will hold true, over the next 2 to 5 years?

VW: Okay, I think some things will stay. So, for example, I still think a simple test would have its role because they are essentially, they don't cost you anything extra. When you

ask for a liver panel, most likely you will have those different enzymes. And it is also not expensive to ask for a platelet count. And therefore, those simple tests would be very appealing, particularly if you use that as initial screening. I think it would be there to stay.

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Now, regarding liver stiffness measurement, again I think it would continue to have its role, mainly because it is a point-of-care test. So, in some settings when you have the machine nearby, you can perform the examination at the same setting, and therefore you can give the patients the results, and make the next management decision right away.

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Now, on the other hand, of course, we have to anticipate new changes. There are two tests that I may specifically highlight. So, the first test would be specific fibrosis biomarkers, mainly because nowadays there are several agents entering phase 3 development for the treatment of non-alcoholic steatohepatitis, and some of these agents may be registered for the treatment of this condition in a few years' time.

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And in almost all the phase 3 studies, multiple biomarkers are measured together with sera liver biopsies, and therefore we would know the performance of those biomarkers, not only as a surrogate for the histological features, but also whether or not they can predict clinical outcomes in the future.

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Now, among the blood tests, I think two particularly stand out. The first test would be the ELF test, or what we call the enhanced liver fibrosis panel. So, it is a combination of three specific fibrosis biomarkers. Now, there will be presentations at the upcoming EASL meeting this year, so what we know is that, compared with other known invasive tests, although it has a similar performance as some of the other blood tests and also transient elastography, but on the whole it has less variation over time. So, the coefficient of variation is particularly low, compared with liver stiffness measure, for example. And also, because it has been correlated with so many trials, so we will know whether it can be used to monitor treatment response. So, this is something that we anticipate.

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Now, the test has already been recommended in the United Kingdom by the NICE guideline as one of the initial tests for fatty liver disease. So, we will have to see the subsequent data to see whether it will have a place as some of the routine measurements.

Now, another blood biomarker that has gained a lot of attention would be the PRO-C3, which really measures the new formation of collagen. So it is a real biomarker of fibrogenesis. So, in a way, it may be both a reflection of the current fibrosis stage, and also the activity of the disease, so how fast the fibrosis is going to progress in the next few years. So again, this has been incorporated in many clinical trials, and we are going to see interesting data.

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Now, this is – and for the blood biomarker part, and regarding imaging biomarkers, I wouldn't call it a new test, because it has been around for some years already, but the adoption has not been widespread at the moment, except in some – for example, in some centers in the United States or in Japan, there may be more adoption.
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So, the test I'm referring to would be magnetic resonance elastography, or in short, we call it MRE. So, compared with ultrasound-based elastography, such as FibroScan, MRE would have applicability, so the success rates of measurement would be higher. And at the same time, the overall accuracy is also higher. And therefore, some centers have been routinely performing that, and again, this has been used as a monitoring tool in some clinical trials as well.
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What is lacking would be the responsiveness of the MR elastography, if we want to evaluate a _____ 0:25:11 response. Now, many of the studies so far would be cross-sectional in nature. But if you want to use it as a monitoring tool, you really have to ask how fast would fibrosis improve over time, and how fast would MR elastography improve over time. So, we need that bit of data to finally recommend how to use it in clinical practice, not only for case selection, but also for treatment monitoring.
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FK: Things are going to be moving fast, and we will see more progress in the field. My sense is that the platform, or just our way of thinking will be the same, that you start with a first-tier simple test, and then go on to a more sophisticated second-tier test. I think

the first-tier test probably will stay the same, as you mentioned. The second tier, I think there is going to be some movement and advances that we I think will stay tuned to, as you referred, both from blood as well as imaging biomarker ends.

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I want to go back to transient elastography, because I think it has a space, a place right now, and I think it will stay the same. Many of our patients are obese, and there are issues with performance of these tests in obese patients. What should clinicians think about, both at the low cutoff and at the high cutoff, for some of these tests, and when to go and look for an alternative test?

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VW: Okay. Now, this is a very important point. Whenever we order an investigation, we need to understand how it is performed, and also the limitations and precautions for that matter. Now, for transient elastography, the major hurdle would be severe obesity. So, because when you perform liver stiffness measurement by transient elastography, essentially you are sending a shear wave across the liver parenchyma, and then you would use an ultrasound beam to chase the original shear wave, to measure its velocity.

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And therefore, if a patient has severe obesity with thick subcutaneous fat and pre-hepatic fat, there may be trouble transmitting the wave across the liver parenchyma properly.

Now, the manufacturer has produced the Accelprop(?) to cater for obese individuals. In various studies, even in the obese population, the success rate of

measurement can reach more than 80 to 90 percent. So, this has partially solved the problem of obesity, but this is still not perfect.

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Another controversial issue is that in patients with severe steatosis or severe obesity with extreme BMI, it appears that the test may overestimate the liver stiffness, resulting in a false positive diagnosis of advanced liver disease or cirrhosis. And therefore, in such individuals, one may consider having an alternative test, like MR elastography, if that test is available.

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But if not, then my personal take is that you can still perform transient elastography first because, although we say that there may be issues with false positive results, the test negative predictive value where you mix(?) excellence(?)0:28:26. And therefore, so far, if the patient has low liver stiffness, even if we understand the confounder and potential caveats, we can still conclude that the patient doesn't have advanced liver disease, and you can exclude those patients.

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On the other hand, if you have a positive result, you have a patient with high liver stiffness, this is when you have to think whether there may be confounder factors at play.

FK: That is, I think, a very important take-home message. Because it's a large population, we are more likely to find patients who have a lower risk of having advanced disease, and that strengthens the negative predictive value and the fact that it works

well at the low end. I think it's an important clinical piece. And given the safety of this test, and also wider and wider availability, I think it is a useful test clinically, and I think will remain so.

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But point that you noted and I want to highlight is that the positive predictive value of the test is higher than the cutoff of 12, let's say, and there are reasons to believe the test performance might be at risk, one has to just think a little bit more than a high test doesn't always mean that a patient has advanced fibrosis. And if there are other factors that are not going, not consistent with that diagnosis, then having another test, a third test is recommended, and it's a good idea, because once patients are classified as having advanced fibrosis, that diagnosis could stay with them for a long time. So, some duty of caution is important.

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And that's where understanding the test and the test performance, especially in patients who are obese and who have a higher cutoff, is important to recognize.

That brings two important points, Vincent. One is the role of liver biopsy. We still do liver biopsy, still required in many clinical trials, most clinical trials. Clinically, in your practice, when do you do it? And where do you think it would be in the next 3 to 5 years?

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VW: Okay. When I learned medicine, my teachers always taught me that when you order an investigation, it has to change your clinical practice. If you would do the same

regardless of the results, you have to rethink why you are doing that, particularly for a test that is invasive like liver biopsy.

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So, at present, I would say that I still do liver biopsies a lot, mainly because I'm in an academic center and I'm involved in clinical trials. And therefore, if I diagnose steatohepatitis, particularly together with significant liver fibrosis or cirrhosis, I will have a treatment protocol for my patients. And also, as you said, for many of the late-phase clinical studies, in phase 2b or phase 3 development, pared liver biopsy is really required, not only for study entry, but also for the determination of a treatment outcome.

Now, I must say that this is unsatisfactory. Our patients don't like it, and many doctors don't like it either, because of its invasive nature. And more than that, although we are using that as the most important yardstick to evaluate treatment effect, we know that it is a flawed test, in a sense, because of the many issues of variability.

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So we know that there are sampling variabilities, so when we perform a needle biopsy, we are only obtaining 1 in 50,000 of the entire volume of the liver parenchyma, and therefore if you happen to biopsy the less severe part of the liver, you are going to underestimate the disease severity.

And secondly, even if you get a good chunk of liver tissue, there is intraobserver and interobserver variability. Because after all, it is the pathologist's subjective assessment of the clinical tissue. And experience, of course, would also play a part. In

particular, hepatocytes ballooning is the defining feature of steatohepatitis. If you don't have ballooning, the steatohepatitis is gone, so we call it resolution of NASH.

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However, ballooned cells are particularly difficult to identify, so you really need a pair of experienced eyes. And therefore this is something that would also introduce to the variability in the interpretation.

In fact, last year, in the *Journal of Hepatology*, there was one important paper that would be a post-hoc analysis of the EMINENCE trial. So, what the investigators did was to ask three pathologists to look at the baseline and post-treatment liver biopsies, and then each of them would give a score, and eventually they would determine whether the patient had resolution of NASH or fibrosis improvement.

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Now, it is really not surprising. We know that study is interobserverability. But what this important study shows is that if you look at not just one, but two liver biopsies, then the variability would add up together. So essentially, at the end of the day, it would be all over the place. So the _____ value would be horrible to look at.

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So, I would say that this can't continue forever, so that's why we are so keen to develop non-invasive tests. Nowadays we have already got many non-invasive tests correlated with histological severity in a processional manner. So, just now I have been emphasizing on the importance of responsiveness, meaning that whether the change in

those non-invasive tests can faithfully reflect a change in the histology. So this is some data we need get up.

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Now, in a few meetings, investigators meetings, some other colleagues would ask, “Why are we still conducting such studies, doing pared liver biopsies? This is not good for the patient.” And my usual answer to them is that Yes, eventually we have to get rid of that. So it doesn’t make sense to do two liver biopsies for every patient you need to treat in the future.

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However, as investigators, I will see that we would have the responsibility to work together to gather enough data so that we can eventually move the feud(?) forward and spare our patients from the pain of having repeated invasive measurements in the future.

FK: Well said, Vincent. We are working with an imperfect standard, but at the same time, as you know, lots of work is happening in the field to find a better alternative. I think we are getting there – not there yet completely, but movement is in the right direction.

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Clinically for non-trial patients, who are the patients that you send for a liver biopsy now?

VW: Okay, so, nowadays it is quite rare that I only do a liver biopsy just to stage the fibrosis, because frankly speaking, unless you want to give a new treatment or end a

clinical trial, most of the non-invasive tests would be reliable enough for you to make some decisions.

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But there are situations in which liver biopsy would be useful. So, for example the diagnosis may be uncertain. The initial test may suggest that there is some fatty liver, but the clinical features may not be totally compatible, so you have to consider something else.

So, I would quote a few examples. So, for example, for steatohepatitis, most of the time the ALT level would be high, but not very high. So if you see a patient with an ALT of two or three hundred, I would say that this is quite atypical. And it is worth considering for other liver diseases.

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Now, if you see reversed AG ratio, albumin to globulin ratio, this would suggest an inflammatory process, and in such individuals, we would also like to think about autoimmune hepatitis. And, of course, many a time we would also check the other serologies. Of course we will screen for viral hepatitis – that will be quite clear-cut. But occasionally we may also see some positive autoimmune markers. So in those situations, you may also need a liver biopsy to exclude other liver diseases, or on the other hand, you may confirm an alternative diagnosis and treat accordingly.

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Now, finally, of course liver biopsy is a very important research tool, not just in the clinical trials that I've talked about. For many years we have been using liver biopsies,

both histological analysis and also subsequent biochemical and molecular analysis, for us to understand the pathophysiology underlying most of the liver diseases. I think this will still go on with the availability of different _____ 0:37:25 tests, and the liver tesis (?) would be pivotal for our understanding of the liver disease, and also what would be the best treatment in the years to come.

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FK: Great, Vincent, I agree. I think for clinical practice, the use is for diagnostic purposes when there is unclear or conflicting data to support a clinical diagnoses when I think there are biopsies used. And you're right, it's getting less and less frequent for us, common for us to order liver biopsy.

This was great, Vincent. Great conversation. And I am very confident that our listeners are going to enjoy it as well.

VW: Thank you very much.

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FK: Thank you, Ken and Jay, and special thanks to my guest, Vincent Wong. Thank you all for joining us for this episode on diagnosing NAFLD and NASH. You can find the other five episodes in this series, the NASH Clinical Care Pathway, and more resources at the program's website, NASH.Gastro.Org.

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Thanks also to our sponsor, the American Gastroenterological Association, and for the medical education grant from Novo Nordisk.

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