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Assessing Non-Invasive Testing for Liver Fibrosis

Dr. Buch:
Non-invasive testing to assess patients for liver fibrosis is becoming increasingly popular. They can be subcategorized into non-invasive tests that use direct and/or indirect markers of fibrosis, tests that utilize either basic labs or proprietary panels of biomarkers, and then there are even elastography tests. So how do we know when it's appropriate to use each of these assessments?

This is *GI Insights* on ReachMD. I'm Dr. Peter Buch. Joining me today is Dr. Richard Sterling, Professor of Medicine at Virginia Commonwealth University and the co-author of "Non-invasive Assessment of Liver Fibrosis," published in *Current Treatment Options in Gastroenterology, 2020*. Dr. Sterling, thanks very much for being here today.

Dr. Sterling:
Thanks for having me.

Dr. Buch:
It's a pleasure. Let's get right into the discussion. What are the pros and cons of non-invasive tests that use algorithms like APRI, FIB-4, and NFS?

Dr. Sterling:
So, one of the things that I like to say is the only things worse than doing a liver biopsy yourself is either teaching someone else how to do a liver biopsy or having one done on yourself. So as a result, non-invasive testing for liver disease severity has really increased in popularity. And knowing how much fibrosis your patient has is important because it's important with prognosis, particularly if they have advanced fibrosis, and who's gonna be at risk for liver cancer, as well as to identifying treatment strategies for patients, particularly those with viral hepatitis or fatty liver. So, when we look at a patient, there are several questions that we ask. Who needs to have this assessment done? Why do you need to have it done? What non-invasive assessments are gonna be available to you in your setting? Which ones should you use? And how should you really use them? And when we look at these non-invasive assessments, often they can be divided up into simple blood tests that are based on routine available data such as the AST, the platelet ratio index, or APRI, or the test that I prefer – the fibrosis-4, or FIB-4 test, which includes two liver enzymes – the AST and the ALT, the patient's age and the platelet counts. And these simple, essentially free tests work just as well as some of the more complex tests that are proprietary and cost money. Alternatively, if a serum-based test doesn't work or doesn't give us the answer that we want, we then use imaging-based tests, and right now the most common imaging-based tests are ones that look at elastography, or how stiff the patient's liver is. And there's a couple of different tests, either that are ultrasound-based or MR-based, that can give you that answer.

Dr. Buch:
That's great. Which non-invasive tests would you recommend to our primary care colleagues who are following patients with non-alcoholic fatty liver disease?

Dr. Sterling:
So, as we know, non-alcoholic fatty liver disease is one of the most common liver conditions out there. And I think, in our practice, the first test that we tend to do when we see a patient is we use one of two essentially free tests. We use the FIB-4 test, and we also use another test called the NAFLD fibrosis score, which includes some similar tests as the FIB-4, such as AST, ALT, age and platelets, but it also includes two additional tests – the BMI and the albumen.

Dr. Buch:
How would we select the best test for our patients, among the various proprietary tests for fibrosis, like FIBROSpect, FibroSURE, and

FibroMeter?

Dr. Sterling:
So, many studies have shown that the simple, non-invasive tests for first-line testing work just as well as these other tests that you've mentioned, like the FibroSURE or the FIBROSpect. But if you wanted to use them, it really may depend on the insurance company, and what tests that your lab can offer. Many of those tests are proprietary, so they are run through commercial labs such as LabCorp, and so it really may depend on what laboratory that your laboratory contracts with to determine what test that you can get.

Dr. Buch:
So again, just coming back to my previous question, between the simple tests that we talked about – the non-invasive tests and the proprietary tests for checking for non-alcoholic fatty liver disease what you're saying – keep it simple!

Dr. Sterling:
Yeah, so again, in our practice, we start out with the FIB-4 test and sometimes we may supplement that with the NAFLD score or the NAFLD fibrosis score. And that usually gives us very high negative predictive value, meaning if those scores are low, your patient is very unlikely to have advanced fibrosis or advanced non-alcoholic steatohepatitis, or NASH. The problem with these simple tests is that although they have very good negative predictive value and specificity, their sensitivity and positive predictive value aren't as good, and so sometimes you'll see a patient who has the suggestion that they have advanced disease based on these tests, when you really don't know. And that usually, in our practice, leads to the second-tier testing, which is liver elastography.

Dr. Buch:
That's great. That clarifies it. So, for those of you just joining us, this is *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today I'm speaking with Dr. Richard Sterling about non-invasive assessment of liver fibrosis. So, getting right back to our discussion, Dr. Sterling, between elastography and magnetic resonance elastography, which is preferable?

Dr. Sterling:
Well, I think that depends. If you look at the best test that gives you the best amount of information, that's gonna be the magnetic resonance elastography, or MRE. The problem with MRE is that it may not be covered by insurance companies, and it does require the patient to come back to the hospital for a second visit, and even if it was covered by the insurance, it may or may not be offered at your center since many places don't have the equipment to do it. So as a result of all those things, because it's very expensive, because it may not be offered, or it may not be covered by insurance, in our practice our next line test that we tend to do is transient elastography and we currently use the technique called, "vibration control transient elastography," which also goes by the trade name of FibroScan. And the advantage of that test is that it's almost a point-of-care test. We have the machine right in the office, and I can do it as part of that visit with the patient, so that the patient doesn't have to come back. It not only tells me how stiff the patient's liver is, which may tell me how much scarring they have, but that also has a feature to tell me how much fat is in the liver, called a CAP score. So, I can get two pieces of information right there at the office, for just another five or ten minutes of the patient's time and the patient doesn't have to come back to the office. And that is usually covered by almost all insurance companies.

Dr. Buch:
Just to clarify for those members of our audience who are not familiar, can you differentiate elastography from transient elastography, please?

Dr. Sterling:
Sure, so elastography is the general mode of measuring how stiff a patient's liver is, and there's several different techniques that can do that. We talked a little bit about magnetic resonance elastography, which in some respects is different to vibration-controlled elastography, where there is a vibration wave that's set up by a transducer, that goes through the liver and then the technology, whether it be MRI or ultrasound, then measures how quickly that wave propagates through the liver. And the theory is, the stiffer the liver, as a result of more scarring, the faster that vibration moves through, and therefore your higher your elastography goes. There are three types of vibration-controlled elastography: the one that we talked about, the vibration-controlled elastography, or FibroScan, but there are two others. One is called the acoustic radiofrequency imaging, or RFI. And the other one is shear wave elastography, and it just really depends on the technology of how things are done. But transient elastography is by far much lower in cost than, for example, MRE.

Dr. Buch:
Thank you. How often should non-invasive tests be performed?

Dr. Sterling:
So, I think non-invasive tests should be considered in every patient as their initial liver disease diagnosis, when the evidence of advanced fibrosis or cirrhosis is not evident. So, if I have a patient in the clinic who clearly has evidence of hepatic decompensation –

they're jaundiced, they have ascites, they have hepatic encephalopathy – those are not the patients that we're talking about. We're talking about the patients who it's not really clear if they have end-stage liver disease or not. So, I think it should be done on all patients as part of their baseline evaluation. It's a little bit more challenging to decide when to do the second test, or the follow-up test, because most liver disease doesn't occur overnight, and certainly you can consider it in patients to follow them to see if things have gotten worse without treatment. There's a lot of controversy about repeating the test to see if things have gotten better. For example, if I have a patient with chronic hepatitis-C, and I do a liver stiffness test or even a blood-based test to assess them, and then I treat their hepatitis-C to cure it, it's unclear how to interpret the follow-up test after the patient has been cured. That may hold true for fatty liver patients, or NASH, once treatments become available.

Dr. Buch:
That's a perfect segue into my next question – the gold standard. When should we still consider a liver biopsy?

Dr. Sterling:
So, liver biopsy is not completely gone, and there are certainly other indications when we do it. Transient elastography, or even the blood-based tests can tell us how stiff the liver is, and it may give us an indirect assessment of how much fat is in the liver, but non-alcoholic steatohepatitis, or NASH, can still really only be diagnosed by a liver biopsy, where we can see hepatocyte ballooning, and inflammation, and Mallory's hyaline and the other histological features of NASH. So, if you have to know whether a patient has simple steatosis, steatosis with inflammation, or non-alcoholic steatohepatitis – NASH, that may still require a liver biopsy. The other places where liver biopsy still has a role are in patients with autoimmune hepatitis, patients with abnormal liver enzymes of unclear etiology, where we need to see the pattern of inflammation, as well as our liver transplant population, where we're trying to see if the patient has rejection or recurrent disease that led them to get a transplant to begin with. So, although we do far fewer biopsies now than we used to do, liver biopsy still plays a role in my practice.

Dr. Buch:
Thank you. And before we wrap up, are there any other insights you would like to share with our audience today?

Dr. Sterling:
We've talked a lot about the use of non-invasive testing, but there's also a misuse. If you do it too frequently you may see changes that aren't there, just from the variation, or you may not get a chance to assess changes, and so sometimes I'll get patients referred for non-invasive testing – for example, a FibroScan – when I'm not really sure what to do with the data when I get the result. So, it's important not to misuse these tests, but as it is, it's important to understand how to use them.

Dr. Buch:
That's great. Well, that's all the time we have for today, but I want to thank Dr. Richard Sterling for joining me to discuss non-invasive testing for liver fibrosis. Dr. Sterling, it was great speaking with you today. You provided a tremendous amount of insight for our audience.

Dr. Sterling:
Thank you.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this episode and others from *GI Insights*, visit reachmd.com/giinsights, where you can Be Part of the Knowledge. Thanks for listening.