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Assessing Non-Invasive Monitoring Techniques for Liver Fibrosis

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm your host Dr. Peter Buch. And joining me today to shed some light on how we should be incorporating noninvasive techniques to assess liver fibrosis in our practice is Dr. Maurizio Bonacini, who's an Associate Professor of Clinical Medicine at the University of California-San Francisco. He's also the CEO of Mission Gastroenterology & Hepatology.

Dr. Bonacini, welcome to the program.

Dr. Bonacini:
Good morning, Peter. Thank you for having me.

Dr. Buch:
It's a pleasure. Let's begin with some background, Dr. Bonacini. What is the accuracy of blood tests to assess liver fibrosis for different liver diseases?

Dr. Bonacini:
Well, so that's a very good question. By these blood tests, I think we mean what's called the APRI, which is a relation between AST and platelets, or the FIB-4 test, so the blood test that you actually can calculate based on a simple blood sample that we would take from the patient. There are other blood tests like the FibroTest in Europe. The ELF test is fairly widely used, but these are proprietary, so there is some charge involved. Basically, these tests typically have been compared in a certain disease, so people ask the question: What is the prediction of these tests for fibrosis in, say, hepatitis C or in nonalcoholic fatty liver disease? So it's hard to compare them across diseases, but looking at the area under the curve, which really measures a combination of sensitivity and specificity of the test, depending on the cutoff that you use for each of these tests, which has been variable in the literature, you come out with a flavor that's pretty close in any given disease, but in those in a certain disease, there is sort of a pecking order where some tests are a little bit better than others.

Dr. Buch:
So when assessing hepatitis C, how do we decide whether to use AST to Platelet Ratio Index, also known as APRI, or the Fibrosis-4 Calculator, or FIB-4 for short?

Dr. Bonacini:
If you don't mind, Peter, I'd like to expand a little bit on the question. I would throw in the mix other noninvasive tests for fibrosis. I think the best performer for fibrosis is a magnetic resonance elastography, so MRE; of course, an MRI test is expensive, but it does perform best.

The second is vibration-controlled transient elastography, so the FibroScan, which is fairly well available in the United States. The third performer are the blood tests, and there's basically multiple studies to show that the best performer is actually the FIB-4, slightly better

than the APRI test. The FibroTest or the ELF performs similarly, even though one recent paper that was presented in London would support the fact that the ELF is actually performing better than the FIB-4. But I think for the audience, if one would pick a simple, inexpensive test to screen for advanced fibrosis, the FIB-4 performs basically the best.

Dr. Buch:
So, Dr. Bonacini, how often does the APRI or FIB-4 score miss significant fibrosis?

Dr. Bonacini:
Well, that's a very good question, and basically what you're asking is what is the sensitivity of the FIB-4? It depends on which level you're going to use, the cutoff. The cutoff will make a difference in sensitivity and specificity. So the question you are asking is, What is one minus the sensitivity? To make it simple, if we look at F3 and F4, and if you use the cutoff of 1.3—so below 1.3 the test is very predictive of the absence of stage 3 or 4—and if you calculate the sensitivity, you come out with the answer of within 5%. So it's possible to miss advanced fibrosis stage 3 or 4 at minus 1.3 in about 5% of cases, probably a little lower than that. Although, there was one paper that was just presented hinting that percent may be higher, but I like to believe that the FIB-4 across a wide variety of patients is actually performing quite well, and the false negative is less than 5%.

Dr. Buch:
Thank you very much. So putting this all together, and again, especially for our primary care colleagues out there, when should we move on to transient elastography or FibroSURE from APRI or FIB-4?

Dr. Bonacini:
I think in the population at risk for liver disease—in this day and age, NASH or NAFLD is the most common one—the risk of advanced liver disease is pretty small, say 15% or so in stage 3 or 4. Most of my patients that I see have low fibrosis, so you want to sort of table those patients and reassure them and not really go forward.

So the bottom line is that we use the FIB-4 with a cutoff of 1.3. If it's greater than 1.3, then the algorithm pushes you to do a vibration-controlled transient elastography. If the elastography number is greater than 7.4, then you go to a third test. If it's less than 7.4, then we tell the patient, "Your FIB-4 greater than 1.3 was not correct; you have low fibrosis." If elastography is greater than 7.4, the recommendation of the EASL is to do a noninvasive test like the FibroTest or the ELF, which the patient will be charged for. And the price is about $150 for the test. And then there's different tests at different levels. So if the level suggests high fibrosis, then probably the patient should be offered a liver biopsy. So that's how the algorithm goes.

Dr. Buch:
Thanks for clarifying that. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Maurizio Bonacini about noninvasive tests to assess liver fibrosis.

So, Dr. Bonacini, can you describe the techniques and role of both ultrasound-based 2D shear wave elastography and MRE elastography that you alluded to previously?

Dr. Bonacini:
We are basically measuring tissue stiffness by any of the techniques that you mentioned, and this stiffness has been correlated with fibrosis, again using a liver biopsy as the gold standard. Then I will compare briefly vibration-controlled transient elastography, which we call FibroScan, and that shear wave elastography. Shear wave elastography in my experience here in San Francisco is more on the realm of radiology because the machine is basically an ultrasound that has the advantage of being able to sample the stiffness of large tissue, particularly the 2D version. And the bottom line is that both techniques use an ultrasound beam to assess the velocity of transmission through a medium. The faster the velocity, the stiffer the tissue is, and therefore the more fibrosis. The softer the tissue, the slower the propagation.

Dr. Buch:
Great. And moving on to more invasive things, when is it time to do a liver biopsy these days?

Dr. Bonacini:
In terms of how useful a liver biopsy is, let's divide it into three categories. One is diagnostics. To make a diagnosis of autoimmune hepatitis, for instance, or primary biliary cirrhosis, you may want to use a liver biopsy to make an ironclad diagnosis. Likewise, if you want to measure copper in the liver or iron in the liver, you may want to do a liver biopsy, which is a diagnostic test.

Then we have the prognostic value of the liver biopsy, and I want to divide it in two categories. One is the rare event where you want to find out what is the likelihood of the liver that is undergoing massive necrosis, as what we call acute liver failure, will recover, so the patient may not need a liver transplant. Again, usually it's not an issue, and it's very rarely an indication.

So the last one is the more common indication. How often do we need to do a liver biopsy for fibrosis? As you remember, maybe 15, 20 years ago when hepatitis C was treated with interferon, we did liver biopsies to select patients with advanced fibrosis so we could better allocate treatments that were not very effective and that were fairly toxic. Then after hepatitis C oral medications were developed, the need to assess fibrosis by biopsy really fell by the wayside. Now the issue is the new epidemic on nonalcoholic fatty liver, so this made us question when we need to do a liver biopsy.

Well, I do a liver biopsy because I do clinical studies where liver biopsies are really crucial. There is no clinical study that I know of that does not require a liver biopsy before the intervention and at the end of the intervention. In my practice, who would I biopsy in reality? Well, I biopsy very few patients because notwithstanding the algorithm of the EASL that I told you, I tend to be more conservative. Even if my algorithm suggested the patient has stage 2 fibrosis, then I may not want to confirm that with a liver biopsy because probably I will not do anything different. I would sill ask the patient to lose weight, to improve their sugar control, and so I follow the patient with yearly FibroScans. But to answer the question, if we were to really scientifically assess the need for a liver biopsy, I would say let's follow the EASL algorithm. We first do a FIB-4. If it's greater than 1.3, then we do a transient elastography. If it's less than 7.4, we'll do it once a year and we won't do a liver biopsy. If it's over 7.4, we move to another noninvasive test. If the third noninvasive test says you have low fibrosis, we leave it at that. If it's higher, then we discuss with the patient the need for a liver biopsy, and that's how I would use the liver biopsy in this algorithm.

Dr. Buch:
Well, this has been a great discussion on the importance of using noninvasive tests to assess liver fibrosis, and I want to thank my guest, Dr. Maurizio Bonacini, for sharing his insights. Dr. Bonacini, it's been a great pleasure speaking with you today.

Dr. Bonacini:
Thank you so much. The pleasure was all mine.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights, where you can Be Part of the Knowledge. Thanks for listening and see you next time.