Featured Cases: Highlights from the 2014 EASL Meeting

Our guest authors are Mark S. Sulkowski, MD, Professor of Medicine, Medical Director, Viral Hepatitis Center in the Divisions of Infectious Diseases and Gastroenterology/Hepatology at the Johns Hopkins University School of Medicine; Raymond T. Chung, Associate Professor of Medicine, Harvard Medical School, Director of Hepatology, Vice Chief of Gastroenterology at Massachusetts General Hospital; and Laurent Castera, MD, PhD, Department of Hepatology, Beaujon Hospital, AP-AP, INSERM U773 at the University of Paris-Diderot.

After participating in this activity, the participant will demonstrate the ability to:

- Summarize recently released data about non-interferon-containing regimens for the treatment of hepatitis C.
- Describe any performance gaps for interferon-free regimens in cirrhotic patients.
- Describe the role of ribavirin as a component of HCV treatment in new interferon-free regimens.
- Describe newly presented information about non-invasive markers of liver disease.

This discussion, offered as a downloadable audio file and companion transcript, covers highlights from the 2014 EASL meeting.

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Dr. Chung has disclosed that he has received grants and/or research support from Gilead Sciences and Mass Biologics, and has served as a consultant for AbbVie, Inc.

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- Primary: primary care physicians (PCPs), OB/GYNs, physician assistants (PAs), nurse practitioners (NPs), community gastroenterologists and others who care for patients of Asian and West African descent in areas of high HBV prevalence
- Secondary: gastroenterologists, infectious disease specialists, and other clinicians involved in the care of patients at risk for HBV

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HCV
- Clinicians do not adequately identify which of their patients are at highest risk for HCV infection or effectively interpret testing results.
- Clinicians need to understand best practices in how to identify and manage HCV treatment-related side effects.
- Clinicians need improved awareness of how newly emerging therapies impact therapeutic decision-making in HCV infected and HIV/HCV co-infected patients.
- Clinicians are unaware of new non-invasive techniques to stage liver disease.
- Clinicians need to understand best practices in identifying cirrhosis and HCC in patients infected with HCV.

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- Raymond T. Chung, MD, has disclosed that he has served as a consultant for AbbVie, Inc., and has received grant/research funding from Gilead and Mass Biologics.

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eViralHepatitis Review is jointly presented by the Johns Hopkins University School of Medicine and the Institute for Johns Hopkins Nursing. This program is supported by educational grants from AbbVie Inc., Boehringer Ingelheim Pharmaceuticals, Inc. and Genentech.

The format of our program today is a bit different. We’ve asked some expert clinician-educators in hepatitis to share their thoughts about new information presented at the 2014 European Association for the Study of the Liver — EASL — meeting.

And so we’ll be joined today by Dr. Mark Sulkowski from the Johns Hopkins University School of Medicine, Dr. Raymond Chung from Harvard Medical School, and, a bit later in the program, by Dr. Laurent Castera from the University of Paris-Diderot.

This activity has been developed for primary care physicians, gastroenterologists, infectious disease specialists, OB/GYNs, physician assistants, nurse practitioners, community gastroenterologists, clinicians who care for patients of Asian and West African descent in areas of high hepatitis B prevalence, and other HCPs involved in the care of patients with or at risk for hepatitis.

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Learning objectives for this audio program are, that after participating in this activity, the participant will demonstrate the ability to:

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By way of introductions: I’m Bob Busker, managing editor of eViralHepatitis Review. Dr. Mark Sulkowski is Professor of Medicine and Medical Director of the Viral Hepatitis Center, Divisions of Infectious Diseases and Gastroenterology/Hepatology at the Johns Hopkins University School of Medicine in Baltimore.

Dr. Sulkowski has disclosed that he has received grants and/or research support from AbbVie, Inc., Boehringer Ingelheim Pharmaceuticals, Bristol-Myers Squibb, Gilead Sciences, Janssen, Merck, and Vertex. He has served as an advisor for AbbVie, Inc., Boehringer Ingelheim Pharmaceuticals, Bristol-Myers Squibb, Gilead Sciences, Janssen, Merck, and Vertex and has served on a steering committee for Pfizer.

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Doctors, welcome to this eViralHepatitis Review Podcast. Dr. Sulkowski, let me ask you to start us off with a quick overview.

DR. SULKOWSKI: Today our focus will be on new developments in hepatitis C therapeutics. We’re going to look at data presented at the International Liver
Congress. This was the 49th annual meeting of the European Association of the Study of the Liver, and this will be remembered as the meeting at which we turned the tides on treatment options for hepatitis C. At this meeting we saw multiple antiviral combination regimens that yielded cure rates or sustained virologic response rates in the 95 percent and in some populations 100 percent range. This will set the stage for the approval of these drugs in many parts of the world over the next year, and more important, delivery of these effective regimens to patients with hepatitis C infection.

MR. BUSKER: Talk to us specifically, if you would, about some of the most important new information presented.

DR. SULKOWSKI: Well there were a number of different regimens presented and I think one of the major problems we’re going to face is for clinicians and patients to try to keep track of these. One way that at least in my mind I’ve organized these is antiviral regimens that have a NS5B nucleotide analog polymerase inhibitor as their backbone, in this case sofosbuvir, and there is a family of different combinations being based on this very potent, highly effective, FDA-approved nucleotide analog sofosbuvir. And then the other side we have regimens that one could say are based on the combination of a protease inhibitor and an NS5A inhibitor and these include things like ABT450 boosted by ritonavir, asunaprevir and daclatasvir and a number of different combinations that were presented. So I’ve come to think of them being broken down in that way.

So perhaps we can start by focusing on just one family of studies, that’s the nucleotide analog bases regimens. So these regimens all include sofosbuvir, and one that I’ll start by covering is the COSMOS study. The final data were presented by Eric Lawitz at this meeting, and essentially this was the combination of simeprevir plus sofosbuvir, so this is a protease inhibitor plus a nucleotide analog sofosbuvir. And then the other side we have regimens that one could say are based on the combination of a protease inhibitor and an NS5A inhibitor and these include things like ABT450 boosted by ritonavir, asunaprevir and daclatasvir and a number of different combinations that were presented. So I’ve come to think of them being broken down in that way.

And in a nutshell what was presented was cure rates greater than 93 percent. And overall, even patients with genotype 1A had very high response rates with a highly tolerated regimen. So what’s unique about this regimen is it’s currently available, at least in offlabel combination. This is something that is being used in clinical practice, and we finally have the data.

Ray, what are your thoughts on this regimen and where will it stand?

DR. CHUNG: It’s a terrific regimen for those who need to treat their patients now. And what was unique about COSMOS, Mark, is that they tested the populations that we would have imagined need to be treated now, namely those patients with advanced fibrosis, METAVIR fibrosis stages 3 and 4 including bridging fibrosis and cirrhosis. Whether those patients were treatment-naïve or null responders, they were each included in the study and as you pointed out, the excellent rates of sustained response really give us a terrific amount of encouragement to take those patients whom perhaps we can’t counsel watchful waiting for much longer and if we need to get about the business of treating them now, which is I think a fair statement for particular cirrhotic patients, then these data certainly arm us with the confidence that we can succeed in that context.

A brief note I think of caution, and it’s one that, that I think we have to be concerned about in general when it comes to the seeming ease of use of these all oral regimens, is that even though the data here are from compensated cirrhotics, in practice the temptation may exist for patients to be treated who may not be quite so compensated. That is to say their synthetic function is completely intact.

We have certainly seen examples of this in older days with PEG, ribavirin, and first-generation protease inhibitor-based regimens, where patients who were not quite so fully compensated were treated and whose hepatic function deteriorated. There is some concern here that in an even mild to moderate hepatic impairment, that intrahepatic levels of simeprevir, the protease inhibitor, are quite unpredictable and concerns exist potentially that in a person who may not be so intact, we might see untoward effects.

I think we have to be careful about the indiscriminate use of these medicines in those patients, and we need to be careful to be sure that that cirrhotic patient is actually a fully compensated cirrhotic. But that said, the news is very encouraging for this particular group of patients.

DR. SULKOWSKI: Well, Ray, as you talk about that I think you hit on one of the major themes, at least in
my mind, that emerged from this meeting held in London in early April, and that is that when someone asks the question what’s a difficult to treat patient in 2104 and beyond, we’re taking away a number of the factors we used to talk about—race, high viral load, genotype 1—those types of things are no longer defining the hard to cure patient, it’s really cirrhosis. And as I look through a family of studies presented there for both the nucleotide analog polymerase inhibitor based regimens and then the protease NS5A regimens, we really do see that the cirrhotic patients, while excellent results are seen, it’s the one place where perhaps we’re falling a bit short of 100 percent or so.

The studies that I wanted to get into were the ION-1 study, as well as the ION-3 study, that focused on patients who were treatment-naïve, the majority of whom did not have cirrhosis and were treated for 12 or 24 weeks with sofosbuvir and the NS5A inhibitor ledipasvir and patients were randomized both to duration, 12 versus 24, as well as ribavirin-yes or ribavirin-no, and weight-based ribavirin was used.

So when we look at this family of studies, ION-1 did allow patients with cirrhosis to enroll. Roughly 15 percent had cirrhosis, and the overall SVR rates were phenomenal. These patients were treatment-naïve with or without cirrhosis, and the SVR rates ranged from 97 to 99 percent. We were left with the conclusion that 12 weeks looked as good as 24 and ribavirin appeared to add very little. In fact, only two patients had virologic failure in the form of relapse, so things look very good in this treatment-naïve group.

And then among non-cirrhotic genotype-1 naives, 8 weeks of therapy without ribavirin yielded 94 percent SVR. So we get this idea that treatment naïve non-cirrhotic and treatment naïve cirrhotic might be relatively easy to treat.

Which brings me to ION-2 which was the exact same design as ION-1, 12 versus 24, sofosbuvir/ledipasvir, ribavirin yes/no, but this time the patient population had genotype-1 and were treatment-experienced, including nearly half the patients who had failed telaprevir or boceprevir in combination with PEG-interferon and ribavirin, and 20 percent had cirrhosis. By any definition this patient population would be difficult to treat, and overall the results looked very good, 94 percent for 12 weeks, no ribavirin, and 99 percent for 24 weeks.

Things got a bit interesting when Dr. Afadhul, who presented and then published the ION-2 data, showed the breakdown by cirrhosis and no cirrhosis. We see that for the 24 week group it was 100 percent with and without ribavirin, but for the 12 week groups in patients with cirrhosis, he reported 86 and 82 percent, and it looked like ribavirin didn’t make a difference there; 12 weeks seemed to be somewhat short for patients with cirrhosis.

So let me stop there, and Ray, let me get your thoughts on the ION family, 1, 2 and 3, and where you see this regimen being used in practice over the next year.

DR. CHUNG: As you have pointed out, there is nothing quite like the patient without cirrhosis who is treatment naïve. If we were imagine that there is low-hanging fruit in this group of patients, it’s that very population you’ve described. Something about the lack of advanced histology appears in some ways to be consistent with excellent virologic response rates, which I think brings us to the larger question about what it is about cirrhosis that appears to limit response rates. I think at that level it’s worth thinking perhaps in a couple of different ways about what those constraints might be.

At one level there is certainly I think a physical or architectural set of constraints that accompany advancing fibrosis in the liver. Imagine now that you’ve deposited scar tissue around your hepatocytes where drug levels need to be at optimum concentrations to provide the desired antiviral effect. In a densely settled scar that accompanies advanced fibrosis or cirrhosis, one might envision that access of drug to those very same infected hepatocytes may at some level be somewhat attenuated.

For the most part, the dosing strategies appear to be successful in most patients, but one could envision that access may become more limited, particularly in the most advanced forms of fibrosis. As we think about patients with cirrhosis, we might think that, that when we try to take away duration of therapy we may, in fact, be seeing an impact on performance of these regimens.

The other point to be made, though, which is one you brought out in the distinction between ION-1 and ION-2, where it appeared that patients with cirrhosis who were treatment-naïve appeared to do well, but those who were treatment-experienced did not do as
well. So receiving and failing previous therapy may speak to a couple of other issues, one of which may be the inherent responsiveness of those patients to regimens that once contained interferon. That could speak to a limited innate immune response that may be important to close out the deal in terms of clearing out the last remaining infected hepatocytes, even with a successful direct-acting antiviral-based regimen.

I think the treatment-experienced patient with cirrhosis then may very well be a selected group of patients who have, by virtue of their prior nonresponse, be in an impaired position, even in the face of very good concentrations of antiviral drug, still not be able to close the deal. They may require more help from the antiviral, in this case perhaps in the form of extended duration of these therapies. There may be both structural or architectural concerns that accompany cirrhosis and innate immunologic concerns in that group.

DR. SULKOWSKI: Let me follow up on that last point you made about patients with cirrhosis and get into the TURQUOISE-2 study. One of the interesting points of this patient population is, we do continue to see some very subtle differences in these treatment-experienced patients, and we’ll circle back to that.

But let me give you an overview of TURQUOISE-2, which was presented and published by Fred Poordad. This was a 12- versus 24-week study of the ABT regimen which included the coformulated ABT450/ritonavir/ombitasvir tablets and has a protease inhibitor called 450, an NS5A inhibitor called ombitasvir, and ritonavir coformulated into two tablets once daily. All patients took that in combination with dasabuvir, a nonnucleoside polymerase inhibitor, as well as ribavirin.

The study design was quite simple: 380 patients with cirrhosis, who could be treatment naïve or PEG-interferon/ribavirin treatment-experienced; relapsed, partial responder or null responder; who received 12 weeks of the 3D regimen with ribavirin for 24 weeks. The demographics of this study showed some patients with advanced disease, about 12 percent had albumin less than 3.5 percent and about 20 percent had platelet counts below 100,000.

What’s interesting about the sustained virologic response rates are, when you break down the categories by genotype subtype, with this regimen patients with the 1B subtype tend to respond very well and probably don’t require the addition of ribavirin. In the patient with 1B for whom this regimen is very effective, 12 weeks looked equal in patients with cirrhosis, regardless of previous response.

When we got to the genotype-1 subtype A patients, in previous studies, the PEARL studies of this combination had shown that ribavirin led to a 7 percent higher SVR rate, but in this population where everyone got ribavirin, the naïve SVR rate was 92 percent and 12 was equal to 24 and we saw 12 equaling 24 among prior relapers, prior partial responders, but when we got to the prior null responders, so these were patients who were given PEG-interferon and ribavirin but it was really an incredibly ineffective regimen, less than 2 log drop, and here we saw 80 percent SVR for prior null responders of 1A for 12 weeks, jumping to 93 percent when one gave 24 week.

So it looks like if one is treating cirrhotic patients you really need to ask the question are they previously treatment experienced and at least in my mind I’ve been thinking that cirrhotic prior treatment failures may benefit from 24 weeks. But I think this study really gets to this idea that perhaps the immune system is contributing something to the eradication event and these prior null responders are immunologically impaired, but that is of course speculation.

Ray, what are your thoughts when you approach a patient? First, it sounds like we need to know whether they have cirrhosis, yes or no, and then we need their treatment history. How will be determine cirrhosis in the coming year: by biopsy, or is there a role for other measures?

DR. CHUNG: It’s a great question, Mark. As we look at this breathtaking array of regimens that are now being developed, with 95 percent rates of sustained response or better, we’re now in a position to say it’s not a matter of whether we treat but when we treat. I believe that the onus on us to accurately and precisely stage treatment for our patients becomes somewhat diminished, as it largely will not influence our decision to treat.

But as you have pointed out in these studies, it is important to understand whether a patient has cirrhosis, given these subtle but real differences in
outcome, and our choices about duration of therapy that rely on that ascertainment. I think that if we had tools — and those tools appear to be emerging — allowing us to make that clear distinction between patients with and without cirrhosis, I think that help us not only define the regimen for those patients, but also identify patients who need continuing primary care of the liver, That is to say screening for hepatocellular carcinoma and even screening for portal hypertension in the form esophageal varices. These are important dimensions I think of, of course, sorting the cirrhotic patients from the non-cirrhotic.

As we’ll hear from Dr. Castera shortly, the emergence of transient elastography and other serum noninvasive markers of fibrosis, have really done well from a performance vantage point in helping us make that very distinction between the cirrhotic and the non-cirrhotic patient.

**MR. BUSKER:** We will be hearing from Dr. Castera in just a few minutes. But first, talk to us about the NS5A agents. Dr. Sulkowski?

**DR. SULKOWSKI:** As we look at these various options that we anticipate our patients may have in this protease NS5A family of combinations, there’s the ABT combination that we have already discussed and we also saw some very compelling data from a phase IIIB trial of the Merck compounds, MK5172 and MK8742. This is a once daily protease inhibitor plus a once daily NS5A inhibitor. And what was tested in the so called C-WORTHY Study was this regimen for various durations as short as 8 weeks, 12 weeks and then 18 weeks, with or without ribavirin. What was unique about the C-WORTHY Study was they investigated a number of different patient populations. They had cirrhotic patients, they had cirrhotic null responders, they had HIV co-infected patients and they really put this regimen to the test if you will and yielded very high sustained virologic response rates. They did determine that 8 weeks was probably too short, and there was some suggestion that the longer therapy might be more effective for cirrhotics, the 18 weeks.

Ray, what are your thoughts on this regimen and the role of ribavirin: will this be another one pill, once a day regimen, will they need ribavirin, or how will we use this?

**DR. CHUNG:** One thing that seems to emerge from our studies is that if you have a superb regimen that consists of two very potent direct-acting antiviral classes, you will do well in a very large swath of populations. When you start getting into the more challenging populations, there may be some slight lag in performance.

In this regard the two strategies that have been used — and we highlighted some of them earlier — have been either to extend duration or to add ribavirin, or in some cases both. They appeared to help get a little extra measure of efficacy in those populations by either prolonging the duration of and presumptively enhancing the antiviral concentrations in those difficult-to-reach reservoirs, particularly in patients with cirrhosis. What is interesting with ribavirin is, even though we haven’t nailed down its precise mechanism of action after many, many years of using it clinically, it does appear to continue to confer some enhancement in performance even with these potent classes and regimens in combination. And we believe, at least one of the theories here, is that ribavirin might not be acting so much acting as a direct antiviral so much as it is perhaps increasing the rate of virus mutation. Once you have the virus down to a very low concentration but not quite at extinction, as you might with these DAA regimens, the mutagenesis rate may actually be the final crowning blow in terms of clearing out those reservoirs of viable virus.

It’s an intriguing notion that ribavirin does appear to add to difficult, more difficult to treat groups of patients. This is why we see that with the 1A patients, for instance, that in regimens that don’t contain the nucleotide polymerase inhibitors, sofosbuvir as you alluded to earlier, where other classes perform a little less well against 1As, where ribavirin appears to be a more important part of that regimen. And hence the use of ribavirin in 1As appears to bring up performance.

**DR. SULKOWSKI:** Ray, I think you have hit on one of the other important themes over the next several years is to really once and for all sort out the role of ribavirin in the treatment of hepatitis C. It sounds like we’re getting closer to figuring out exactly what ribavirin does, but I also hope that we’re close to getting rid of it from most patients that we treat in terms of a therapeutic regimen. So certainly major advances and a number of different regimens
that are all oral, interferon free, that can eradicate or cure hepatitis C in excess of 90 percent of patients treated, and the Merck regimen is certainly one of them along with the ABT regimen from AbbVie and the sofosbuvir based regimens from Gilead. So the future really does look quite bright for patients.

DR. CHUNG: I concur.

MR. BUSKER: Dr. Mark Sulkowski from Johns Hopkins, Dr. Ray Chung from Harvard — thank you both for being part of this eViralHepatitis Review Podcast.

And we’ll return, to speak with Dr. Laurent Castera from the University of Paris, in just a moment.

MS. JULIE MCArTHUR: Hello. I’m Julie McArthur, Adult Nurse Practitioner in the Division of Infectious Diseases at Johns Hopkins University. I’m one of the program directors of eViralHepatitis Review.

eViralHepatitis Review is a combination newsletter and podcast program delivered via e-mail to subscribers. Newsletters are published every other month. Each issue reviews the current literature in areas of importance to hepatologists, infectious disease specialists, primary care physicians, nurses, nurse practitioners and other clinicians caring for patients with viral hepatitis.

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MR. BUSKER: Welcome back to this eViralHepatitis Review podcast. I’m Bob Busker, managing editor of the program. Continuing our discussion of the new information presented at the 2014 EASL meeting, I’d like to turn to Dr. Castera to talk about non-invasive markers of liver disease.

Dr. Laurent Castera is from the Department of Hepatology at Hospital Beujon, AP-HP, INSERM U773 at the University of Paris-VII in Clichy, France. And he has advised that he has no potential conflicts to disclose, nor will he be referring to the unlabeled or unapproved uses of any products or devices.

Dr. Castera, welcome to the program.

DR. CASTERA: I’m very glad to be there and share some experience about noninvasive methods.

MR. BUSKER: Let me begin with the overall question — and I know Dr. Chung answered part of this — why it’s important for clinicians to assess liver fibrosis in patients with hepatitis C.

DR. CASTERA: Why is it so important to assess liver fibrosis in patients with chronic hepatitis C? Because not only prognosis and outcome, but also treatment indications are related to the amount of liver fibrosis.

For many years liver biopsy has been considered the reference standard for evaluating liver fibrosis. Over the past decade, because of its limitation, invasiveness, and sample bias, liver biopsy has been challenged by noninvasive methods. This method relies on two different but complementary approaches: the dosage of a serum biomarker and the measurement of liver stiffness. These methods are now widely used, especially as first line for staging of liver fibrosis in patients with hep C. Actually, the measurement of liver stiffness using transient elastography is currently the most accurate noninvasive approach for diagnosing cirrhosis. There is also increasing evidence for predicting clinical outcome and survival in patients with cirrhosis.

MR. BUSKER: There were a number of new findings presented at EASL that addressed this issue. One of them was “Liver stiffness assessed by Fibroscan is a major prognostic factor in primary sclerosing cholangitis.” Please tell us about that, if you would please.

DR. CASTERA: This is a study from France. The setting is PSC, primary sclerosing cholangitis.

So basically this is a large series of PSC patients, that is a rare disease, with a follow-up of four years, and
there are two interesting findings. The first finding is that if you have liver stiffness value above 10 kPa, as the outcome is different because the survival rate is close to 40 percent after 8 years, whereas if your liver stiffness value is below 10 kPa, sorry, your survival rate was 80 percent. So that makes a difference.

The second interesting finding, even more interesting, is the fact that these patients underwent several liver stiffness measurements over time, once a year, and for instance, if you have an increase of liver stiffness over time, let's say above 1.3 kPa/year, the risk of developing complication of dying is even higher. And for instance, the survival rate was 20 percent after four years in these patients, as compared to 85 percent in patients below 1.3 kPa/year. This is consistent with other data, especially in patients with hepatitis C showing the prognostic value of liver stiffness, especially in patients with cirrhosis and the relationship with the outcome.

But the interesting finding of this study is the dynamic perspective that if your liver stiffness increases over time, then you are even at higher risk of developing complications, liver-related complications. And, of course, these results need to be validated in other populations and especially in hepatitis C patients. But they suggest that liver stiffness value at baseline, and the evolution over time could be used to stratify cirrhotic patient in different risk groups together with the usual scores like Child-Pugh or MELD score.

MR. BUSKER: Thank you, Doctor. Now another presentation that you highlighted was “Prothrombotic Genetic Risk Factors Are Associated With Liver Stiffness In The General Population: Results From The Rotterdam Study.” Summarize this research for us, if you would please.

DR. CASTERA: So this study targeted a large population of elderly patients, this comes from the Netherlands, the so-called Rotterdam study, and there were more than 1,000 patients over 65 that were evaluated for liver stiffness measurements using FibroScan.

The concept of the study was to use noninvasive methods and FibroScan, particularly to phenotype the patients for liver fibrosis or cirrhosis. And this is a very innovative and attractive approach to phenotype a population, for instance, for cirrhosis. And it has been previously shown that you could detect cirrhosis in so-called normal or healthy population using this method.

So in this study there have been also previous studies using genetic factors or factors that are associated with fibrogenesis, like adiponectin, for instance, in NAFLD or in hep C patients, and in this study the authors studied the coagulation factor including factor V Leiden, factor II and blood group non-O that may increase the risk of liver fibrosis in the general population. And actually what they could show using a cutoff of 8 kPa as clinically relevant fibrosis, that in the subgroup of 100 patients with elevated liver stiffness values, the heterozygosity of factor V Leiden and factor II were associated with a two-fold increased risk of clinically relevant fibrosis in this population.

MR. BUSKER: How can these finding be applied to patients with hepatitis C?

DR. CASTERA: So the way I will extrapolate to hep C is the fact that there is so many people with hep C that you will not be able to provide a liver biopsy in all these patients and the use of noninvasive methods may be accurate to pick up the most severe patients with liver fibrosis or cirrhosis in large populations in order to refer them to the specialist and to treat them.

MR. BUSKER: Thank you, Dr. Castera. I’d like you to discuss one more presentation from EASL, if you would please. And I understand this is about new research into portal hypertension?

DR. CASTERA: So recently there have been a lot of interest for spleen stiffness that could be a better surrogate for portal hypertension than liver stiffness, even though this remains to be demonstrated. Also transient elastography is challenged for the measurement of liver or spleen stiffness by other methodology including ARFI (acoustic radiation force impulse imaging) and supersonic imaging.

MR. BUSKER: And the limitations of FibroScan?

DR. CASTERA: So the main limitation of FibroScan in clinical practice is the applicability, especially in patients with ascites or obese patients.

So in this study, entitled “Prospective Comparison of Liver and Spleen Stiffness and Composite Scores, Using Supersonic-Shear-Imaging or Transient
Elastography for Detecting Clinically Significant Portal Hypertension in Patients with Cirrhosis,” around 80 cirrhotic patients undergoing HVPG measurement were studied and liver and spleen stiffness was measured using either FibroScan or supersonic imaging.

The first interesting finding is the applicability of supersonic was far better than that of FibroScan because around two-thirds of patients had ascites and supersonic was applicable in almost all patients, 97 patients, as compared to 45 percent of patient with FibroScan.

So the second finding is that spleen stiffness did not have a good diagnostic accuracy for portal hypertension in this population, and the best method was the measurement of liver stiffness using supersonic imaging with, for instance, 82 percent diagnostic accuracy at a cutoff of 24.6 kPa.

Overall, this result suggests that the new technology, especially supersonic imaging, may be interesting for detecting clinically significant portal hypertension, especially in patients with advanced cirrhosis.

So although these results are preliminary and need to be confirmed by other groups and in other populations, they emphasize the fact that there are new technologies challenging the standard to be beaten that is currently FibroScan, and may be helpful in the future.

**MR. BUSKER:** Dr. Castera, thank you for sharing your thoughts with us today in this eViralHepatitis Review Podcast.

**DR. SULKOWSKI:** Okay, thank you very much, I hope this new information will be helpful for your clinical practice.

**MR. BUSKER:** This podcast is presented in conjunction with the eViralHepatitis Review Newsletter, a peer-reviewed literature review certified for CME/CE credit, emailed monthly to clinicians treating patients with viral hepatitis.

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