[MUSIC PLAYING]

RAMON BATALLER: I put a title with an intention. I want to deliver you to you one message that I hope you remember. If one talk, you get one message that you remember, to me, it is a definition of a successful talk.

We need to treat the cause. We need to talk about alcohol use in these patients. We learned that from the hepatitis C world. We were trying to treat hepatitis C people with a lot of drugs, a lot of medicines to slow down the disease. Nothing worked until we cured the hepatitis C.

In alcohol, we're still very behind in our knowledge and our attitude, sometimes, to face the cause of the disease. And the first step is to diagnose that they are drinking-- which is very challenging, as you know, because patients under-report all the time.

So to do, please, always focus in the alcohol intake. Talk to the patients. And ideally, as I will show you, you have to have a multidisciplinary team. You have to have an addiction person working with you.

And so this is a natural history of alcoholic liver disease. It's very similar to what Dr. Bihari showed about NAFLD-- very similar. The fat in the liver, the progressive fibrosis, the cirrhosis, and the hepatocellular carcinoma or decompensation.

There's two differences. Number one, people, throughout their life, they drink very irregularly. When you see a patient that has been decompensated eight years ago with ascites and encephalopahy, then five years were fully compensated, then decompensates again now, you have to think about ethanol 100%. NAFLD doesn't cause that when they decompensate.

Number second difference. When you drink very much for a long period of time, sometimes, you can develop, sorry, an episode of alcoholic hepatitis-- that is when you get yellow and you fail sub-acutely. That is unique of alcoholic hepatitis. It doesn't occur if you eat excessively for many years.

So what which are the determinants of drinking? One important concept-- alcoholism is a very genetic disorder. When we ask, and lately, we are asking more and more about these to our patients, 2/3 of our patients have family history of alcoholism.

And there is no studies. We would like to do one, if that impacts the relapse rate, the resistance to anti-craving therapies, et cetera. But a lot of patients have that, I used that to remove the guilt for many of these patients. And it's helping a lot, especially with women, that they are more stigmatized in this society when they drink. It helps.

We did a study that I didn't think was so important, but it became vital. We were in many TVs and radios all over the world. So we were the first to demonstrate when it's cold, you drink more, and you have more liver cirrhosis due to alcohol.

And the mother of one of the surgeons at UNC where I used to work, he was from Mexico. She told me, maybe it's not the cold. It's the sun. I said, what an idea you gave to me. I promise I will study that. And I went [INAUDIBLE] in the paper. That became the most important result. And not only the cold, the lack of sun that I suffer as a Mediterranean guy here.

[LAUGHTER]

A lot. Why you say that? This is America. The amount of alcohol that you consume and the cold weather, you see there is a-- except for some, this is the cold weather, and this is the alcohol, there is a north-south degree, OK? And in the world, we found the same.

Interestingly, the something that many journalists were very interested has led that towards another study that we're doing now with our team-- thank you, the team is there. We're working whether the vitamin D deficiency associated with the lack of sun causes depression, but now there is a lot of data that it causes, as well, addiction.

So we're trying to see whether people with bariatric surgery, that they have this tendency to become alcoholics. The deficit of vitamin D precedes the onset of alcoholism and also predisposes to alcoholism.

I have to be very-- I have never thought in my life there will be my name in *Elle* or in *Cosmopolitan,* because I have never dated a model. So it's interesting that some of the journalists even quoted our study.

So we're talking more-- as I say in my introduction of the course, hepatology is facing a life event. I'm from Spain. You will notice a thick accent. And they are closing many liver centers, and they are merging to GI because of the lack of patients. In Valencia, my hometown, this is happening and [INAUDIBLE]. We are safe, guys. In America, due to the obesity and the amazing amount of alcohol intake, especially in Pittsburgh, we're safe.

So because our clinic today in the inpatient clinic that I have my colleagues here, 70-- 2/3 of the patients are alcoholic-- So we're not talking about a marginal disease. We're talking about marginalized disease, but not marginal.

Which are the causes of early liver disease? All this study is done in France. But you have to remember that 88% of the people, or most of the people with a kind of fibrosis in the general population are not due to hepatitis C and B. It's due to NAFLD or alcohol, or the combination.

In science when we do studies, when we do papers, we try to isolate a cause. We only-- even for FibroScan studies. So what is the cause? Like humans can only have a cause of liver disease. In real life, when we see our patients, don't have one cause-- so there typically is hepatitis C, then NASH-- and forget about the others.

In my common practice, it's very common that a patient is labeled with hepatitis C or NASH and the alcohol is ignored. Because the patient lies, because biomarkers are in order, et cetera. When you see the patients and the acute hepatitis C, the disease progresses, it's because the main driver of the liver disease was alcohol.

OK, so we are now doing a position paper-- and hopefully, Jay and I, we will collaborate in that-- to the term [INAUDIBLE] dual, the people with-- we call it in Spain, [INAUDIBLE], which is a typical, here you call "beer belly." This is very common, OK? This is very common.

With this team, in my clinic, in the alcohol liver disease clinic, I have seen few patients in my life with early alcoholic liver disease. Those patients that go to the [INAUDIBLE] clinic continuously. They don't come to me.

Why? Because we don't have campaigns for early detection of fibrosis among drinkers, OK? We are trying to convince UPMC, with some difficulties-- and this is recorded-- to start a program for early detection of silent fibrosis among alcoholics.

Among other reasons, you cannot give Antabuse or disulfiram to someone with silent cirrhosis. I have seen four people die. You need to check for liver disease before you give anti-craving drugs, for example. So but also, you can save lives and save money, because we detect alcoholic liver disease patients too late.

This is a global study that we did and we published this year, with all over the world, including Kenya, Australia, India, China, South America, et cetera. In blue, you see when the patients are see more frequently early disease versus late disease, and in the red is when the patients are seen more frequently late versus early. Look at alcohol. It's always minus 8, minus 10-fold.

We did, also, in this study, which is the disease that is less represented at AASLD and EASL, et cetera. It was alcohol by 10-fold. So alcohol always has 10-fold-- needs more attention, OK? We are getting more attention, but still, the data speaks by itself-- we are behind. We need to detect these patients early on.

You know what is the main cause of hospitalized liver patients in America? Alcohol, 2/3 of the cost. Not detecting patients early not only doesn't save lives, but also doesn't prevent all the burden, economical burden of the disease.

So as I say, obsessive, I think we need to start campaigns to detect liver disease among addiction centers. And we are working on that. There is a trend to start in the world. There are few, few liver centers like this in the world, where we did collaborations, we only learned-- we only knew two centers in Europe doing that. So it's really amazing, the lack of this.

And why do I say that? Look at this. This is in a study we published two years ago with a group in-- that I helped a group in Austria. People with F3 or 4 of liver disease, alcohol, have a high mortality.

This is more than to have a dysplasia in the colon polyp. This is more, no? You have a dysplasia in a colonic polyp-- so detecting silent liver disease can impact people to stop drinking. It can impact people to stop drinking.

I think with the FibroScan that we have now, we can start screening for fibrosis in our alcoholics. And the FibroScan scan can be very good for positive and negative reinforcing. If you continue the drinking, you will worsen. If you stop drinking, you will quickly improve. So it can help to motivate the patients, because the patients respect the liver.

When you tell the patients you have a risk factor of something potential in the future, they say, this guy's a little exaggerated. When you show you have fibrosis in the liver, they respect it, and it's likely that detecting that can contribute to stop drinking.

What is the management of patients with moderate or silent alcoholic liver disease, the ones that I tell we barely see and I have barely seen in my clinic? I am really happy when, in my clinic, we've seen one of these. Obviously, this happens with the NAFLD. You have to rule out other causes. But you cannot hide having a metabolic syndrome or BMI of 40, but you hide very frequently that you're drinking.

How to reveal the drinking in someone who is lying? You have to be motivational, to approach the patient well. You can talk to the family members or friends. And sometimes you can use biomarkers of alcohol, because people lie all the time.

There are three biomarkers. The alcohol in blood is one day. So I have seen patients getting drunk in the clinic. One day, he was so drunk that when I went to see my colleague, they were you smell alcohol. I go, no, I have not drink. That was my patient. They had high levels of alcohol in the blood. I was smelling the alcohol.

So the other thing is the urine alcohol test. We're doing a lot of the alcohol metabolites in the urine. Two drawbacks. It's urine, so if your center is not equipped for drug testing, you do not check if the patient goes alone to, without any peers, the temperature of the urine. And UPMC, we don't have that capability in our clinic. And I have seen a lot of savvy addicted people cheating,

OK, and going even with the family members to the toilet to pee there. So OK? We have the screen for drugs that the patient was not taking it. [INAUDIBLE] showing that the urine was not from the patient.

But now we have a new thing that is a PEth-- phosphatidylethanol. That is in the blood. Now it's a little costly-- 180, 200 bucks. You cannot do it as a screening. But it captures three weeks of alcohol, the PEth-- P-E-T-H.

Now we have in since last week-- think you, Andreas for that. You are really contributing to our unit. And we have these in UPMC. And yesterday-- no, Thursday was the first day with Samantha that we ordered these to a patient that I have my doubts that he's drinking. This is the most sensitive and better when you have, really, doubts-- for example, in the setting of a transplant evaluation, remember PEth.

If you detect that the patient has a liver disease, they don't have all the causes, you should use non-invasive techniques such as Jay has described for NAFLD. NAFLD is much more advanced than ALD in terms of research, but these techniques are also useful for assessing fibrosis in alcoholics.

Knowing that someone has drank in the last hours, alcohol, you get reddish. It is very vasodilatory. It increases the blood flow in the liver, and it increases the stiffness of the liver, and you can overestimate the degree of fibrosis. You have to make sure that the patient is abstinent at least for one day.

You know, when you drink a lot how bloody and reddish you become-- some more than others. When you do a biopsy in these patients very rarely, and you do rarely in alcohol and in NASH, it's exceptional to do biopsies of these patients. But once you have the ALD, you can give antioxidants. You can give vitamin B complex. And you can do motivation, either yourself or with the help of a counselor.

I would highly recommend to have a counselor in your clinic. We have, finally, a counselor at UPMC in the clinic. We have counselors in the patient service. This is the way to treat these patients. But still, most patients won't accept to go to a counselor because it's stigmatizing. You need to be a good counselor.

With the new-- Christian-- that I'm blown away, because he looks fantastic, the new counselor, we want to do a training course to train everybody working at UPMC for motivational interview. I still see when I round that we don't ask, don't tell the alcohol. We don't ask too much, we don't tell too much. We kind of ignore.

Of course, when I'm running, they cannot ignore that. And I say, what is the last drink? Last drink? I'm sorry. No, no, we have to ask for the last drink. And the patients under-report all the time.

Sorry that I'm being too practical. Maybe you expected more data. But I think I can be more useful giving you practical advice. And needless to say that the FibroScan, as Jay has shown for NAFLD, there is a lot of studies that accurately measures their estimated fibrosis. Especially I see these very much for early patients as a motivational, also, tool, because you have positive and negative reinforcement.

OK, let's focus a little bit in the last six minutes-- I have to stick with the time after my warning-- about the alcoholic hepatitis, the yellowness that you get suddenly. This is very frequent in America compared to Europe. Where I come from, people drink, as a whole, more, but more steadily, more-- here, the drinking is concentrated in fewer people, and they are crazily drinking. They come with a lot of effects of drinking in the nerves, with a lot of neuropathy, with cognitive impairment, with pancreatitis, with a lot of problems. So alcoholics here are extremely severe compared to other countries. And the data speaks by itself.

So typically, one of the things I wanted to say that we studied a [INAUDIBLE], we did a study, is that when an alcoholic hepatitis comes to the clinic, many times they have a little fever and a little leukocytosis, and not always, they are infected. This can be an [INAUDIBLE] inflammation leading to multi-organ failure and death.

But one of the things that most or many cirrhotics are hypertensive because cirrhosis is a vasodilatory condition the drops your blood pressure in general. So we noticed that we did in a study that was presented in SLE that people with a MAP of less than 80, independently of the MELD, do worse, OK?

So probably because of SIRS, the systemic inflammation induced by alcohol, mixed with [INAUDIBLE] is responsive to vasoconstrictor. This is, we're doing some mechanistic studies to see. We'll figure out why.

But I think we have to do a trial. And we have here the albumin company, already we met them to start to give albumin in patients with systemic inflammatory response, [INAUDIBLE], to prevent acute kidney injury, multi-organ failure, and death.

So probably these patients have a vasodilatory state leading to hypotension that is one of the contributors to early diagnosis, you can see the difference is massive about the mortality of these patients. One of the cultural things in this disease that, when I came from Europe, everybody was biopsied. Everybody gets a biopsy. In America, it's an anathema. You cannot do it. Why you cannot do? We are in the evidence-based medicine. Why?

So when we tried to, some experts, we came out with some guidelines when the liver biopsy is advisable. When you don't have any atypical thing-- you have an alcoholic that has not taken any drug, that is yellow, that has all the picture in the labs, et cetera. My goodness, he should be in alcoholic hepatitis, and the imaging doesn't say you something wrong, you don't need a biopsy, I agree.

But what about if you have atypical labs? For example, recently-- and some remember this patient-- we see a patient, drinker, with all the picture of alcoholic hepatitis, but the alkaline phosphatase was a little too elevated for my experience.

We ordered an MRCP. He had a cholangiocarcinoma. He was an alcoholic with an alcoholic hepatitis and a cholangiocarcinoma. He had stopped drinking immediately. All the labs associated with [INAUDIBLE], the transaminases improved, but the bilirubin remained 20 because the cholangiocarcinoma did not respond for the abstinence.

So now, this cultural-based medicine I don't like. You had to have evidence-based or experience-based medicine. I think evidence and experience shows that patients with a typical thing, you need to do a biopsy for a definitive [INAUDIBLE]. If you don't do the biopsy in these patients, you cannot label in the note, this is a definitive [INAUDIBLE]. You can see it's just impossible.

What is the-- we are very good at predicting the death of these patients-- very good-- but not so good treating these patients. Recently, one of the studies that we're doing in Italia, we are doing a global study in many countries in the world. We have showed that the male is, again, the best discriminatory function for alcoholic hepatitis mortality.

Please don't use the discriminatory function. The [INAUDIBLE] is the worst by far. We have done-- there's many papers for that. Please, if you do it, you will hurt my feelings, OK?

So the patient underwent a liver biopsy, and we did several studies showing that the degree of cirrhosis, where the cirrhosis was [INAUDIBLE], they have worse prognosis. And then these patients, for example, I am putting here, it was horrible. It was all this [INAUDIBLE].

The patient was given prednisolone, but unfortunately, he did not respond. He died.

What do we do with these patients with severe alcoholic hepatitis that do not respond? We have a program in UPMC, and more than 50% of the programs in the country, about early liver transplantation in these patients. My talk at AASLD was about this. It was a controversy talk, OK?

We have large discussions at UPMC when we have these patients. When I have one of these patients, I know I will not arrive home on time, because we can be one hour. And there is a very opinionated, well, you have been turned down one of your patients, you're hurt. Next time, you say no to the next one. That is real life, is it not true? I don't know, Jordan-- you have the same in Toronto?

When I spoke to the audience, everybody was laughing. Oh, my god, don't tell me. If we have two patients, I call my wife, I am not going home today. Because the discussions are super long.

In general, when you have a patient with major comorbidities, and it's the first episode ever, these patients who deserve a shot for [INAUDIBLE]. We have done roughly 10, it's only 2% to 3% of the whole population of these patients. So we're not using all the donors for that.

And I will show you just one final slide, which is this. So we talk, because I have 13 seconds. I have to be straight, talk [INAUDIBLE]. Here's my last slide, linked to the message they I told you at the beginning. Precise medicine, where we talk always about precise medicine. This is modern medicine. We only think in polymorphisms, the genetic background.

In alcohol, it's to know why the patient is drinking. Remember, depression and anxiety, pain, poor sleeping, and trauma. We have a growing population of young ladies without help in their 30s, even their high 20s. 2/3 of them were abused in the past. It's another, other consequence of the macho society.

We're trying to do a publication with that, and we are talking to the counselors that these ladies have to be treated for their trauma, especially. So treat alcoholism, go to the underlying cause. This is the best way to save lives to our alcoholic patients. Thank you for your attention.

[APPLAUSE]