

[MUSIC PLAYING]

RAMON Hello, good morning. My name is Ramon Bataller. I would like to thank the organizers. Thank you Chris, Harvey,
BATALLER: [INAUDIBLE]. Also thank you everybody that I see all the people here. Thank you for your work and your support
in a daily basis.

So Jay talked to you about a good diet. And I will talk to you about not drinking. So I hope after these two sessions, you're in a good shape.

So my next three minutes is to talk about alcoholic liver disease. I will try to be as practical as I can to give you practical tips. So when Monday you face a new patient, you identify and recognize alcoholism in some of your patients, which is the number one step.

Number second step, you go for the patients. You really care about them. You try them to stop drinking. The same way, Jay has very nicely explained that there's nothing better to stop eating excessively, in alcohol it's even more true. Alcohol is such a harmful thing when you take it in excess. There is nothing any pill will ever cure the disease if you continue drinking.

So I have been 15 years with these patients. So, I always say to my patients, I don't know about anything else about except for this disease. I know about these patients, this disease. And I will try to commend you some of my experience because there are not so many studies compared to NAFLD, but that is B and C.

Many of the aspects of alcoholic liver disease are unexplored. It's not evidence-based. You go to the guidelines, and it looks that everything is low of evidence. So based on my experience, I will try to give you some practical tips.

The first thing I want to tell you is a teaser, which is the burden? Is alcohol so important? When I moved to America-- I'm from Spain-- you will notice an accent. I was afraid. They claim that they don't drink so much. My fear was over in two days. There's a lot of alcoholism here.

When I moved to Chapel Hill to Pittsburgh, it's still more exciting. I have a lot of business here. Pittsburgh has a lot of alcohol, and drug abuse, and addiction. So that's why a lot of my talk will be about addiction, motivational interviewing, et cetera, because these patient sense if you care about them.

This is a study that we published recently showing that in America from based in the World Health Organization-- [INAUDIBLE]-- here in the US and Canada, 62% of cirrhosis are due to alcohol or alcohol is involved. So we're not talking about a weird disease and genetics. No, it's the most common and [INAUDIBLE] today.

And all the patients in our service are or NAFLD or alcohol. We don't have much more Hepatitis C and B severe. So this is where we will-- especially the young people here, this is our patients that we will see in the next years.

What about the cost? In Hepatitis C, why it would put so much attention? Because the drugs a very expensive, very useful. By the way, their great.

The money in these disease is put to cure the disease. That's why everybody-- [INAUDIBLE] pays to identify the disease. And we treat it now universally everybody. And in 12 weeks, we beat the disease.

In the alcohol field, the money is put to cause the disease, not to cure the disease. So this plays in a different way. So we don't have much support to treat these patients. That is the reality.

But what happens with these patients? They are the most costly in our system. They are readmitted more frequently than the other patients.

And look at the cost. This is a paper that we did with American data. This is under revision now. We're responding that we were common.

But alcohol causes much more than Hepatitis C in in-patients in America. And they accumulate because they are readmitted very frequently. So by treating better these patients, maybe we won't make much money, but we can save lives and save money. And the money thing is something that we're using now with the hospital to motivate them to invest more in this disease.

This is a naturalist story of alcohol liver disease. And this is very similar to NAFLD, very similar, but has some differences. If you drink in excess, you get fat, fatty liver disease. You drink more, you have fibrosis and steatohepatitis-- fibrosis and inflammation. And you drink more and more, you develop cirrhosis and decompensations.

There is one difference. You can eat as much as you want. You remember the *Super Size* movie? You can eat, you have belly pain, a little transaminitis? Well, you will never become jaundice and your liver suddenly will fail.

By eating, your liver can fibrose, can develop the cirrhosis. But you don't have these super acute failure that we call alcoholic hepatitis. This is a unique thing that happens in alcoholics.

People, even at young ages, I have seen-- and it's been typically we saw in the 40s and 50s. In America, I see more 20s and 30s. Especially now that's several studies, but we have seen a super population of young ladies heavy alcoholics linked to previous abuse, which is a very topical thing in today's society. So that's why we have to tackle the underlying cause of the alcoholism. If we don't treat the trauma, how can we beat alcoholism?

In any alcoholic that you talk-- and will talk a little later-- that you face, see the underlying cause. Is chronic pain? Is depression, and societies, and trauma? Is a lot of family story. You have to go into the cause.

So in this field, compared to Hepatitis C, and B, and NAFLD, in the alcohol, we only capture the patients when they are dying, when they're yellow, when they are decompensated. We have done a worldwide study the now is under the revision showing that compared to all of the other diseases that they have captured more earlier than later, alcohol is always captured late. We don't go to early detection. There are no programs for early detection of alcoholic liver disease.

So this is one of the things that we will like to-- we are trying to engage and to start at UPMC, early detection in rehab centers for example. And we do a fibroscan and discover a silent cirrhosis in the alcoholic. Don't wait until the patient get yellow and decompensated.

How we treat early alcoholic liver disease? I have seen very few with early in my life. In the clinic, typically I see late, advanced, yellow, decompensated, very few with early steatohepatitis. Sometimes I see early because the ferritin goes up and they refers a hemochromatologists.

And before I see my patient, while these in the waiting area, I say, oh my god, he looks alcoholic. Alcoholics have some stigmata of alcoholism. And I wonder how some of these alcoholics have gone to so many providers and nobody say alcohol, no, no, no, oh my goodness.

Review a little in Google, it say, all the stigmata of alcoholism, there are some facial stigma of alcoholism and signs of alcoholism. And the patients tend to under-report, more women because the stigma of the society, religious. There are others. Latinos, for example, they under-report more

So you have to uncover the under-reporting alcohol. You have to be a skilled in how to-- so I don't have time, a half an hour, but if some of you are interested, you can email me, I can tell you my tricks how to identify alcoholics, how to uncover alcoholism in patients who deny it, very common, very common. It's a skill. It's like to detect Hepatitis C, you have a test. And the test, now they are perfect.

To detect alcoholism, you don't have that test. It's your brain, your sensitivity, your skill to communicate to the patient. It's a little more difficult. That's why this disease is not captured early. It's not a single test.

So the first thing I want to tell you is what are the causes of early liver disease in the world? This is one study in France that they did fibroscan in many patients that went to a primary care center for whatever reason. And they discovered that 7% of the patients have fibrosis without knowing that they have any liver disease.

Which are the causes? Fatty liver. The most important cause is NAFLD then alcohol. But then look at this, one-third have what you guys call beer belly, we call "barriga cervecera" in Spanish. So it's a very common association.

There is not a good term-- how can you have a non-alcoholic and an alcoholic together? It's like A and non-A together. So the terminology doesn't help to these association. That's why there's some now movement maybe to call [INAUDIBLE] dual because many patients have both.

One interesting thing is they can be sequential. When you stop drinking, and you will see a lot, you start eating like crazy. The center of craving for sugars are the same of craving for alcohol. In the alcohol centers, they don't have candies anymore because the alcohol is eat the candies immediately because they have a lot of coke addiction in candy. They gain weight very much.

And the other way around, if you have a bariatric surgery for NAFLD, for obesity, this predisposes to alcoholism. And the alcohol is more harmful to the liver. I have talked many times with our faculty, with Jay, with [INAUDIBLE], et cetera, how many of these are LHAPs we see after bariatric surgery. Nobody knows exactly why, although they are addicted to the solid, and then they go to the liquid.

And also, the stomach has some protective things. By removing the stomach from the GI tract or just making it dysfunctional, you don't secrete ghrelin, for example, for the circulation that makes you less addicted. So remember the sequential thing.

So one of the things that is under a study is which is the main parameter that influences the outcome of the early alcoholic liver disease, as in NAFLD is fibrosis. You have an f3 or f4, and you have an early alcoholic liver disease, look at your survival in 10 years. You're very likely to decompensate soon after. That's why detecting a three or four with a fibroscan, it would be fantastic because you will prevent-- you know how many lives you can save if you detect these patients here, how many costs, how many ER visits, et cetera? So we have to go early to these patients, to detect fibrosis as an endpoint of release.

And one of the movements that we're trying to do in UPMC is to get approved the fibroscan. You know what is the fibroscan? It's a device that is very-- I think there's not a picture here-- so a tiny device.

They have now developed a backpack. It's like a portable one that you can in 10 minutes detect the degree of fibrosis in a patient a lifetime. And the training is four or five hours. So we're trying to get it approved for non-Hepatitis C indications to start early detection in our primary care centers and the rehab centers.

How can we treat early? The first thing is the identify that you have a alcohol use disorder. You can do an audit. You can do a test. But also you have to see signs in the body. You have to see signs in the labs. For example, DGT, DGT that we don't order enough, is very, very, very good to detect alcoholism. When you have more than 200 or 300, only you're a heavy alcoholic or you have cholestasis, it will go so high.

Most of the times, if you rule out other diseases, you have signs of alcoholism in the labs, in the patients, or the family except that you have that diagnosis of alcoholism, sometimes it's superimposed with NAFLD. You don't know which is-- what is playing a key role-- when you have an obesity and alcohol abuse, what is causing more damage to the liver? We don't have good biomarkers.

What advice that I gave is to start the counseling with the alcohol first and the diet later. This is what most of the counselors have told me to do. When you have a patient with both, sometimes should I start with everything? Stop drinking, and stop eating, no smoke, don't go with-- it's too much for a patient.

So typically you do it stepwise. You start with the alcohol, which is the more harmful thing for the fibrosis, and then you shift to the diet. But what I told you is sometimes I feel more difficult the diet then the alcohol sometimes because you don't need to drink everyday, but you need to eat everyday. So it's more difficult for patients to keep up with the diet.

So typically, we assess the fibrosis with only basic tools. We don't have to do a biopsy. We do very few biopsies in alcoholic liver disease, only if you have doubts. And typically, these patients are no well biopsy.

There's one study showing that you do a biopsy, the patients are more likely to remain absent, which is interesting. I've had two or three times in my life because a patient was, I don't care, the liver. And then you do a biopsy, you show them the results, and suddenly they get scared. People respect the liver. Remember that.

There's a saying in Spanish. It's "el hígado es el señor," "the liver is a sir" because people respect the liver. Don't mess up with the liver.

What is the therapy with ALT? Number one is counseling. And maybe you can give vitamin complex. And some of them are malnourished, et cetera.

And then number second is, can I give any anti-craving drugs to all my patients? Importantly, never give this sulfa and the antibiotics to any patients with liver disease. We have seen four or five severe DILI, severe drug-induced liver disease, two of them life threatening, in my life. All of them with f3 or f4 silent, they give the sulfa and without checking the liver.

The only medication with little evidence is baclofen. Are you familiar with baclofen? Baclofen is a GABAergic agonist that is sometimes craving for [INAUDIBLE], for eating, and sometimes I wonder I should take some. And has been proven to be efficient to decrease craving in alcoholic liver disease patients.

I ask for craving. You have to ask for the desire and control decide to drink to the patients. If it is positive, baclofen is quite safe. Only gives some dissonance, but it's quite safe for the liver. And it can help not to start with craving with sugars when you stop drinking.

There are some other studies showing that is good for withdrawal syndrome. So when you have a patient that has difficulties to stop drinking because he has shaky and doesn't want to go in house, you can give high dose of baclofen to prevent withdrawal syndrome and facilitate that the patient stop drinking. And as in NAFLD, there is nothing approved, FDA-approved, to slow down the disease yet. These two diseases, we have to rely mostly on lifestyle. That's why all of you today, you have to have the skills to be a good motivator to all these patients.

And remember, that this will be 80% or 90% of their patients in 5, 10 years. So any provider that see liver patients had to be almost like a psychologist because, my goodness, to change lifestyle, you have to have the skills. I had to learn over the years.

It helped me a lot to have a counselor with me. I learned a lot with her because I thought I knew a lot and I knew nothing. I learned a lot. And also experience, but you have to develop-- go to YouTube, see motivation interview, and YouTube can-- even cooking today with YouTube. So YouTube will help you.

I was going to now go to the LHAP, which is the typical thing that everybody talks. But I wanted to talk to the early a little because typically we don't talk much about the early alcohol liver disease. But this is completely blocked. I don't know who can he me.

Anyway, so the other syndrome that is the most famous is the yellow thing. When you get yellow, decompensated suddenly, you go to the hospital, for the most part you have a chronic liver disease. Most of the patients have a cirrhosis already. Some of them are very young. This is alcoholic hepatitis. And this is the most famous alcoholic liver disease study.

So one of the questions is not every alcoholic that gets yellow has an alcoholic hepatitis. You can have a metastasis for colon cancer or breast cancer and be an alcoholic. Or you can have sepsis with a cirrhosis, get yellow, and you don't have an alcoholic hepatitis.

Or you can take Augmentin, and you'd be an alcoholic. You get yellow because you have a DILI with Augmentin. And you shouldn't be labeled to have an alcoholic hepatitis because you are yellow.

So recently there was a consensus when you need a biopsy to diagnose alcoholic hepatitis, you have a clinical picture. And my whole message is, when you have any confounding factor-- some of the labs are-- for example, you have an alkaline phosphatase of 500, this is not typical of LHPA. Maybe you have metastases. Maybe the ultrasound of the CT scan, they have defused metastases. You need to do a transjugular biopsy. You need to do a transjugular biopsy to do transjugular vein-- thank you-- because these patients can bleed easily.

So we come up with some algorithm. These algorithm you can see in a recent guidelines for the American College of Gastro basically when you need to do a biopsy and when you don't have to do a biopsy. And this is very important if we want to trust from these patients. You don't want to transplant to a DILI, a drug-induced liver disease. You don't want to transplant someone with a metastasis. That's why we're using this protocol to identify those patients with definite, really clinically-diagnosed alcoholic hepatitis.

So another thing that I want to tell you is how we can identify those patients requiring a specific therapy, those with severe alcoholic hepatitis. There's a slight change. Are you familiar with the Maddrey score, the famous Maddrey score?

So there are several studies, and one study that we published in *Journal of Hepatology*-- not myself, other group from Glasgow-- showing that Maddrey is the worst of the existing scoring systems. It's difficult to-- so definitive and I remember I told the authors, can you put that in the title, Maddrey is no longer the best in the title because nobody-- I remember the first time I say that it was in John Hopkins a few months ago. I didn't realize that Maddrey was there. And I showed this.

[CROWD LAUGHS]

That was horrible. But anyway, so don't use the Maddrey. Please use the MELD. MELD more than 21 is severe.

So some other predictors of if the patient's going to die or not comes from the biopsy. The biopsy can give you some information not only in the diagnosis of the prediction. And we did a big study showing that, for example, the more inflammation you have in the liver, the better.

The more inflammation you have in a wound, the more likely that the wound will heal. When the wound is open, zero inflammation the skin, that is burn out. This will never heal. So there is a simplistic concept but tells you that when you have inflammation in alcoholic hepatitis, still is repairing going on.

Why this is so important because our research has shifted from trying to treat inflammation to trying to recover the parasites. The parasites have a lot of karma. The parasites is the opposite of the neurons. The neurons are very protected by all the barrier here. They're not exposed to anything, but they can not regenerate.

The liver is the opposite. The liver is exposed to all that, but is not reactive. It can regenerate. Can you cut half of the liver-- our surgeons know very well-- and you grow.

So in alcoholic hepatitis, is the liver loses the karma. It's very reactive to the gut products. And the parasites start to regenerate poorly. And that's why you die. So we focus in our research more in the parasites' failure.

So what to do with a patient with alcoholic hepatitis, a couple of things, number one, nutrition. So when I was resident, all the patients were alcoholic. But that does has a parenteral in nutrition because everybody as a default, have a white.

Today, we don't care about nutrition, no. There are some papers showing that nutrition can improve survival. These papers show overall negative results. But when you identify those patients been deeply malnourished, giving parenteral nutrition increases survival.

So these patients with LHPA that come really malnourished with toxic, with neuropathy, they don't have vitamin B. They can not walk well. They have anemia because their erythrocytes have wall very, very thin, et cetera, these can benefit from intensive nutrition.

What about the specific therapy? Well, there is a lot of controversy about if we should continue giving cortisone, prednisolone, or is futile. The results of the largest paper published a couple of years ago seemed the cortisone have a transient beneficial effect in one month. But after one month, it's lost.

Honestly, I don't have argument to say you don't want to give cortisone because something that improves at one month, but after one month, you have any beneficial. Maybe you can sign your papers or something in one month. There's not much benefit. And has some harm effects. So it's not clear if the only existing therapy's even effective. So we need new therapies.

What to do when you don't respond to prednisone or prednisolone, and you have an LHPA severe. But this is nothing, except for one thing. All the therapies that I show you one to change the [INAUDIBLE] was negative. There is nothing to prove except for one thing, liver transplantation.

And this is the last part of my talk, these three slides, to show that the first study with Philippe Maatran in the north of France in Lille-- they drink like crazy. That's why a lot of things, Lille scoreless-- no, really. And they did a study that when you have an LHPA, you're 21, or 29, or 31, you didn't know you were sick of the liver, it's the first ever decompensation, you have not failed 20 rehabs attempts, you a naive patient for therapy, you have a decent family support, everybody's such a psychopath, if you don't offer a liver that will die, look at the survival without the liver. And you offer a liver, they have a similar survival, the patients with six months afterwards.

And I will ask you a provocative but an ethical question to the audience. If you don't offer these patients a liver because they don't deserve because they're drunk, are we punishing morally a person? You know how many patients we have transplanted two organs with NAFLD, smokers. They have been eating despite knowing that they have 10,000 problems. Some of them with bypasses of the heart 10 years ago, still smoking-- excuse me?

Are we giving anti-therapy for hepatitis C those who got the hepatitis C see with IV drugs? All of them are self-inflicted diseases. But they are not punished morally. So we have to be doctors, not police or priests. We have to be doctors. If you demonstrate that some population can benefit from an organ, go for it.

And this study was corroborated. But a couple of studies in America, this is from the Mount Sinai with very similar results. Look at the difference. Have you ever seen many differences in survival of any therapy?

UPMC recently-- and I have to thank [INAUDIBLE] and [INAUDIBLE] for their help-- we have approved this indication for very selective patients. They have to be patients that failed the cortisone, very selective in the sense that we have good predictors that these patients would not relapse later on.

But if we save life to young people-- remember, and this is the last phase of my talk, that 40% of these patients have family story of alcoholism as a genetic disease. And how many ads of alcohol linked to success or power in the TV we have? So we have a genetically-predisposed disease with misleading advertising in TV. And when they get drunk, and [INAUDIBLE], we punish them.

So morally, I have my problems that we don't offer this liver. But of course, very selective patients because we have to think in the whole population. So this is all. Thank you for your attention.

[APPLAUSE]