[MUSIC PLAYING]

BENJAMIN SAMSTEIN: I'm going to start with a couple of questions. And I hope you will participate a little bit, because some of this talk is meant to be a little more interactive. So I want to start with a show of hands of how many of people in this room have had an orthopedic procedure.

OK. So please keep your hands up for a sec. So look around. OK. It's about half the room. So you can put your hands down. So how many of you who had surgery or a procedure for orthopedics were told by your orthopedic surgeon that it wasn't severe enough and you should come back when it was worse?

All right. Much less. Many fewer hands. Orthopedics is one area where-- Clearly, sometimes we do replacements of joints. Hopefully, most of you were having procedures that didn't involve joint replacements, although they're very, very common procedures.

But transplantation is one of the few procedures where whether or not you need the procedure has very little relationship to when you get it. If we think about anything else, for example in cancer therapy-- and I'm not going to take a show of hands of that-- we don't say, well, you have early cancer, and colon cancer, breast cancer, prostate cancer, and you would benefit from treatment.

But we're not going to give you treatment because somebody else I saw today is sicker than you. Their cancer is worse, and we only have chemotherapy for one of you.

I don't know how you all feel about that, but that would feel frustrating if you heard that, oh, well, honey, I have colon cancer, but the guy who came in before me has stage four colon cancer. So they're going to treat him, and when it gets to be stage four, then they're going to treat me. That would be a strange conversation.

But at the same time, that is the conversation we're really having with many patients. You have an indication. I'm going to put you on the list. But, of course, I'm not going to actually give you a liver transplant, even though, as one of the previous speakers, Doug Tapper, just went over, your chances of being re-admitted, your chances of dying this year from your liver disease might be 20%.

And so transplantation is really unique in terms of how we have to communicate those

resource and rationing that's part of what transplantation is about. So today we're going to talk a little bit about a source of organs that can enable transplantation for many patients.

So I have no disclosures, although I will tell you that I believe LDLT is a good thing. And what we're boiling it down to is actual people with decompensated cirrhosis who need transplants. And I'll give the example of three recent cases.

So a 55-year-old man. Hep C. Cirrhosis. Treated and cleared. Refractory ascites. SBP times two. Still had significant portal hypertension requiring LVPs every two weeks. Encephalopathy. Controlled on rifaximin and lactulose. As long as he took them, he was all right. MELD's 14.

That patient in most parts of the country has no access to transplant, clearly the most important therapy for that patient. We just had a discussion about how important rifaximin and lactulose can be. But trying to explain to the patient that what they really need is a therapy that you cannot give them.

A 37-year-old woman. Primary sclerosing cholangitis. She works as an LPN. Her fatigue and encephalopathy keep her from working. She's able to do her ADLs, but the quality of her life is dramatically reduced by her symptoms. MELD's 15. No access to transplant.

A 57-year-old woman. PBC. Admitted with hyponatremia. Sodium to 124. Ascites. MELD's 18. Bilirubin's normal. INR is 1.5. Creatinine's basically mildly elevated. Again, very little access to transplant.

And so LDLT is something to be considering in those scenarios.

So LDLT started with children. Fortunately, in the United States children do not-- not children with liver disease-- but in general, children do not die and become brain death at very high rates. And as a result, in the 1980s the mortality rate for children on the waiting list was 50%.

And so two parents would be standing at the bedside. Help my child. And we would say, we have no organs. And 50% of the children died. Today, through the utilization of living donation and split liver grafts, techniques developed in part in living donation, the mortality risk for children on the wait list is markedly reduced. It's below 10%.

And so this began with experience out of the University of Chicago, the transplantation of two livers, two patients with one liver. And then discussion progressed to the utilization of healthy parents, and then now has become routine with adults.

I'm going to go back to the idea of what waiting means. And so I'm going to start with a tool that's available online called the SRTR waiting list calculator. And this is the University of Michigan. It's true of all the centers, essentially, in Michigan and throughout the United States. This is aimed at helping patients understand what their risk of getting a transplant, of dying, of still being on the waiting lists.

So I ran this a few weeks ago. So this is a patient, any one of the few that I just mentioned. MELD's 15 to 24. Let's say they're 18, whatever. And they have a blood type O. And they don't have cancer.

They come to Dr. Fontana and they say, what are my chances of being transplanted? What is going to happen to me over the next year? Say, well, I put you on the list.

OK, that's great. Thanks, I'm on the list. OK. What actually will happen to me? Say, OK. So 60% of those patients will still be waiting. OK. 20% will have a liver transplant. And 16%, 16.7%, will die.

So depending on how symptomatic the patient is, those are not wonderful statistics. That means-- And the University of Michigan statistic, this is at least as good, if not better, than centers throughout not only Michigan but the rest of the United States. This is what we have to tell patients.

Because I think we often feel that we're doing something by putting person on the list. You can be on lots of lists, but being on a list doesn't get you anywhere if you never get to the top of the list.

So this is for someone with a MELD score of 15 to 24. What if they're symptomatic but their MELD's lower? So MELD's 12. Predominantly they have portal hypertension, but MELD's 12. What's their chance of what's going to happen to them?

So again, this is non-tumor patients. Blood type O. So 13% of people will have a liver transplant, and 70%, 75% basically, will still be waiting. So for patients who are on the list, who are symptomatic, and you say, well, you are going to have to wait until you get sick.

And, of course, what drives people to get sick? So encephalopathy. So we are waiting. But encephalopathy doesn't really drive their MELD score up. We're really waiting for an infection. We're really waiting for SBP.

So we're waiting for you to develop an infection in your ascites or pneumonia that you survive, drives up your MELD score, puts you into renal failure. That's what we're waiting for so that we can transplant you.

That's the conversation that sometimes we-- For those patients who can understand it. Because they want their MELD score to go up because they want to get a transplant, if we've determined that they medically need it. But who really wants peritonitis? It's a hard thing to wish for.

So I made that point earlier. This is basically when we start to fight the war against liver transplant. When people have SBP and they're really sick and their MELD's 27 in the hospital, that's when we give them a liver. And the ones who don't survive because they get too sick die.

So I would suggest that that is not the best time. The best time is actually when they're medically stable to do transplant.

So living donation. Basically, the first adult living donation in the United States was performed in 1998. And the numbers, and we're going to talk a little bit about this, why they basically dropped in 2002 and then have stayed stable, around 200 to 300, over the last 15 years.

And so-- I'm just going to make sure I stay on time. So kidney donation. So how many of you-- Does anybody know anybody who's don-- None of the University of Michigan people. Like the transplant people. Does anybody know anybody who's donated a kidney? Does anybody know anybody who's donated a liver? That's about even.

In general, 34% of the kidney transplants in the United States are done with a living donor, and only 5% of the liver transplants. So there is a seven-fold difference in the utilization of living donation in kidney versus liver. And I thought I might explain part of why that is.

So the first is that living kidney donation has been part of the core of kidney transplantation since the very beginning. The very first kidney transplant was done between two brothers, who were identical twins, in 1954. One had kidney diseases and the other didn't. And so living donation, at its core, has always been part of kidney donation.

Laparoscopy started in 1995 in kidney donation. And it was routinely adopted, more than 50% of all kidney donations by 2004.

Liver, in contrast, the first liver transplant was in 1963. Living donation, basically the first living donor wasn't until more than 35 years later. Laparoscopy just began in 2002. And routine adoption of laparoscopic liver donation has not in any way been adopted.

In addition, kidney is very explainable, in large part because a lot of kidney allocation is based on time. So if I say to someone, when your kidneys fail, you will go on dialysis and you will wait four years, five years. You'll have to go to a machine three times a week.

And you can explain all the complications that go along with dialysis. But it is easily understandable. It's like if someone said to you, you need to be on a waiting list for lunch today, and you said, well, when will I eat? You say, well, it depends how hungry the people in front of you are. And the chances of you getting fed is like--

Versus, OK, I'm going to be on a list. Lunch will be served at 4 o'clock. And so for you all, you might say, you know what? I'm going to go out to eat, because 4 o'clock is too late and I'm going to be hungry way before then. So you say, all right, since I know exactly when I'm going to be served lunch, I will go out and get an alternative pathway for getting lunch.

Kidney is similar, in the sense of, if I know that I have to wait five years and I know that I have to go on dialysis, I understand that. And when you're explaining it to patients, that is so important to be able to explain it in a way that's understandable.

I don't know how familiar you are with MELD, but MELD is a very complex formula with logs and math. We all know how good Americans are at math. And so there's no way you can expect most patients to understand that a MELD score will lead them to have a transplant at any one time.

I was giving a similar talk at Mayo Clinic. And I asked Russ Wiesner, who helped develop the MELD system, I said, well, how long do patients with a MELD score of 17 wait in Rochester? He said, well, it's very complicated. I can't really tell you. And I say, is that what you tell the patients? And he said, uh--

So my point being, the very people who came up with our system, it's very, very difficult to explain.

So living donation. So what can I tell you about living donation? So we know that people who receive a living donor have a lower probability of dying. It's reduced by about half. And maybe

the faster you get a living donor and the faster you get transplanted, the better you do.

When we've determined that liver transplant is the therapy that you need, what matters probably more than anything else is that you actually get the organ that you need.

So this is a slide which basically shows-- Let's see if I-- OK. Only people on this side of the room will be able to see my pointer.

That this is probability of death. And basically, they were broken down into different MELD scores. But that patients who were waiting on the list died at a steady rate, and patients who are a little sicker died faster. And patients who had a living donor overall did better. Patients who had a living donor did better than those who waited.

And for those who prefer bar graphs, I put it into a different-- So basically, at every MELD, whether your MELD's 6 to 10, 11 to 14, 15 to 19, or greater than 20, if what you need is a liver transplant, then getting a liver transplant saves your life.

And one of the things that I try to explain to patients is that really that's what it's about. If you're 37 and you have PSC, that's what you should be focusing on, not waiting until you get sick.

And then, after transplant, basically, patients who get a living donor usually do a little bit better. The main reason they do better is because they're healthier. They're in a better state. They're not in a morbid state.

It just says patients with earlier cancer do better, have higher cure rates than patients who have more advanced cancer. And I think a previous speaker was talking about decompensation. So we know that, whether you have ascites, whether you have encephalopathy, SBP, worse portal hypertension, all of these things lead to worse outcomes.

And, of course, none of these things are in the MELD score. They used to be in Child-- Though they are in Child-Pugh. But we took them out of the system because it was felt that they could be gamed.

So maybe people think Chris has encephalopathy. But if we wanted, we could put him in the ICU and then say he's severely encephalopathic. And then he would be expedited, versus using only his labs, which turn out to be normal and therefore he has no access to transplant.

Using a system in which there was subjective parameters actually may have facilitated the

patients who had symptoms from their decompensated cirrhosis, but we took it out to replace it with a calculator.

And this basically is showing that among LDLT we're getting better. Basically, trends over time, and this is true of all liver transplant, we're just getting better at identifying who will benefit from transplant and how to manage them post-op.

And there's no doubt in my mind that the impact-- One of the most significant reasons why people had trouble after liver transplant was recurrence of hepatitis C. We are likely to see substantial improvements in the overall survival of patients after liver transplant.

We will probably see the five-year survival, which is generally around 70%, may rise to over 80% in the era of hep C. So five-year survival is over 80%. And 10-year survival is for healthy patients probably in the same range, 75% to 80%. So really long-term survival at very, very high rates for patients who otherwise face very high mortalities.

So why are we better? Well, in living donor we're better for multi-modality reasons. We're better because we do better pre-operative imaging. We have a real pathway to transplantation.

So we do good MRCPs. We plan out how to rebuild the veins. We see the arteries. And we basically have to have a surgical map that tells us exactly how we're going to do it.

When we started in 1998, my mentor, Jean Emond, basically, they did a hepatic angiogram and an ultrasound. And then, in the operating room, it was like, it looks pretty good.

Now, we do complex volumetric analysis and we do 3D reconstructions, excuse me, reconstructions of all of the graphs planning for the operation. Intraoperatively, we do cholangiograms so we can precisely divide the bile duct.

I'm running out of time, so I'm going to move a little quickly.

So why isn't living donation used more? And I think that one of the things is that the major barrier comes from the recipients and the families.

There are people who are willing to donate often. But we feel, we as the health care providers, feel, wow, if I really told someone that they had very little access to transplant, that would be coercive. That would make me feel uncomfortable to tell them about the risk of dying on the

list.

And probably the recipient, he doesn't come with anybody. The recipient doesn't have any donors. His brother lives in Philadelphia. It's too far. Or maybe I've heard that the risk to the donor is too high. So what are the risks to the donor?

This is a probably illegible slide, too far away. But basically, we estimate the risks of a right hepatectomy to be somewhere in the range of 1 in 500 to 1 in 2,000. To give you an example-- So what does that mean? Because most people have no idea.

So the risk of dying, for example, in a car accident in your lifetime as an American is 1 in 84. The risk of all of us having appendicitis and dying as a result of that operation is about 1 in 2,000. So having a donor hepatectomy in a planned, controlled fashion falls somewhere in the risk of lifetime risk of dying in a car accident and having your gall bladder out.

Obviously, it is modified by the age of the donor, by the volume of the remnant, and by the experience of the team. The complications for donors include hernias and surgical wound problems.

I just want to point out that, in general, a significant portion, maybe 10, and depending on the-- 15% of patients who are transplanted in the United States are in an ICU at the time of their transplant. As many as 25% to 50% of patients may be hospitalized.

Living donation is usually done at healthier patients, patients who electively plan their operation. They're much less likely to be on a ventilator, on dialysis, and, as a result, have better outcomes.

And I'm just going to mention-- So living donor is a technically little-- It is a more difficult operation. The recipients are more likely to have technical complications, the most common of which is bile leaks. But most of that is handled with non-operative techniques today.

And so now that I've convinced you that you should convince your patients to have a living donor, the main issue then is, should we us the right side or the left side? And sometimes it's easy because the patients come to us and they say, OK, I'm going to be a left donor.

Many living donor centers have introduced smaller scars. Most of the early donors had a transplant scar across their abdomen and up and down. At New York Presbyterian, where I do most of my surgery, we now do either through a mid-line or laparoscopic. In our center, we've

done over 325 donors. No donor deaths and no liver failures.

And I think a lot of this comes from the experience and the operative planning that is now routine, and avoiding the smaller grafts.

So I want to go back to these cases. 55-year-old man with hep C, cirrhosis. 37-year-old and 57-year-old. So many of the patients will have children, adult children who are capable of making informed consent about this issue. There are spouses who are healthy and appropriate for donation. There are siblings who are healthy and appropriate.

And at our center. We use altruistic donors. That means someone who has stepped forward, a non-directed donor. They're more likely to not be appropriate donors, but we consider them. As well as lifelong friends. So look to your right, look to your left. Maybe somebody will donate to you.

There are certainly some challenges and controversies. I don't know how many of you know this gentleman. But this was a person who was very, very sick in Canada and sought out a living donor. And the cause of his--

So one of the challenges is that, if suddenly you have organs for everybody, should you transplant people? So if you have people who have cancer in which their risk of recurrence--

So right now, today, we only transplant people if we think that you're going to be cured of your liver cancer 8 or 9 times out of 10. What if your cure rate was 2 out of 10? 3 out of 10? Much worse.

But without a transplant, your cure rate was zero. Would we consider a living donor? I don't have an answer for that. Most centers do not do living donor for those cases. But if you had organ--

So right now, we do pancreas surgery routinely for patients who we expect that only a small portion of them, less than 2 or 3 out of 10, will be alive at five years. But we still offer them pancreas surgery. Would we offer living donation? Patients with alcoholic hepatitis, another scenario in which we might consider living donor. And patients who are really sick out of the ICU.

So, in conclusion, I've tried to impress upon you that, really, organ replacement outcomes are improved by optimal timing. And living donor liver transplant surgery and outcomes have

improved over time. And the donor hepatectomy can be done safely.

And, of course, I'd like to thank Chris, John, Dr. Fontana, and the group here at Michigan who have helped put a lot of time into organizing the LDLT program at the University of Michigan.