Ex Vivo Heart/Lung Perfusion

Announcer: Welcome to the Mayo Clinic Cardiovascular Continuing Medical Education podcast. Join us each week to discuss the most pressing topics in cardiology and gain valuable insights that can be directly applied to your practice.

Dr. Friedman: Hello, my name is Paul Friedman. I'm chair of the Department of Cardiovascular Medicine, and I'm delighted to be speaking today with Dr. Mauricio Villavicencio, who's an associate professor of Surgery and a leader in heart transplantation. And today we're gonna talk about ex vivo heart perfusion. So Dr. Villavicencio, welcome.

Dr. Villavicencio Theoduloz: Well, thanks very much for having me and to speak about this kinda hot topic of ex vivo heart perfusion and transplant.

Dr. Friedman: Hot topic seems like an appropriate description for this particular therapy. So why don't we start with the basics. What is ex vivo perfusion?

Dr. Villavicencio Theoduloz: Well, I think to understand it a little bit better, we have to go a little bit back on how we have done heart transplantation for the last 30 years since the pioneers of heart transplantation. And we have done it, you know going to a brain dead donor, which the heart is beating. And we have taken that heart and give essentially a cold flush with solution and put it in a cooler essentially. And that has given us around four hours most of the time to perform the transplant which obviously has some, you know, logistical limitations and distance, and then for more complex operations problems. But that has been pretty much the success of the heart transplant. Doing it this way with cold storage, as we can say.

Dr. Friedman: So, the basic idea with cold storage is cool the heart down, limit its metabolic activity to limit ischemia so that it can safely travel before it's reimplanted. And that's sort of the fundamental. And that's what's being upended with this new intervention.

Dr. Villavicencio Theoduloz: Yes, that is correct. And then we have tried to travel to stretch it a little bit in that way, but it is not really that safe, you know to stretch the time that can be out. So it's cold, it's immobile, it's not working. So it is, you know, prolongs its time. And then of all organ, that transplant is the one that tolerates less time, you know, so compared to the lung, the liver, the kidney, you know, you could preserve a heart for a way less time than other organs. So it is a handicap of the cold storage.

Dr. Friedman: Got it. So what are the major advantages then of ex vivo heart perfusion and how does it work? What is it?

Dr. Villavicencio Theoduloz: So ex vivo heart perfusion is, you can take... Again, for that brain dead heart-beating donor, we will talk a little bit later about the non-heart-beating donor. And you take it from that heart-beating donor, and then you hook the heart to a device. This device, the one that's FDA approved, is called the OCS heart device. And then essentially what it does is that pumps blood into the aorta. So the aorta is hooked to a cannula. So the blood goes and the pressure that normally, is kinda normal pressure, 60 blood pressure, and perfuses the coronaries, and then comes back through the coronary sinus. And then what you have to do surgically is

close the inferior vena cava and the superior vena cava. And then to let that heart go, and go through the right ventricle, the pulmonary artery. And then we capture it in a cannula that is on the pulmonary artery. And then there's a little bit of blood that is spilled over that goes through a receptacle that again, is collected again. So we got the venous blood connected through the pulmonary artery and from some that is coming down from the reservoir, and then goes... It's very similar to an ECMO concept. So in terms that then goes through a pump, then it goes through an oxygenator, and then gets pump into the heart again. So that is the concept. Ex vivo heart perfusion, and the one we use now in the clinical setting is one that is mobile so you could, you know, take in the device, you know, transport in an airplane or in ambulance. And then you perfuse the heart and you normal temperature. So you bring up the temperature up to 36 degrees to do the perfusion. So in that you can get around... It is not clear how far can you go, but most of the people who have done, total out of the body time of around eight hours or even more. So that's the beauty of it.

Dr. Friedman: That's really remarkable. Now, is this being done for lungs or other organs as well, or just for the heart at this stage?

Dr. Villavicencio Theoduloz: Yes, it's done for the lungs that... You know, my other expertise is lung transplant. But I think the benefits in the heart side are, you know, are more than on the lung side. And the reason for that is that you could do cold storage in the lung side for easily 10, 11, 12 hours, which we don't have on the heart. So in the heart is more critical. There's certain situations in the lung that can, you know, be useful. For example, the DCD donors. We can talk a little bit more about what are the DCD donors. But in general, I see on the heart side to be more useful.

Dr. Friedman: Tell me a little bit about the role of this technology in heart-liver transplants and how it could be helpful.

Dr. Villavicencio Theoduloz: Well, you know, cause the history, you know, heart-liver transplant have been a very high-risk operation. You know, most of the patients that have Fontans have multiple sternotomies previously, and that they're very sick. And then they are sensitized so they have antibodies again, human tissue. So I think one of the, you know, great advantages of having those CS device is that we are doing heart-liver transplant, but with the liver first. So we do the liver first, which is an easier operation. It says that it doesn't have... I mean, there's no previous operations. And then... So you do the liver transplant, and then the heart has been out, you know, six or seven hours, and then you go and do the heart transplant. And it has the beauty later on. You know, when you come off the heart-lung bypass machine, there's less vasoplegia because the liver is already in. And then there's less coagulopathy, so the liver is working. And then, so the patients bleed less. So that's quite a bit an advantage. And there's a third very important advantage, that these patients are sensitized. If you do the liver first and you do some pre-treatment, you know, with medication, the liver can take of, you know, the antibodies, again HLA antigens. So you could use it, you know, to treat very highly sensitized patients in a, you know, liver-heart transplant, liver first. So it's very exciting technology.

Dr. Friedman: Oh, amazing really. And the time interval between the liver transplant and the heart transplant is usually how long?

Dr. Villavicencio Theoduloz: Well, it's almost nothing, because what happens is when you do the liver implant, and then you do the reperfusion... When you do the reperfusion of the liver, there's quite a bit of hemodynamic instability. So what happens is then, when you have instability, you have to go on bypass-

Dr. Friedman: I see. So this are one right after the other.

Dr. Villavicencio Theoduloz: One right after the other, but it's important in terms that, you know, it manages the antibody. So we're always worry about, you know, hyperacute rejection with the antibody. So having the liver first, you know, give us, you know, peace of mind. You know, we have published this, you know, that today lead the way on this.

Dr. Friedman: How can you tell if a heart that's placed in ex vivo perfusion is a good heart?

Dr. Villavicencio Theoduloz: Well first, you know, I'm a surgeon so I'm a little bit like, you know, plumber if you would say. So I like to see that heart beating strongly, directly in there.

Dr. Friedman: Yes. Yes.

Dr. Villavicencio Theoduloz: You could see there. So whatever something looks weakened there, you know, I get nervous. So that's, you know, more sort of a macroscopic standpoint that you could see how the heart is looking like. But then, what it has been a study in the clinical trials on the OCS device is the lactate. So the heart has this unique capability that can metabolize the lactate, and then... So the heart is working fine instead of, you know, producing lactate because it's ischemic or damage. Then start metabolizing the lactate. So the lactate that is produced by the heart during the perfusion on the OCS device should most of the time will, depends on the type of donor, but most of the time will at least have to get stable or start coming down. So once if a lactate starts coming down then you would think that heart is working, and then that you want to use it. And then I think that it's important because you perfuse this heart very long, sometimes on the OCS device. So what happens is for a reason that we completely do not understand, the heart gets a dermatose. So you have to examine the heart before implanted to make sure you know that it hasn't gotten that much a dermatose. So it's still a little bit limited in the time that you could use. I mean, because who would like to do what elective heart transplant if you would like, you know, will be way better for the team. But so far, with the management that we have, how we know the technology has not allowed us this yet. So that is the lactate, how you look at it, and whether or not there has gotten a dermatose. And then you have to also, you know, do an integration. How sick is your patient just to move forward with a transplant or no, or you can wait.

Dr. Friedman: Now for our listeners who maybe have never seen a device. I know we'll have a link available where they can watch a video, but just for now, how big is the device, and is it battery-powered, or do you have to keep it plugged in? Is it on wheels? You know, give us a picture of what the actual device is like that the heart is in.

Dr. Villavicencio Theoduloz: Yeah, so the device would be like the size probably of a dishwasher machine or something like that. And then it will have wheels that you could get it

around. But... And then it has an area where it goes the disposable where the heart goes. So it's a device, and you could monitor over the hematocrit the saturation of the blood. You could monitor the blood pressure. It has a monitor that monitors the blood pressure and the coronary flow. Most of the time, it will be flowing around 750, 800 cc per hour on the coronary flow. And then it has batteries, but it is safer, you know, of course, to get it plagged, to have a batteries always as, you know, backup so you don't wanna get in trouble. So it is, if you ask me, I mean, sometime we have a little bit of problems in the planes to put it in. So you know, probably in, hopefully in the future versions will be a little bit smaller so it's a little bit easier to handle. But so far, you know, we don't have any other portable device, not even at I think, clinical trials or FDA approved. And so that's what we're using, and it's, you know, it has all these capabilities. It's very nice. Probably, I like to say that other thing that it makes it a little bit difficult to use the device is that we would like to perfuse the heart obviously with blood. And then that is a little bit of a limitation because when you do the donor, essentially what we do if we put a cannula in the right atrium, and at the time right before crush clamp, we drained the blood of the donor to use it on the circuit. You know, you have to remember that this is kinda portable ECMO circuit for the heart. So in that period that, you know, we have to drain the blood of the donor. All the other organs that are getting procured in the same door, they get a little bit nervous, because, you know, the blood pressure goes down obviously.

Dr. Friedman: Sure.

Dr. Villavicencio Theoduloz: Cause you know, this sort of goes down the, you know, obviously the preload of the heart of the blood pressure, but it's a very short period of time. You could get the blood normally in one to two minutes, and then all the organs can get flushed for, you know, transplantation.

Dr. Friedman: Hmm, yeah, fascinating. While the heart is in the machine, in the OCS machine, are there any therapies that can be applied?

Dr. Villavicencio Theoduloz: Well, there has been in a heart. I'm not that aware, maybe some experimental work. I'm very aware in lung that while the heart is, you know, getting perfused, that there's some group of investigators that have applied, for example, UV light. UV light to get rid of hepatitis C virus. So, for example, we have to-

Dr. Friedman: Interesting.

Dr. Villavicencio Theoduloz: We have to understand that there's around 20% of our donors are from a drug overdose, and from those 20% have hepatitis C. So now, what we do is that we treat the recipient, you know, with antiviral to get rid of the hepatitis C donor. But it has demonstrated that, also if you could perfuse an organ, you know, on ex vivo perfusion, and then use UV light, you could get rid more virus. So you could kinda decrease the viral load before implantation on the recipient. So I can, you know, I can imagine that there are several therapies that we would like to have, but we haven't gotten to the point really, particularly in lung. I think, I like to see, you know, for lungs with the pneumonia, for example, that you would be able to be perfused for a long period of time with antibiotics and probably recover the next morning. But the time so far is not enough, but it has potential. So we need to understand better what produces the edema in

the tissues because this is something that, you know, it gets produced in the lung and the heart with a long perfusion. So we can figure out that probably, we will be able to have longer perfusions, more therapies, and probably more elective transplants.

Dr. Friedman: Absolutely remarkable that what had been a limitation for the transport stands to potentially become a therapeutic window where infections may be eradicated before an organ is donated. Really conceptually, that's just a remarkable thing. Are there any special advantages for the kinds of patients that we often see at Mayo Clinic?

Dr. Villavicencio Theoduloz: I think one of the most thing that can have a greatest impact, I think there's multiple, so we could talk a little bit extensive about this. Sorry about this. If it is my passion, I could get very long. I mean talking about-

Dr. Friedman: Well, it's fascinating.

Dr. Villavicencio Theoduloz: So one is the DCD donors. You know, so everybody can understand because our traditional way, as we were talking about the cold storage, the traditional donors have be the donors after brain dead. The sprain dead. The donors legally dead, and we could take the heart. But there's many donors that they have had neurological injury. And what happens is there's no future and the family decides to withdraw the care. So essentially, there's a plan withdrawal of care, and then that most of the time will happen in the operating room. And then withdrawal care happens. Palliative care has just started. And normally what happens is the blood pressure gets low, saturation gets low. There's a period of cardiac arrest of five minutes and after five minutes you could declare death. So as a separate from the transplant team, death is declared. And then you could go in and you will open the donor, but the heart will be stopped, and will be distended, and will look terrible. And we don't want that for transplantation. So what we do is that, this was pioneer in Australia, and then come back to Europe and now to the US, and then we take the heart and put it on the ex vivo heart device and we resuscitate essentially the heart. So you will see in those hearts that have very high lactate, you know, to start. And then as, you know, the heart starts beating and then gets better, lactase is stabilized and, you know, decreases and we could do that heart transplant. So there has been already a trial in the US comparing using these hearts versus just using cold storage and the survival has been the same. I think that was the data that was presented in ISHLT shows survival is the same. DCD versus brain dead donors, you know, recover with with ex vivo heart perfusion. So same survival. And then there's a little bit more of primary graft dysfunction. So you put the heart on it, then you do the transplant. And there's more dysfunction of the heart at the beginning, so you have to be quite comfortable on doing ECMO for a couple of days. And then it usually quickly goes away because we normally take, you know, young strong hearts and then they get better. So we have done around, for example, this year seven DCD heart transplants here at Mayo. And it continues to grow. In our region, the live source around 30% of the donors are DCDs. So it's a very important source, you know, for heart transplantation.

Dr. Friedman: And by the way, just to clarify for listeners, DCD stands for donor after cardiac death as opposed to donor after brain death, right?

Dr. Villavicencio Theoduloz: Well, we have tweaked a little bit what it stands for, because we call it donor after circulatory death.

Dr. Friedman: I see.

Dr. Villavicencio Theoduloz: Because, you know, we think about the cardiac death as an irreversible thing. In this case, you know, circulation has been stopped, but we could recover the heart, you know, transplanted successfully and then have good function. So it has been change a little bit to donors after circulatory death.

Dr. Friedman: That makes good sense. You know, I have maybe one more question for you, and that is these capabilities to travel with the heart eight hours potentially longer. In essence, they stand to limit geographic boundaries of where donors and recipients are, and could fundamentally change organ distribution rules. Do you see a change in transplantation on that basis in terms of how organs are distributed? The UNOS rules, you think there'll be a modification coming from this technological advance?

Dr. Villavicencio Theoduloz: Well, you know, the allocation for heart transplantation has been modified recently, so we're a little bit getting adjusted at this point. But certainly what it happens, it has prioritized urgency. So for example, you have somebody on ECMO, you will be status one. You will have an, you know, you are supported on an Impella. You will be status two, and then it comes down, you have an assist device that you'll be status four. And then you could take, you know, first that has get offered to, you know, 500 nautical miles. So of, you know, a good range. That's quite a long range. So I haven't seen any, you know, sort of discussions about this, about get it broader. But what happens is that, I mean we have gone all over the country. You know, I mean, we have gone to New Mexico, to Florida, South Carolina, here from Mayo, Oakland, Rochester to, you know, Northern New York, and that's the beautiful thing. And then, you know, we don't have to, you know, get in an urgency, you know, to show the hard end. So it is quite remarkable. So it might happen later on, when it gets more widespread use, but I don't think I've seen something, you know, happening these days. Yeah.

Dr. Friedman: Well, Dr. Villavicencio, absolutely fascinating discussion. Thank you for joining me. It's remarkable to see the advances that you and your colleagues have been bringing to this space that continue to evolve. And thank you for sharing some of that with us today.

Dr. Villavicencio Theoduloz: Well, thanks very much for the invite and look forward to see you all, you know, in the cardiology side working. Thank you.

Dr. Friedman: Thank you.

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