

Mayo Clinic Q & A - Dr. Sudhir Kushwaha & Dr Richard Daly -...

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SPEAKERS

Dr. Sudhir Kushwaha, Dr. Halena Gazelka, Narrator, Dr. Richard Daly

- N** Narrator 00:01
Coming up on Mayo Clinic Q&A:
- D** Dr. Sudhir Kushwaha 00:04
The more organ donors we have the more lives we can save.
- N** Narrator 00:08
As with any organ transplant, there is a considerable risk of rejection of the new organ. But at Mayo Clinic a new technique is being performed for patients that receive a combined liver-heart transplant, the liver is transplanted prior to the heart, with remarkable results.
- D** Dr. Sudhir Kushwaha 00:24
We made the observation that those patients really have zero rejection. In fact, we almost guarantee that somebody who gets the combined organ transplant the chances of them rejecting the heart if there's a liver present as well, is extremely low.

D

Dr. Halena Gazelka 00:42

Welcome, everyone to Mayo Clinic Q&A. I'm Dr. Halena Gazelka. April is Donate Life month. When it comes to organ transplantation, patients with high levels of antibodies, also called highly sensitized, can face major challenges waiting for suitable organs, and they also run a higher risk of organ rejection. There is new hope for these highly sensitized patients who need a combined heart liver transplant thanks to an innovative approach being researched here at Mayo Clinic. The reverse order heart-liver transplant. Here with us today to discuss this exciting field is Mayo Clinic cardiologist Dr. Sudhir Kushwaha and Dr. Richard or Rocky Daly, a Mayo Clinic cardiothoracic surgeon. Thanks for joining us today gentlemen. Can you explain what it means for our listeners if someone is highly sensitized in the context of receiving an organ transplant?

D

Dr. Sudhir Kushwaha 01:39

I'm happy to try and answer that question. Sensitization refers to the presence of what we call preformed antibodies, and usually, if an individual is exposed, and the most common example, is women of childbearing age who are pregnant, and they develop antibodies to their baby. And so, these antibodies will circulate in the blood and will always be there. The other common scenario is if somebody receives a blood transfusion, and usually even though the blood transfusion is ABO matched, and is compatible, there are other components of that blood, which will result in the recipient of the transfusion, forming antibodies, and those antibodies will remain in the circulation really for the rest of one's life. And so, if then a subsequent antigen, in other words, is transfused in or given, then the antibodies will react to that. So, that's really a simple explanation. Rocky, I don't know if you want to elaborate further on that.

D

Dr. Richard Daly 02:59

The presence of antibodies in the recipient to other people, and if they happen to be against a specific donor that we're using for a transplant, then that can be a catastrophic rejection, because of the presence of the antibodies already being there.

D

Dr. Halena Gazelka 03:20

So just to clarify, the antibody is against a type of protein or antigen in another person or that could be present. And that is one of the ways that we match organs, is that we try to have blood types and antibody antigen matches, is that true?



Dr. Richard Daly 03:42

Not everybody has these antibodies like this. Some people have it, and they develop antibodies against other people either through a pregnancy or through blood transfusions, or through a transplant where they're exposed to these antigens from other people. And then the antibodies are present. And if the antibodies happen to be against a donor for that person for a heart, they will reject that heart in a pretty catastrophic way if the antibodies are high level.



Dr. Halena Gazelka 04:19

So, in a typical scenario, if an individual is highly sensitized and needs a heart and liver transplant, how long may they typically wait on the on the list to receive a transplant?



Dr. Sudhir Kushwaha 04:32

Well, it depends on a number of factors. It depends on the ABO blood group and the degree of sensitization, and how many of these antibodies they have, and at what level. And we have ways of measuring the quantity of antibodies and generally speaking, if there's a high antibody burden, then it's difficult to remove those antibodies. We've worked temporary ways of trying to remove them, there's a procedure called plasmapheresis, for instance, which will filter the blood of these antibodies. But they'll always come back because the cells which produce them, the B cell population, in the bone marrow, and in various other organs, will produce these antibodies. And so, even if we remove them in a temporary way, they'll come back. So, if a patient is waiting for a heart transplant, for example, which is the situation we're talking about, trying to get rid of these antibodies is challenging and trying to get a match for that patient which doesn't have the antigens to which the recipient has the antibodies, makes it a bigger challenge and greatly reduces the number of potential donors which might be appropriate.



Dr. Halena Gazelka 05:58

Now, I was an anesthesia resident, so I participated in some of these surgeries, probably with Dr. Daly. I am wondering, in the past it was traditional to transplant the heart first and then the liver. What made you think of reversing the order of that?



Dr. Sudhir Kushwaha 06:17

Well, we made an observation. Previously, Mayo Clinic has traditionally done a high number of combined organ transplants, for various other conditions for which the heart and the liver is affected. And in that setting, when we looked back at our experience with

our combined heart-liver patients, we made the observation that those patients really have zero rejection. In fact, we can almost guarantee that somebody who gets a combined organ transplant, the chances of them rejecting the heart, if there's a liver present as well, is extremely low. And so, with that in mind, we thought, well, what's going on here, there must be some biological process. And a simple way of thinking about it is that the liver is acting like a sponge and removing these antibodies from the circulation. So, we had our own data, which we published previously, which really reinforced the idea. And then we went from that, we projected ahead and thought that well, what can we do for these individuals, perhaps, as Rocky so clearly stated earlier, when we put a heart in and there's a high antibody burden there, you will get immediate and catastrophic rejection. So, if we put the liver in, and the liver removes those antibodies, and then we put in the heart, then we're sort of protecting the heart from that exposure, because the liver has taken all the antibodies up, and it seems to tolerate it just fine. Rocky, do you want to add to that?

D Dr. Richard Daly 08:14

That's well said. There was also some work from our liver transplant colleagues, Dr. Tanner, and others that have shown that the liver does reduce antibodies, but it's not all the antibodies, it's just the antibodies to that liver, to that donor. But those are the ones that count, you know, at transplant.

D Dr. Halena Gazelka 08:42

Because those antibodies would be in both the liver and the heart, correct Rocky?

D Dr. Richard Daly 08:47

Yes, the antibodies would react against the donor tissue, whether it's heart or liver.

D Dr. Halena Gazelka 08:52

Right, sorry, I said that backwards.

D Dr. Richard Daly 08:56

I'll ***** both of those. And there's such a large *****vein bed in the liver, that large surface area is a place for those antibodies to bind. And so, it kind of works like it's absorbing them, but it's really just providing a place for all the antibodies to bind. And they seem to bind in the liver in a way that doesn't harm it the same as it does in other

organs. So, it really does sort of sponge up the antibodies against that specific donor.

D Dr. Halena Gazelka 09:33

That is really just fascinating. I'm always amazed when people figure things out like this. I think it's wonderful. And I know Rocky and Sudhir that you have published the outcomes of seven patients who've had this reverse procedure. What did you find out?

D Dr. Richard Daly 09:51

Oh, go ahead Sudhir.

D Dr. Sudhir Kushwaha 09:52

Yeah, well, basically, I think that what we found, what we observed is that the high levels of antibodies, which we measured prior to transplant in the first 12 to 24 hours after transplant, their levels dropped to very low levels in the blood. So, in effect, the liver, well we speculate the liver has removed those antibodies, but those antibodies, which we were so worried about pretransplant as potentially causing a problem, they dropped down to very low levels, and we, in the paper, we demonstrate that these levels stay low consistently, for a good period of time following the transplant. And so, they're removed from the circulation effectively and can't create the damage, which would be possible.

D Dr. Halena Gazelka 10:48

With this reverse process, does it just not matter anymore? If a recipient who's going to get the heart and liver have antibodies, or are there only certain antibody antigen combinations that this works for?

D Dr. Richard Daly 11:04

It has to be organs from the same donor. The liver has to be from the same donor as the heart because they're absorbing antibodies that are specific to that donor. That's one thing. Around the time of the surgery, we do plasmapheresis, which reduces the total number of antibodies. So, that initially, it gives the liver a chance to be on top of it as much as you know it can. And we also administer medications to prevent really bad antibody mediated rejection. But it turns out that the necessity for those medications may be very low, and we initially were doing it because we weren't sure whether the antibodies would actually be gone. So, does it matter whether there are, if the patient needs a heart and liver transplant, it probably doesn't matter. We've also been worried that when the

levels were really, really high, which they are in some people, that that might be more than the liver can deal with, but in the experience we had, it actually was able to deal with even the higher levels.

D Dr. Halena Gazelka 11:08
Right.

D Dr. Sudhir Kushwaha 12:29
Yeah, I mean, as Rocky just stated, when we started this out, we really had an abundance of caution. We really didn't want to compromise any of our patients, and so we took these extra precautions, but as we've done these patients, it's probably become apparent that we probably don't need to be as cautious with these other medications, and even the degree of plasmapheresis which we undertake. But, I think it's always better to be a little bit careful. But, I think it's ended up being pretty successful, in fact, I saw one of our patients this morning in the clinic, and this is a young lady who was waiting in the hospital for transplantation for almost five years. And the reason she was waiting so long is because she needed two organs, and we wanted a good match. And she also had a complex history of congenital heart disease with multiple previous surgeries, and a credit to Rocky and the surgical team that we were able to take this on, because technically it was difficult surgery, and I'll let Rocky comment on that. But one of the reasons she waited so long is we wanted to get the best possible match, and we also knew that the surgical procedure would be lengthy.

D Dr. Richard Daly 14:07
Yes, it's true that the surgical aspect of this was for all of the patients that we reported, was complicated. It really takes a very close relationship and working with the liver transplant team because it's a choreography between the two teams through the surgery where we start and do some of the dissection for the heart and then the liver team comes and they do their work, and then they have to be a little bit ahead of where they usually are, so that they can sew the liver in very quickly when it arrives into the room because the heart, you know, is waiting. We're waiting to put the heart in. And the time that we have is very limited. So, the liver team needs to work, and then then we all are working together, and we're trying to get the heart in as well before too much time goes by. So, it really is kind of choreography, and when they've had multiple previous surgeries and they need reconstruction of various structures to be able to accomplish the transplants, then it becomes even more complicated. But I would just credit the fact that we have such a good working relationship with our liver team, and that some of that has to do with

having done so many transplants together, you know. We had established a long relationship doing combined organs where we put the heart in first and then the clock is not ticking quite as aggressively against us.

D Dr. Halena Gazelka 15:41

Okay, that is just fascinating to me. So, I knew that our listeners would be wondering, are you doing this all at one time in the operating room? And how long does it take the liver to sop up these antibodies that you can go on and put a heart in?

D Dr. Richard Daly 15:58

Well, we make sure the liver gets blood flowing through it for a while. And it's probably about almost an hour of time that the blood is flowing through the liver. So, the liver has at least that long to reduce the antibody load. And then we reperfuse the heart, that is we give the heart blood and get blood flowing through the heart. And hopefully we have everything's kind of lined up so that we can put one in and the other in and not too much time goes by.

D Dr. Halena Gazelka 16:34

So, they're on a cardiac bypass machine while you're doing this?

D Dr. Richard Daly 16:37

Yes, yes. So, for the heart transplant, they have to be on a bypass machine. For the liver portion of the surgery, we are not always on bypass for the liver portion. We have been for a few of our combined cases, but for the most part, we limit the bypass to the time we need for the heart.

D Dr. Halena Gazelka 16:59

Very interesting. Do you know of other transplant centers who are doing this reverse procedure as we are here?

D Dr. Richard Daly 17:07

No. The combined heart and liver transplant is becoming more common in our country. When I look at the numbers over the last five to seven years, it's been gradually coming up a little bit. But it's still a fairly uncommon surgery. So, doing this in a reverse manner,

you know, we just happened to have enough experience and a good relationship with our liver colleagues that we are able to work on this. But, it would be challenging to start a program. That's for sure.

D

Dr. Sudhir Kushwaha 17:09

I don't think so.

D

Dr. Halena Gazelka 17:47

I guess one of the questions that popped into my head is that knowing the risks of these antibody antigen, what made you brave enough to try this in the first place? How did you know that this might work?

D

Dr. Sudhir Kushwaha 18:02

Well, I think as I mentioned earlier, you know we have the experience of having done 30 or more. In fact, I think it was close to 40 combined heart-liver transplants. And then when we look at our outcomes, we saw that the rejection rate was so low. And because it's not uncommon after heart transplant alone to see some degree of rejection, whether it's mediated by T cells, which we call cellular, or whether it's mediated by antibodies, which we call antibody mediated or humoral rejection. It's not uncommon to see that in the first year or two following cardiac transplant, but these patients really didn't have any. And then when we get these potential recipients who really have no place else to go, I mean, there's really no other options for them. And you have a young individual who has got catastrophic, severe cardiac failure and liver failure. It's very difficult because there's no medical therapy to offer them. There's no conventional surgical therapy to offer them. So, this becomes the only possibility of giving any kind of quality of life to these individuals who would otherwise die. And so, for the individuals, it's really the only lifesaving procedure. For us, it was a graduated risk, I would say. I mean we when we did the first lady, and it was successful, it really opened up the doors for us to consider other possibilities and other individuals with similar problems. So, it's been a bit of a process, I would say over the last 10 years or so, since we started doing this.

D

Dr. Halena Gazelka 20:03

What are some of the reasons that someone would need to receive both a heart and a liver transplant?

D Dr. Sudhir Kushwaha 20:10

Well, sometimes, when there's severe failure of the heart, the right side of the heart is involved as well. And the inability of the right side to pump blood will lead to back pressure on the liver. And over time that will cause cirrhosis of the liver, and the liver will start not being able to function very well either. And that's often the case in many, particularly younger individuals, who have congenital heart disease. Because of the nature of their anatomy, and the anatomy is variable, they may get congestion of the hepatic circulation and over time the development of progressive cirrhosis. And then there are also other conditions where you may get a disease affecting both organs. I mean amyloid is one disease, which we've done that a lot of the conventional heart liver transplants, hemochromatosis, sarcoidosis, variety of conditions, which can affect multiple organs are considerations. But I think, basically, when I think back on the individuals we've done, a fairly high proportion are complex congenital, wouldn't you say Rocky?

D Dr. Richard Daly 21:34

Yes, in this group, it's a high proportion. Because they also tend to get sensitized, tend to get antibodies. Most of them have had several operations, three, four or five operations, and lots of transfusions with all of that surgery. So, they are really at a high risk for having these antibodies.

D Dr. Halena Gazelka 21:56

Well, this is just a fascinating topic. We know that in the United States and elsewhere, that there are far more people waiting for organ transplants than what we have available. What would you say to individuals who are considering becoming an organ donor, or registering to be an organ donor in the future?

D Dr. Sudhir Kushwaha 22:18

Well, I think that the more organ donors we have, the more lives we can save the people who may benefit from a new organ, you know. So, I would say consider it but do it. I think a lot of people have some reticence, but there's really no reason to be reticent, I think the process is a smooth one, and everybody's very respectful and appreciative of somebody who has chosen to make their organs available for use in somebody who may benefit.

D Dr. Halena Gazelka 22:57

I know that in some states, you can put this on your driver's license, for instance. But is that

the only way to register for organ donation?

D Dr. Richard Daly 23:04

I think the really important thing is to make sure your loved ones know what your wishes are. You can do it on your driver's license, and in some states that would even overrule your next of kin in terms of what they would say. So, it carries sort of the weight of will or law, but it doesn't in every state. In some states, it's just indicates your wish. So, if your loved ones know that you'd like to be a donor, that is probably the most important thing to do. And one donor can save seven lives.

D Dr. Halena Gazelka 23:49

Wow, isn't that's something.

D Dr. Richard Daly 23:52

So, it's not just one organ that we're talking about or one person that a donor can help.

D Dr. Halena Gazelka 23:59

Well, Rocky and Sudhir, thank you so much for being here with us today to share about this very important topic. Our thanks to Mayo Clinic cardiologist Dr. Sudhir Kushwaha, and Mayo Clinic cardiothoracic surgeon, Dr. Rocky Daly, for being here today to share what they have discovered about reverse order heart-liver transplants. April is Donate Life month, so we wanted to make you aware. I hope that you learned something today. I know that I did. And we wish every one of you a wonderful day.

N Narrator 24:30

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