

Advances in Live Donor Kidney Transplants
Webcast
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Dr. Joseph Leventhal

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Andrew Schorr:

This is Andrew Schorr on Patient Power. Thanks for being with us once again on Northwest Memorial's innovative webcast series.

Lately we've been discussing transplants, and Northwestern Memorial has been a leader in that. You know, there's a shortage in donor kidneys and other organs that unfortunately we need to help a lot more sick people who could benefit from transplants, but there's a shortage of organs. We spoke about that in our earlier webcast with Dr. Abecassis who leads the transplant program at Northwestern Memorial. And now we have on a surgeon, Dr. Joseph Leventhal. Dr. Leventhal is a surgeon on the medical staff at Northwestern Memorial and he's also an associate professor of surgery and director of the Living Donor Renal Transplant Program at Northwestern University's Feinberg School of Medicine.

Dr. Leventhal, thanks for being with us.

Dr. Leventhal:

My pleasure.

Andrew Schorr:

Sir, help us understand, why do we if need so many kidneys and pancreases and livers? But particularly kidneys, what's going on in America's health that people need transplants?

Dr. Leventhal:

Well, I guess, very broadly, organ replacement therapy has emerged as a treatment of choice and in some situations the only treatment for certain disease conditions that we've seen improvements made in managing to keep people going and alive, but ultimately really represents the best that we have available to offer patients who are afflicted with certain conditions that lead to the failure of particular organs.

Now, in kidney transplantation specifically we've seen a dramatic increase in what we call end stage renal disease, which doesn't necessarily mean that you are immediately on dialysis but are beginning to experience failure of your kidneys. And this is because we are seeing dramatic increase in certain health conditions that we know lead to kidney failure.

Andrew Schorr:

Well, we have an epidemic of diabetes, right? I think more than 15 million people, and that's often a cause, isn't it?

Dr. Leventhal:

Correct, and hypertension as well. And these are the two most common causes of kidney failure. We're also doing a much better job of keeping people alive who have progressive failure of their kidneys. And there simply aren't enough kidneys that we obtain each year from individuals who give the gift of life when they have a tragic death, what we call deceased donor kidneys.

So increasingly we see living donors who are donating one of their two healthy kidneys to a particular individual who has kidney failure as emerging as playing a larger role in what we're doing for people who need a kidney transplant.

Andrew Schorr:

So this is your effort to try to get around the problem, the shortage of donor kidneys from people who've died. And I have a question about that. So many of us, and I'm someone, I'm an organ donor on my driver's license. A lot of states have that. Doesn't that fix it?

Dr. Leventhal:

Well, I think indicating that on your driver's license helps. Ultimately, what's also very important is letting people in your life know that this is your wish because it's one thing that it's on your driver's license, it's another thing if nobody knows that this is what you really want to do. And of course we do have situations where family members, loved ones who are approached after an individual, let's say, has an accident and is brain dead who choose not to allow donation to proceed. So it's very important to discuss your choice to be an organ donor with people in your life so they understand this is something you want to do.

That being said, even if we were to maximize organ donation, not all donors have healthy organs that can be used for particular individuals. We are seeing individuals who are deceased donors reflecting the general population. So the population is an older population, a population that has certain health conditions that we see throughout the general population. So we're seeing fewer individuals who are donors who are a younger age. A major impact, for example, in traumatic death of certain things such as safer vehicles, helmet laws, seat belts, what have you, which is great that we're not seeing those sort of tragedies occur, but the organs we do get are coming from individuals who are older and perhaps have as a disease condition hypertension and diabetes, the very situation that we're trying to treat in the person who has it very bad and whose organ ultimately failed.

So I think we're always going to have a gap between the people on the waiting list and the number of organs we have available each year from deceased donors.

There are more than 60,000 people on the kidney transplant waiting list right now and we have, at best, maybe around 13,000 to 15,000 kidneys that we can transplant from deceased donors each year. So the waiting times are increasing steadily, and that's where the living donation is playing more of a role.

Andrew Schorr:

Okay. Let's talk about that. So you helped lead the way I believe beginning in 1997 at Northwestern where you've been perfecting Living Donor Renal Transplant Program, and I know since 1997 you've performed close to one thousand minimally-invasive living donor operations. And I know it's one of the most active programs in the country. And I also understand that you increasingly have ways of doing it, where we used to think we had to be a really close match and that's not the case any more. So help us understand how you've been perfecting this and where we are today.

Dr. Leventhal:

Certainly. Well, first and foremost, living donation, the act of undergoing the medical procedure of giving up one of your kidneys is much less invasive in 2007 than it was over a decade ago. In 1997 we were the first program in the midwest to perfect what is known as laparoscopic donor nephrectomy. Instead of making a foot- to a foot-and-a-half-long incision between your ribs or underneath your ribs, perhaps removing one of your ribs to gain access to the kidney, we use a series of small thumbnail-size incisions, kind of what we call keyhole surgery, to remove the kidney through a two-and-a-half to three-inch incision after working through those small incisions with small certain instruments, what we call laparoscopic instrumentation.

This has had the impact of shortening the hospital stays of individuals dramatically, resulting in much less postoperative discomfort, a more rapid return to normal activity. And since the program began in 1997 we here at Northwestern have paved the way in introducing new instrumentation techniques that have made it even less invasive so that the operation is shorter than it was in 1997. We use fewer small incisions to do the procedure. The stay in the hospital now for donors is routinely just about a day. So if they were to be admitted on a Monday to have a kidney removed, they would be going home to continue the recovery in the comfort of their home Tuesday afternoon or Tuesday evening and then getting back to their normal daily activities right thereafter. So that has removed a disincentive for many individuals to donate a kidney and has made the idea of being a kidney donor much more acceptable to individuals.

In terms of increasing accessibility of transplant, in living donor transplant to individuals who have a living donor, we have had advances in several areas that make it possible to offer transplantation to people with less immunosuppression, for one, and secondly to get around certain obstacles that previously were medically very problematic.

First and foremost, we have better medications, better immunosuppression in the new millennium than we did 15 or 20 years ago. So we can deal with individuals who are not identical or closely related in their DNA, what we call the HLA match, with really no increased risk of rejection such that individuals who get a living donor kidney transplant routinely have a risk of a rejection of a tenth, of less than one in ten, and at Northwestern a graft survival that approaches 99 to 100 percent at the end of one year.

Andrew Schorr:

So that's tremendous progress.

Dr. Leventhal:

Right. So we no longer need to make sure that people are matching very closely in their DNA because the drugs help control for that.

The other areas relate to situations where a transplant recipient has developed an immunity against a potential donor, what we call a positive cross match, where they have antibodies against a potential donor, or where there is an incapability in the blood type, what we call ABO-incompatible transplantation, where again an individual has anti blood-group antibodies. Now, previously if you would transplant under these circumstances the graft would be rapidly rejected by what is known as hyperacute rejection where the antibodies would bind to the kidney and would injure it and cause it to be lost in a matter of minutes to hours.

We have developed very safe and very effective approaches for dealing with positive cross matches and ABO-incompatible transplants. Northwestern is one of the few programs in the United States that has an active incompatible transplant program where we can use certain medical treatments in particular transplant recipients to remove these antibodies, prevent their reappearance and safely transplant them with a living donor kidney with low rates of graft rejection and excellent patient and graft survival. And we've been doing this here at Northwestern over the last three to five years.

Andrew Schorr:

I just want to go over some of that again for sort of the lay person, if you will. So what you've been perfecting is a way for the recipient of having less likelihood that they will reject the donor kidney. And even where there's been these bigger obstacles like the ABO-incompatible situation you're finding ways around that.

Dr. Leventhal:

That's right. That's right. Now, one of the things which we have been able to demonstrate here at Northwestern is that it's not necessary to subject the transplant recipient, especially for ABO-incompatible transplantation, to additional surgical procedures to get around the blood type incapability. What I mean by that

is that around 15, 20 years ago when people began to look at ABO-incompatible transplants it was kind of assumed that one would have to remove one of the antibody producing factories in your body called the spleen fairly routinely. And until very recently it was expected that a splenectomy would have to be performed in a transplant recipient in order for them to get an ABO-incompatible kidney. Well, we've used certain antibodies against antibody-producing cells in your body to remove the need for the splenectomy. So it makes the whole experience here of going through the transplants much less problematic for the transplant recipient. You no longer need that additional operation to be able to go ahead and get the kidney transplant.

Andrew Schorr:

Help us understand one other thing that you've helped pioneer there too. What are paired exchanges?

Dr. Leventhal:

A paired exchange is a situation where you have two donor recipient pairs, and there is either a positive cross match or a blood type incapability within each separate pair. But were the recipients to exchange donors, in other words were donor A to give to recipient B and donor B to give to recipient A, you could successfully avoid a blood type incapability or positive cross match. So what we have done here at Northwestern is offer this to specific individuals where there's, with respect to the size of the kidneys and the age of the donors, parity, where things are very similar, and everyone has their donor operations and recipient operations on the same day, what we call mutually assured donation and transplantation, and at the end of the day a kidney donor who was donor their kidney to help their recipient get a living donor transplant has been able to achieve that goal. It's just that their kidney isn't necessarily in their particular recipient because they've been exchanged between recipients. But at the end of the day two people have been transplanted and have normally functioning kidneys.

Andrew Schorr:

Wow. That takes a lot of coordination, but it sounds like it's a blessing for both families involved.

Dr. Leventhal:

It is. It does require a lot of coordination. We're fortunate here at Northwestern to have been a busy enough program and the sort of support from the hospital to successfully offer this to our patients. And it does help an individual who otherwise would have to stay on dialysis or progress to dialysis to have access to that kidney transplant.

Andrew Schorr:

Dr. Leventhal, let's talk about this some more. Your area of research has been in this whole anti-rejection area. Where are we headed? So you've made tremendous progress it seems. What are obstacles you're trying to overcome now? Where is it headed?

Dr. Leventhal:

Well, the last 20 years in transplantation has really been focused in terms of the clinical research that's being in preventing acute rejection and graft loss or kidney loss due to acute rejection. And it's been very successful in that whereas before you'd have an acute rejection risk of around 40 to 50 percent we now routinely have rates of rejection risk that are between 5 and 10 percent. And the risk of graft loss from a rejection attempt is extremely, extremely low. And it's because we have better immunosuppressive drugs for preventing this rejection which most commonly occurs within the first post transplant year.

The challenges that remain are related to minimizing the amount of immunosuppression that an individual might need for the remainder of their life with the transplant, for one. And we are looking at ways of developing minimal immunosuppression protocols. And Northwestern was one of the first centers to pioneer what is known as prednisone-free immunosuppression, where as previously you might have to be on steroids for your life with all the attendant potential side effects from steroids - related to diabetes and hypertension, weight gain and so forth, bone disease, we now have shown very definitively that you do not need to be on prednisone to avoid rejection and have a functioning kidney transplant.

Now, there are other drugs we've identified that we'd like to move away from, in transplantation because they have side effects on the kidney. Specifically, there is a class of drugs known as the calcineurin inhibitors, and the two most common ones we use are cyclosporin and Prograf. These drugs are very good at preventing acute rejection, but they've been shown over the long term to cause injuries to kidneys. And we believe that if we can avoid the long-term use of these drugs in our kidney recipients we can further extend graft survival. And so we here at Northwestern are participating in research to explore the development and successful use of drugs that don't have the specific side effects of cyclosporin and Prograf.

And finally, the area that I think we are still working in and need to make improvements in are in long-term graft survival. We have done a very good job of preventing graft loss over the first couple of years, but when we look at 10, 15, 20 years after a transplant we are still seeing individuals going on to have a transplant fail. With a living donor kidney transplant the average amount of time that will have elapsed will be around 20 years. So if you're a young individual who gets a transplant, let's say at the age of 20 or 30, you're very likely going to have to end up getting a subsequent transplant.

We are looking at ways of avoiding this process of chronic graft loss by again tailoring our immunosuppression, controlling other risk factors in patients who receive transplants, such as hypertension, their lipids. And we're still understanding this process of chronic graft loss by studying patients who are successfully transplanted and as we follow them out after transplant.

Andrew Schorr:

So help us understand. The way it's working today, someone, family member, maybe not, but a living donor donates their kidney. We talked about the minimally invasive nature of that. They go on with their life, and then the donor receives the kidney, and you're trying to perfect the antirejection drugs now so that they can lead a pretty normal life, it sounds like now, and hopefully have that kidney last a long time.

Dr. Leventhal:

Correct. Correct. The patients do extremely well with the transplant, much better than they did a generation ago. The medications that we have are much better in terms of the way the recipients tolerate the medications. But the challenge is for he us--we'd love to have that transplant that that recipient gets be the only transplant that they're ever going to need. That's an area--that's something we've not been able to achieve in transplantation but something we're working very hard towards right now.

Andrew Schorr:

Okay. So it must be daunting though. It's like climbing a mountain. You've really made tremendous progress, and Northwestern is to be congratulated on that. I know you wish that people would work on lowering their blood pressure and work on not having diabetes in the first place, some of these conditions that lead to the need for these transplants.

Dr. Leventhal:

Well, certainly. And I think there are certain risk factors that people have control over and other that they don't have control over. Clearly, there are certain things that contribute to high blood pressure and diabetes, and we all know that weight gain, obesity contributes to this. Lifestyle, diet, exercise.

I must also say that these are very important issues after transplant as well, perhaps more so, because some of the medications that we use to control and prevent rejection have the undesirable side effect of maybe making the blood pressure a little higher, the diabetes a little bit more difficult to control. So getting a transplant is something - the transplant recipients can't be passive. They have to take a very active role. They're a stake holder in their health, not only by taking their mentions regularly and without fail but also by trying to live the healthiest lifestyle possible.

Andrew Schorr:

And for the donor though, they can go on with a normal life.

Dr. Leventhal:

Correct. The donor evaluation process is a very, very careful one to make sure the donors are healthy, that they don't have certain health conditions that we feel will expose them to an increased risk of having kidney problems themselves. So we're fond of saying that we're all born with two kidneys so that we could potentially give one away, but that's with the understanding that an individual has two normal-sized kidneys and is healthy enough to give one of those kidneys away.

Andrew Schorr:

Well, I want to take just a minute. I know we're mostly talking about kidneys, but you've made a lot of progress in the transplantation of other organs at Northwestern too, right?

Dr. Leventhal:

Certainly. I'm also very involved with the pancreas transplant program that's run by Dr. Dixon Kaufman, and there we've also seen over the last 10 to 20 years a dramatic decrease in rates of acute rejection through better immunosuppression that we have available as well as improvement in patients and graft outcomes long term through a better understanding of how to select patients for transplant, how we do the operation and how we manage individuals after the operation.

Andrew Schorr:

And I know in talking to Dr. Abecassis, head of the overall transplant program, even with liver transplant, that's incredible to me how there can be part of a living donor liver taken and it regenerates sort of on both ends, both in the recipients and there's a regeneration on the donor as well.

Dr. Leventhal:

Correct. And that's a very unique feature of the liver is its regenerative capacity. And there's also been a real explosion over the last ten years in living donor liver transplantation, where, as you put it, a segment of the liver is removed from a donor, it's transplanted into the transplant recipient, the liver of both the donor and the recipient grows back and grows to normal size. And although it's technically a more challenging operation than what we routinely do in kidney and there is an increased risk of things such as a technical failure with the liver because of the sort of hook-ups that are needed in the transplant recipient, the rates are still quite low and the outcomes superb. And it's something which, again, a generation ago we just did not have available routinely to offer our adult transplant recipients.

Andrew Schorr:

Dr. Leventhal, what I gather from all this and our discussion earlier with Dr. Abecassis is at the Feinberg School of Medicine and Northwestern Memorial there's a tremendous devotion to living donor transplantation.

Dr. Leventhal:

Absolutely. There certainly is. And part of that is not just paying attention to the needs of the transplant recipient but also having a program that is designed to protect the interests of the donor. I think we need to always remember that individuals who are living donors are having an operation that they don't need to have. They are putting themselves in harm's way, so to speak, for the potential benefit of the transplant recipient. So it's very important that those individuals are making an informed, voluntary choice and that they are being carefully evaluated and educated about the living donor process.

There is a very well identified and detailed evaluation process that living donors go through, either for kidney donation or liver donation here at Northwestern, to ensure that the interests of the donor are always being preserved.

Andrew Schorr:

Yes. On an earlier program we had on a gentleman who had a donation of a kidney for polycystic kidney disease from his adopted son. And they had gone to a seminar, and I know there was a lot of counseling. And I know Michael, the son, felt very comfortable with that. He felt like you really were looking out for him, and it sounds like that's the way to go.

Now, we've described what goes on at Northwestern. It seems to me that this sort of activity doesn't just go on at any hospital, that you are one of the leaders in this.

Dr. Leventhal:

Right. Well, we have one of the most active living donor programs, I would argue, in the world. We performed in excess of 150 living donor kidney transplants last year and I believe close to 30 living donor liver transplants last year, making us one of the busiest programs there are. And part of that is having, I think, an institution that is really committed and has the support to take care of donors and recipients. A lot of centers perform living donor kidney transplants but they perform them in almost an itinerant way where they're doing relatively small numbers.

We have the advantage of a tremendous amount of experience and also because of that experience are comfortable taking care of transplant recipients and potential donors who other centers might not be as comfortable with because they don't have the sort of experience that we do. I think that it's very important that patients these days rightfully can get the information that they need about different transplant centers so they can make an educated choice about the center that they want to go to.

Andrew Schorr:

Right. And I think now with the internet, and of course this program is on the internet, people would do well, listen to this program and then if you want to follow up with Northwestern all the information is on NMH.org, and you can look up Dr. Joseph Leventhal and you can look up the transplantation program. And you have a website for the transplantation program too, don't you?

Dr. Leventhal:

That is correct. And there are details related to the various organs we transplant here, contact information if you're interested in finding more out about transplantation and donation. And we are very happy to hear from individuals in that regard.

Andrew Schorr:

And it is not necessarily a quick process, deliberately so. It's not like somebody needs a transplant, it's going to happen tomorrow. You're very careful in the selection and the evaluation, and I think that's a good thing.

Dr. Leventhal:

Yes. Obviously, with transplant recipients we need to make sure that they are medically suitable candidates to receive an organ. Although transplantation represents a treatment of choice for many individuals, be they have kidney failure or liver failure or diabetes, it is not the solution for all patients. Some individuals simply don't have the reserve that is required to get through an operation and derive the benefit of a transplant. So we carefully evaluate transplant recipients to make sure that there aren't medical problems such that getting a transplant would not be of their benefit.

With respect to donors the evaluation process that helps them make an informed, voluntary choice and carefully evaluates their health status is one that moves through some very deliberate phases and again takes a certain period of time. And again the time is not just for us to do the sort of evaluation that's required but to make sure that everything is looked at properly, but also to allow donors and recipients to reflect on their decision and make sure that this is something they want to be doing.

Andrew Schorr:

So it sounds like you've made tremendous progress. So one last question for you, Dr. Leventhal.

Dr. Leventhal:

Sure.

Andrew Schorr:

If you had a crystal ball, with all the research that is going on that you're doing, your colleagues at Northwestern and the Feinberg School of Medicine and then your peers around the world, if you look forward where are we going to go with kidney transplantation and making the organs last, not be rejected, the medication regimes be simpler, a simpler go for the donor, where are we headed?

Dr. Leventhal:

Well, the Holy Grail of transplantation is something we call tolerance, where by virtue of medications that we can give for a period of time or treatments we can use at or after the time of transplant we can make the recipient take the donor organ and have the rest of their immune system function normal and they would never reject the organ. They would be specifically tolerant of the organ with no risk of rejection in the future. This is something we have been able to achieve in animals but have not been successful in achieving in man.

And I think the future over the next decade is going to be the beginning of evaluation and protocols that may be able to do this in kidney transplantation. We here at Northwestern are actively interested in this and will likely be launching trials of this nature within the next one to two years, where by combining the use of stem cells and cells from the bone marrow along with a solid organ we hope to be able to achieve tolerance, certainly minimize the amount of immunosuppression that individuals will need and hopefully impact on this process of chronic graft loss that I mentioned earlier.

I also think that we will see a change in the sort of medications that we use routinely in patients who we're not pushing the envelope in in terms of achieving tolerance. And by that I think these drugs I've talked about, the calcineurin inhibitors, Prograf, cyclosporin, I think we'll see them phased out of kidney transplantation and replaced with other medications that we here at Northwestern are pioneering the evaluation of.

Andrew Schorr:

Well, it's very exciting all you're doing. I wish you well with all your work. And I think it's very encouraging for people who sit on those lists hoping for a donor kidney and if there can be a living donor to fill that need, even though years ago used to be incapable and now you have ways around it. The pioneering work you've done at Northwestern Memorial is a great hope for people. It must be gratifying to you that you can do this.

Dr. Leventhal:

It certainly is. It certainly is.

Andrew Schorr:

Well, we've been visiting with Dr. Joseph Leventhal who is director of the Living Donor Renal Transplant Program at Northwestern University's Feinberg School of Medicine. And he's a surgeon on the medical staff at Northwestern Memorial and associate professor of surgery also at the Feinberg School of Medicine.

Dr. Leventhal, thank you so much for being with us on Patient Power. We wish you all the best with your pioneering work for you and your staff.

Dr. Leventhal:

Thank you very much.

Andrew Schorr:

This is Andrew Schorr with Patient Power, and as always we wish our listeners the best of health. And remember, knowledge can be the best medicine of all.

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