

Melanie Cole: The combination of a growing number of patients with end-stage renal disease and a shortage of organs poses a significant challenge to the transplant community. Ongoing efforts are required to expand the donor pool and get more patients to transplant and sooner. Today, we're offering a roadmap of innovation in living donor kidney transplantation.

Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole. And joining me in this panel today is Dr. Amanda Leonberg-Yoo, she's the Director of the Training Program, an Assistant Professor of Clinical Medicine and the Medical Director of the Living Donor Kidney Transplant Program at Penn Medicine; and Dr. Robert Redfield III, he's the Surgical Director of the Living Donor Kidney Transplant Program, also with Penn Medicine.

Doctors, thank you so much. This is such an important topic we're discussing here today. And Dr. Leonberg, I'd like to start with you. What do you see as the single greatest challenge? facing patients on the kidney transplantation waitlist today, some of the constraints to meeting that annual demand for kidney transplantation.

Dr. Amanda Leonberg-Yoo: That's a great question to start with, Melanie. So thinking about the prevalence of end-stage kidney disease in the US, we have over 800,000 individuals receiving some form of kidney replacement therapy. Access to transplant is limited, although the number of patients added to the waitlist continues to grow. And access, I think about it in a couple different ways. It's not only access to different types of kidney transplant, living versus deceased. It's also awareness about living and deceased transplant and acceptance that this is really something that can happen to them. And so, I think earlier access to education is key.

Dr. Robert Redfield III: Yeah, I'd also, like to add access is absolutely the number one issue. But, you know, for those that do have access, really the second greatest issue is organ availability. And because we don't have enough organs to transplant patients that are on the waitlist, the wait time is long and that wait time is increasing. So for the most common blood type, blood type O, wait times are now approaching 10 years, and that's a 10-year wait for a high-quality deceased donor organ. And mortality on dialysis is significant, such that patients essentially, over a 10-year waiting time, have basically a 50% chance of surviving that wait.

Melanie Cole: That puts a real perspective on the scope of the problem, Dr. Redfield. So there are a number of ways to abbreviate the wait for the kidney. And one is what we're talking about here today, is living donor transplantation. Can you please speak about your program at Penn Medicine? How does it work? What's the advantage of receiving a kidney from a living donor? Tell us about the survival advantage of living donation?

Dr. Robert Redfield III: Yeah, I think that's a great question. And, you know, there are many advantages. I think the top three that jump out is that if you have a living donor, you don't have to wait. And like I said before, the wait time can be upwards of a decade. And we do know that the data is very clear that the earlier you get transplanted, the better you do. And so patients who ideally could get transplanted before they even have to initiate dialysis do best, and that's a preemptive transplant. And really, the only way to get a preemptive transplant is to get a living donor because we can control the timing, we identify the donor and we can do the transplant many times before dialysis has to be initiated.

The second is living donor kidneys work better. And the data there is very clear. When patients come, you know, to my clinic and I counsel them about needing a kidney transplant, the best treatment option I can offer them is a living donor kidney transplant. And not only do they get to avoid the wait, but these kidneys work right away. And, you know, with deceased donor kidney transplantation, because the kidney has to go through the dying process and is out of the body for a significant amount of time, it can take, you know, many days, weeks, and even a month to kind of wake up, and so that recovery is a little harder. I'm not trying to discourage deceased donor kidney transplantation, but, you know, the recovery is a lot more significant.

And, living donor kidneys have a lower incidence of what we call delayed graft function, and that's where the kidney takes a little while to wake up and patients will still need renal replacement therapy while they're recovering from their transplant until the kidney really kind of kicks in. And, these kidneys also last longer. On average, kidney transplants last about 10 years. If you break things up and look at living donors versus deceased, living donation is approaching a graft half-life of almost 20 years now. And so, when we're looking at those kidneys that are transplanted now and we, you know, asked the question, "In 20 years, what percentage of those kidneys are functioning?" It's going to be about 50/50 at 20 years, which is not perfect, but it's certainly a lot better than deceased donation.

And, some of that is again, these kidneys are coming from healthy living people. They don't have to spend much time out of the body. They don't have to go through the dying process and they're, by definition coming from a healthy person with really not a lot of medical problems.

And it is still a better treatment than dialysis. But, you know, my wish for all my patients is that we can get them access to a living donor kidney transplant because, you know, and this is the last thing I'll say, is, you know, you look at this country of, you know, 330 million people in the United States not everyone can donate a kidney, but a lot of people can. And on the current wait list right now, it's about a hundred thousand people in the United States are waiting for a kidney transplant. There is definitely a hundred thousand healthy individuals that can donate a kidney and get all of these patients off the wait list, and that's really the focus of our practice here at Penn, is to try to get all of our patients access to this best therapeutic option.

Dr. Amanda Leonberg-Yoo: Yeah, and I want to jump in by highlighting that point that deceased or organ supply really is inadequate for our growing needs for kidney transplant. Just looking at the numbers alone, the total number of people on a wait list, a hundred thousand, about a quarter of those individuals receive kidney transplants. But right now in the US, only about 20% of those are living donor kidney transplants. And so that's the area, like Dr. Redfield highlighted, is the area that we have the opportunity for growth. The deceased donor kidney transplant organ supply is present. However, the potential disadvantage that Dr. Redfield had described, is kind of important to think about in terms of longevity.

I also wanted to make a point, so we were talking a lot about the advantages to the recipients, there actually are advantages to a potential kidney donor that we've really started to think about more recently because it's a bit of an ethical dilemma, thinking about living kidney donation because a donor accepts a risk so that a recipient can benefit. So this kind of ethical line of thinking really excludes consideration of the benefit of the donor other than emotional or psychosocial benefit, which is sometimes hard to quantify.

But there are a lot of other tangible benefits that you think about in terms of living donations. So thinking about donating to a loved one, considering reduction in stress or worry about post donation follow-up for that individual thinking about, you know, family member not being

sick anymore. There's a better quality of life. It's hard to quantify, but certainly a tangible benefit from the donor perspective. You know, differences in health habits, you know, less dietary restrictions following kidney donation as compared to dialysis, which can affect a whole family. And finally, you know, at Penn, we really do emphasize the health and wellness of the donor, so thinking about how a donor may become more proactive about their own health and wellness following the evaluation process and following ideally donation.

Melanie Cole: Wow. You both make such great points. This is such a fascinating topic, Dr. Leonberg-Yoo. Donor-recipient compatibility, as we're discussing here today, is a critical part of kidney transplantation. But if a living donor's kidney is incompatible with an intended recipient, for other providers, what do you see are some innovative and necessary steps to increasing living donation?

Dr. Amanda Leonberg-Yoo: Sure. So in general, we think of it as biological incompatibility, so different blood types, different tissue typing and all of these are very important factors for direct donation. Other incompatibility considerations we think about include age or size differences, distance or maybe even chronologic incompatibility.

But I think taking the first biological incompatibility, different blood type, different tissue typing, we're able to overcome this barrier by providing paired donation, donating indirectly to the individual in need or to the intended recipient. So you, as the donor, donate on behalf of someone into a registry. Within this registry, you can find a perfect match, blood type, tissue typing, in which that individual benefits from your donation and your recipient then benefits from another ideally perfect match on the receiving end of things. So I think that's probably the most impactful type of overcoming of incompatibility. And Dr. Redfield has a lot of experiences in this working with the National Kidney Registry.

Dr. Robert Redfield III: Yeah. Really compatibility, biologic compatibility, so blood type or HLA compatibility does not matter. It's actually something that we talk about at the end of the evaluation. And the only thing that matters is that there is a person that is evaluated to be a healthy living donor that can donate.

So if they don't have the same blood type and their blood type incompatible, we used to do blood type-incompatible kidney transplants,

and it required a ton of immunosuppression and a lot of plasmapheresis, and the outcomes were inferior to compatible. Now, with the National Kidney Registry or Paired Kidney Exchange, we can find a compatible transplant, whether it's blood type or HLA compatible.

And you know, there's also some other innovative things that have spun off because of that. Even if the patients are compatible biologically, you know, maybe they're incompatible in time. You know, one person wants to donate now and the person is not ready for a transplant for another two years. Well, they can go ahead and donate into the donor pool and gets what's called a voucher. So when they're ready for a transplant, they let us know and were able to pull a kidney, a living donor kidney from the National Kidney Registry.

So there's a lot of things like that. We have couples, husband and wife and, you know, they don't want to have to recover at the same time. The donor can donate first, recover, get back to normal health, and then the recipient can get transplanted. So there's really a menu of options now to be able to, A, honor the gift or, really kind of figure out what the best kidney is for each intended recipient.

Melanie Cole: Dr. Leonberg-Yoo, Penn Medicine has a significant emphasis on growing its living donor program. Describe a little bit how the program works and the initiatives you have in place to increase this pool of living donors. How would you describe the two or three leading advantages for individuals considering the Penn Living Donor Kidney Transplantation Program and indications for referral to the program?

Dr. Amanda Leonberg-Yoo: So essentially, this Living Donor Center that we have created really shifts the focus away from recipient perhaps and focuses more on the donor. And I'm thinking about the donor as an individual with some short-term barriers to donation and also long-term barriers to donation. So thinking about from a donor perspective, having a center that's truly dedicated to the needs and understands the needs and barriers to living donation is really important.

So at Penn Medicine what we're doing is creating this living donor center that allows for a really streamlined approach to living donor evaluation. So what that looks like is easy access to evaluation. So considering time off work, lost wages, length of evaluation. We can kind of help make impacts in this area short term to make this a tangible thing for the individual interested. Thinking about long term effects of this type of

program, also thinking about the risk of kidney donation itself. There are risks, albeit small. And by streamlining some of the resources that we have in this domain, we can kind of tailor and and cater the individual's needs to think about the long-term health effects and ensuring long-term follow-up for these individuals. So I think the one big initiative that we have is really shifting the focus to the living donor needs and the living donor evaluation.

Melanie Cole: I was actually going to ask a question just about that because we do think about the recipient. Dr. Leonberg, just sticking with you for a second, can you just expand a little bit on what's important to note far as donor protection, support, safety, selection criteria, mentoring? I mean, there are psychosocial aspects for the living donor. How is that addressed at the Penn Medicine Living Donor Kidney Transplantation Program?

Dr. Amanda Leonberg-Yoo: Oh, that's a great question. So it starts with a multidisciplinary team, and this team is separate from the team that evaluates the intended recipient. And there's intention to that. Our goal is to ensure that the living donor is making a decision that is appropriate for them as the individual considering healthcare needs and also, that's free of coercion. Our multidisciplinary team includes a nephrologist, a surgeon, financial coordinators, pharmacists, there's a dietician, social worker, and a coordinator. And at the crux of it is the donor and the center of this living donor team. The living donor sits next to an independent donor advocate who also helps to navigate this system. And so, you know, again, I think the separation is actually quite important in order to have a focus on the living donor.

Melanie Cole: Such an important topic we're discussing today, and Dr. Redfield, last word to you, please tell us a little bit about the Penn Advantage, the experience of your multidisciplinary team that Dr. Leonberg-Yoo just mentioned, and how have been your outcomes. I'd just like you to speak to other providers about what you see coming in the future and what you'd like them to know about the program at Penn Medicine.

Dr. Robert Redfield III: Yeah, thanks for that question. I do think experience matters. You know, collectively, we have some of the most experienced transplant surgeons and medical doctors, in the country. If you look at our outcomes, we also have some of the best outcomes in living donation, in the country. Currently, with our government reports,

we have a 100% 1-year graft survival for all of our living donor recipients and our donors as well.

I do consider us an innovator. I believe that we all lead from the front here. So we are anything that comes down the pike that we think is of benefit to our patients we examine and we deploy whether it's in, you know, clinical trials and innovative immunosuppressants for our recipients. We currently have a trial that's looking to try to perform living donor transplants without the use of immunosuppression, which is I think, you know, for a number of our patients, a great treatment option, you know, innovating on the way of surveillance.

You know, some of the innovations that were talking about on the donor side with the voucher systems and allowing people to advance, donate, allowing better matching instead of just looking at the crude HLA matching, trying to identify people with low eplet mismatches is something that we're rolling forward, here. So, we do have a commitment to innovation in making this great field better.

But I think most importantly is the care that patients receive. And this comprehensive living donor center that we are standing up here, is that at its core it's to provide the best care to donors. And, you know, living donors are a special population. They're the only population that is engaging the healthcare system, because they want to save a life and they're healthy. And I think there's a different care expectation there. I think we all want to, provide the best care for all of our patients. But these are really special individuals who are coming and undergoing surgery and accepting some risk. Although it's very small and it's very managed to save a life. And because of that, we want to make very streamlined approach, a very efficient approach to allow them to honor that gift and to be able to realize that. Anything on your end, Amanda, that I may have missed?

Dr. Amanda Leonberg-Yoo: I think we're also not only promoting the health and wellness of the living kidney donors, we also celebrate the contributions of these individuals. Like Bob has said, these are special individuals that have saved a life by a gift that they didn't need to give. And so I think enhancing that patient experience is really an important part of the care delivery. This is done in a lot of ways.

You've mentioned the mentorship program in the past, and I think the individuals who've gone through this process, kind of they're part of the

group of individuals that are bonded together in this mentorship group is really an outreach of that. So not only do kidney donors give the gift of life, they also mentor people in order to be able to understand the process and move forward with it. So I think that's a pretty special kind of full circle experience that these individuals provide.

Melanie Cole: Very well said, both of you. Thank you so much for joining us today and sharing your incredible expertise for other providers. To refer your patient to Dr. Leonberg-Yoo and Dr. Redfield at Penn Medicine, please call our 24/7 provider-only line at 877-937-PENN or you could submit your referral via our secure online referral form by visiting our website at [pennmedicine.org/referyourpatient](https://www.pennmedicine.org/referyourpatient).

That concludes this episode from the Specialists at Penn Medicine. Please remember to subscribe, rate, and review this podcast and all the other Penn Medicine podcasts. I'm Melanie Cole.