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ABHI HUMAR: Hello, everyone. And welcome to this webinar on "Live Donor Liver Transplant at UPMC-- Changing the Paradigm." My name is Abhi Humar. I'm the clinical director of the Starzl Transplant Institute. And over the next several minutes, I'd like to discuss about live donor liver transplant, and specifically the program here at UPMC.

It's appropriate that we discuss liver transplant at Pittsburgh, because this really was the birthplace of liver transplantation, started by this gentleman shown on the screen, which is Dr. Thomas E. Starzl, who many regard as the father of modern day transplantation.

I started the program here, and over a course of about 30 years, liver transplantation has now become the established definitive treatment for just about anyone with end stage liver disease with survival rates that are well over 90% at most centers at one year post transplant.

So fast forward to today and the present condition of liver transplant in the United States. There are roughly about 13,000 to 14,000 people waiting for a liver transplant in this country. And we do roughly about 8,000 liver transplants. And if you look at the graph, you'll see right away that creates what we call "the gap," which is the gap between the number of people that need a transplant and the number of transplants that are actually happening.

And that creates a waiting list. And that's because there are not enough transplants for all of the people that need a transplant. And therefore there's a queue, so to speak.

And what does that exactly mean for an individual that needs a liver transplant? Well, there are three important consequences to this waiting list. One is that there's roughly about a 15% to 25% chance that any one individual will never make it to a transplant. They will succumb. They will die from their liver disease before they get to the top of the transplant list.

But for the people who actually do make it, what it also means is a longer waiting time. Because priority on the waiting list is decided based on level of acuity of illness. And so therefore, the sicker patients move to the top of the list. And therefore, there's a waiting time before you get to the top of the list. And that can be anywhere from one to two years, depending on where you are at starting.

And then the third important consequence is that we cannot offer transplant to all of the patients that potentially could benefit from a transplant. We have to select the patients who are going to do the very best. Because there's no point having 30,000 people, for example, on the waiting list when you're still only doing 8,000 transplants a year.

A living donor liver transplant then offers a possible solution for all of these main problems that are associated with the waiting list. What exactly is a living donor liver transplant? A living donor liver transplant essentially involves taking a portion of the liver from an otherwise healthy donor and transplanting it into the person with the diseased liver.

And this is possible because of two unique properties of our liver. One is that we have a lot of extra capacity built into the liver. You don't really need 100% of your liver to do everything that the liver does. In fact, you really need a very small portion of your liver to do everything.

And secondly, the liver is one of the few organs that we have that will actually regenerate. And within a very short period of time after a resection or donation, the liver will regenerate back to full size.

So there are several advantages then to a living donor transplant over a deceased donor transplant. The most obvious is that if you are in that 25% that was going to come from your liver disease before getting a transplant, this becomes an immediately a life saving opportunity-- a way to decrease the waitlist mortality.

But even for the other patients that would have normally gotten a transplant, what it allows us to do is decrease the waiting time and allows us to transplant recipients before they become critically ill, essentially turning an emergent operation that's often done in the middle of the night, with a deceased donor, into an elective operation that's done during the daytime. And we can plan the surgery and make sure that the patient is in the best possible condition before they undergo this.

Other advantages include some immunologic advantage to the recipient, the ability to minimize the amount of time that an organ is preserved, and also the fact that we add to the pool of organs. So for every one individual that gets a liver transplant from a living donor, that's one individual that doesn't need a transplant from a deceased donor.

There's also financial benefit to the system of doing living donor transplants, and I'll show you some data to support that. And that has to be balanced by the disadvantages of a living donor transplant. And the main disadvantages of a living donor transplant are the risks to the donor. Now remember, this is an individual who is undergoing a major surgical procedure really for no personal physical benefit to themselves. And therefore, we have to weigh carefully the risks, both the short term as well as the long term, to the donor.

Other disadvantages include possible higher complication rates. Because remember, you're only transplanting half a liver not a full liver, and therefore vessels and biliary ducts can be smaller and there's decreased hepatic reserve. But again, I'll show you data that shows that this really is not as much of a concern.

And as I've shown in this illustration, you can see that the advantages, actually, in my mind, outweigh the disadvantages of this procedure. And in fact, if you look at the national data, look at the outcomes of live donor transplants, this is the national data showing patient survival as a proportion of time. You can see that the live patients who receive a live donor transplant, shown in the red, compared to the patients who receive a deceased donor transplant, shown in the blue, have a survival advantage of roughly 5% to 10% over a period of 5 to 10 years out from the procedure.

So if there are so many advantages to live donor transplant, why is live liver transplant underutilized in the United States? And it is underutilized. If you look at this graph, you can see that the total number of live donor liver transplants in this country has really not changed very much over the last decade and remains roughly at about 400. It has increased in the last few years, but it's still only accounts for roughly about 6% of the total number of transplants that we do. The other 94% come from deceased donors.

Now this is in sharp contrast to many other places around the world. So if you look on the graph on the right, you can see that the proportion of live donor transplants per million in the US is much lower certainly than places in the Far East, such as Korea, Taiwan, Hong Kong, Japan India the Middle East. All of those places, live donor liver transplant actually make up the majority of the transplants that are done.

And there are very few centers actually in the United States that perform a lot of live donor transplants. This is national data from 2018. And you can see that in 2018, there were only 12 centers in the United States that did more than 10 live donor liver transplants in a year. That means roughly about, or not even quite, one transplant a month. And you really have to be able to do a certain minimal volume to maintain the technical expertise.

So why have the number of live donor liver transplants remain so low in the United States? There are really a lot of reasons for this. But some of the important ones are, yes, it is a complex procedure and it requires a degree of technical expertise and investment of the institute in a team that can perform this. We're heavily regulated in the United States by UNOS, CMS, the state. And so the entire program can be very heavily regulated and suffer consequences if there are problems.

Donor complications and deaths, when they have happened in this country, have been highly publicized and can cause risks not only to the program but also to specific team members. And while all of these reasons are important, in my mind, the biggest reason why live donor liver transplant has not flourished in the United States is that people just don't know about this procedure or are misinformed.

And who do I mean by people? Well, essentially, it's really the tripod of what makes up healthcare in this country. That includes the patients themselves and their families who we're looking after. They don't know about live donor liver transplants. The providers, these are the family physicians, the gastroenterologists, even the hepatologists that are subsequently managing these patients, really don't know or misinformed about what live donor liver transplant is about. And then finally, the payers who will have to eventually pay for this procedure really don't have all of the most relevant data.

And we hear this every day when we see patients that come to us. And these are just some of the quotes that our patients repeat to us. And these are things that they've been told by their medical team. My doctor told me that this was a last resort only. My doctor told me that I was not a candidate. My transplant team told me that this was just for pediatric patients because of the amount of liver needed for adult patients. That this is an experimental procedure, this could only be done for kidney transplants. Only family members could be donors.

And these are all misnomers about live donor liver transplants and not the truth. But these are what patients have been told and what people believe.

And definitely there's a need in this country for it. And I'll just go back to the curve that I had shown you. Because there are roughly 14,000 people waiting and only 8,000 transplants done. And I'll submit to you that that 14,000 that we see here is actually artificially low. If I was to list every single patient that could benefit from a liver transplant in this country for a liver transplant, that number may be in fact double what we see over there.

And in fact, if you look, the American Society is actually very accepting of living donation. The general population accepts living donation as a very viable option. And we know this. This is the result of a survey that we had done to roughly about 5,000 US residents, just a random survey, asking, would you be a willing liver donor for someone that you knew? And 70% of people replied yes. And the most surprising statistic is the one below it. Would you be a willing living liver donor for someone you didn't know? Undergo this major operation for someone who you'd never met? 40% of people said yes, that they would. And that's really just a very surprising statistic. I don't think you would see that in any other country around the world.

So UPMC strongly believes in the value of live donor liver transplant and have invested in trying to grow this as a method to help our patients, both at the pediatric as well as on the adult side. This is a graphical display of the number of transplants that we've done over the last decade. And the purple represents our adult transplants, the green the pediatric transplants.

And you can see that, especially in the last five, six years, we've really made a concerted effort to try to offer this to all of our patients and significantly grow our volume. And in fact, last year, we did over 100 live donor liver transplants at our center, the largest at any program in the United States.

Now, if you're going to offer this to patients and believe in it, you have to be well versed in the outcomes. And remember when we talk about outcomes with this procedure, there are actually two patients that you have to discuss, and outcomes in two groups that you have to discuss. And that's both the donors and the recipients. And really both are equally important. And in some ways, the data and the donor is really at the crux of this. Because if you cannot do this with the utmost safety, then it should not be done.

So if you look at the national data in the United States-- and this is available readily for anyone to look at-- as of the end of 2020, there were roughly about 8,000 live donor liver transplants that had been done in this country. To date, there have been six early donor deaths related directly to the procedure. That's roughly about a mortality rate of 0.8%.

And additionally, three donors that themselves received a liver transplant, because their remnant liver that was left behind was not adequate for them.

Overall complication rate-- this is based on surveys that have been done from multi-center studies-- is roughly at about 30% with roughly about 10% major complication rate.

Our own data shows that over a period of 20 plus years that we've been doing this procedure at UPMC, and especially in the last decade, we've had no donor deaths, no cases of liver failure. We have an overall complication rate of roughly about 20% with a major complication rate of about 8% in our donors, and a mean length of hospital stay now down to about five days.

This is our outcomes and our donors looking at complications specifically, and you can see that we have a reoperation rate of roughly about 6% in our donors, of which half are due to early complications such as bleeding and bowel perforation. And the other half are related to late complications, mostly hernias.

We've seen only six bile leaks to date in our donors, all of which have been managed with either percutaneous drainage or ERCP. And then a smattering of the regular medical complications that you would expect in someone undergoing a major abdominal procedure.

Now remember, it's also key to look at other outcomes when you're talking about donors. Because these are healthy individuals that have to go back to normal quality of life. So when we look at recovery at our center, roughly five to seven days in hospital, it's actually, as I said now, down to about average length of hospital stay of five days for our donors. Four to six weeks before they're back to a desk job, 10 to 12 weeks before they back to a physical job. And most of our donors will report that by 3 months post donation, they're 80% to 90% back to their normal level of health,

Now let's look at the recipient outcomes. And this was an analysis that we had done, just been published just recently in the annals of surgery. This looks at outcomes at our center from 2009 to 2019, so a 10 year span. The left shows patient survival. The right shows graft survival. The blue is our live donor transplant cases. The red is our deceased donor cases. And you can see that there's roughly about a 5% to 10% survival advantage in both patient and graft survival with the live donor transplant patients versus the deceased donors over that period of time.

Now partly this is due to the fact that the liver donor patients are not as sick going into their procedure. And this is the demographic makeup of that series. And you can see that the mean MELD score of the patients that are undergoing live donor liver transplant is roughly about 15 compared to about 24 for the deceased donor patients. That's the actual calculated melt.

But that's the way it is, that patients do not have the option of choosing what meld they can get a transplant at. Certainly not if they're going to get a deceased donor, they have to wait until they're at the top of the list. Whereas with the living donor transplant, yes, we do have that luxury. We can do a transplant in patients that have a lower MELD score, as long as they meet the criteria, and as long as we feel that they're going to get a survival benefit from a liver transplant.

And there are other outcomes that are significantly better in patients that do a live donor. And again, from the same series, you can see that the median length of stay in hospital is shorter. The chance of receiving intraop transfusions is less. You can see that roughly about half of our patients that get live donor transplants don't actually receive any intraoperative blood or blood products. And the incidence of major complications, such as early postop renal failure, is significantly less because these are healthier individuals going into their transplant.

One of the concerns of live donor liver transplant, as I said, because this is a technically more complex procedure, there's a higher incidence of technical complications, especially vascular and other complications. And certainly early series did demonstrate this. But what we've seen, with increasing comfort level with this procedure, we've seen a decrease.

And really now, our overall complication rate is really no different between our live donor and our deceased donor. As you can see, our three month reoperation rate is roughly about the same. Our incidence of major vascular complications, such as a hepatic artery thrombosis and portal vein thrombosis, is no different. Our overall incidence of other complications is actually no different between our live donor cases and our deceased donor cases, roughly at about 15%.

And if you look at cost and resource utilization, resource utilization in terms of post transplant care-- how many times are the patients having to come back to the emergency room? How many times are they getting GI or invasive procedures? Or how many times are they needing radiologic scans on an emergency basis? You can see that it's significantly less with live donor transplants, which overall accounts for overall lower costs. And when we did a cost analysis, just look at the bottom line, roughly about 30% lower cost associated with a live donor transplant versus deceased donor transplant when you factor in both the inpatient as well as the outpatient care.

Now this is how our outcomes compare to other centers around the country. And if you're interested in looking at the national data on transplants, you can go to OPTN.org and look at national data as well as any individual center data. And this is how the data is shown. Each circle here represents a transplant center. The x-axis here represents your volume, the number of transplants that you're doing. And the y-axis represents outcomes expressed as a hazard ratio.

So if you're at your expected level, then you're at 1. If you're worse than your expected outcomes, then you're above this. If you're better than you expected outcomes, then you're below this.

And this is our center right here, in terms of graft survival at one month in a year. And you can see that we're a large volume center. We're the largest volume center compared to others. And we have good outcomes in terms of our hazard ratio well below our expected outcomes compared to the patient population that we're doing.

Now we've seen other benefits for our patients. So if you're a patient waiting for a transplant, some of the important things that you want to know is, what's the chance that I'm going to get a transplant at that individual center? That's called something called the transplant rate.

And if you look at our transplant rate over the last five, six years, you can see how much it has increased. It's almost tripled, actually, in the last year compared to what it was back in 2016. And that's obviously advantageous for the patient, because that means that they have a much better chance of getting a transplant at our center.

And the other important statistic that's important for them to know is, what's the likelihood that I'm going to die while I'm waiting for a transplant at any center? The waitlist mortality. And again, you can see that our waitlist mortality has significantly decreased over the last five years, roughly half of what it was back in 2016 to now roughly at about 12%, significantly better than the 25% where we were at before we were significantly utilizing live donor transplants.

So this is how we started thinking about live donor liver transplants. Initially we thought that this would be good for patients that were low on our waiting list but that really needed a transplant that had bad prognostic signs-- patients with liver tumors that we knew that could still benefit but were outside of criteria to qualify for deceased donor transplants. International patients, we thought these were the best patients. Because you didn't want to use a scarce or deceased donor on these patients.

So we started with these patients, and we saw that we could get good results with this group, and therefore started expanding. And so we started to do higher MELD patients, patients that were sicker, utilizing techniques that have been well reported. Larger size grafts, younger donors, and technical modifications to make it work in sicker patients.

We expanded to patients that had tumors, especially tumors that didn't meet the criteria for a deceased donor transplant, because we knew that they could benefit from a liver transplant. Patients with hilar cholangiocarcinomas or metastatic colorectal cancers. Hepatocellular cancer beyond Milan or metastatic neuroendocrine and other rare tumors that all could benefit from a liver transplant but really couldn't qualify for a deceased donor.

To the point where we're at now, where we even offer ABO incompatible transplants using this protocol to desensitize patients, so that we don't really even have to match the blood type of donors now. We can utilize this method to transplant individuals.

So this is where we're at currently, where we feel that a suitable living donor liver transplant is really the first and best option for all of our patients, regardless of the type of liver disease that they have, whether they're low MELD or high MELD, whether they have chronic liver disease or acute liver disease, whether they have a tumor or don't have a tumor. If they need a simultaneous liver kidney, if they're redo liver transplants. All of those patients we feel will do better, or at least equally well, with a living donor.

And this is our own data looking at these what we would call higher risk patients-- retransplants, higher MELD patients, patients with tumors, especially those beyond Milan. And you can see that there's really virtually no difference in terms of outcome in our living donor versus our deceased donor.

And in fact, in certain patient populations-- so for example, in older patients, we have significantly better outcomes with living donor transplants. And that's because an older patient is just not going to be able to tolerate waiting that period of time on the waiting list. They're not going to tolerate having a MELD score of 25 or 30 and then having a transplant. And so we really try to make patients aware of the reality of this.

We often hear that, well, during the COVID time, should we back off on this? Should we not wait to do elective cases like live donor transplants? Well, live donor transplants are really not elective cases. These are life saving procedures in patients. And you have to remember that, for patients with end stage liver disease, the risk of getting COVID is still there. And in fact, we know from data that patients with cirrhosis and other forms of liver disease, if they get COVID infection, their risk of mortality is actually very high.

And this was featured in a great article in the *New York Times* several months ago, which was entitled "The Pandemic's Hidden Victims: Sick or Dying but Not From the Virus." And it talked about patients that were dying from their disease because they couldn't get access to a life saving transplant because programs were not offering it, or were on hold, or were concerned about the virus.

And so we really have not halted our transplant operations at any point in the last year. In fact, this was our busiest year for transplants. Because we offered it really to all of our patients.

And patients sought us out, both on the recipient side as well as the donor side. We had many donors that reached out to us because they were interested in donating. And you can see that over the last few years, the number of donors-- these are anonymous donors, what we call altruistic donors. Or these are individuals who donate to really individuals that they don't know. They're just interested in helping other individuals.

And this has really come about in large part because of the power of social media. You can see that many of these altruistic or anonymous donors actually came through social media, through posts that they read on Facebook about patients in need of a transplant. It just highlights the power of social media and getting the word out about transplants.

So what do we think are the keys to a successful live donor liver transplant? So obviously, you have to have a strong living donor transplant team at your own center. This is not something that can be done by one or two individuals. This really requires a whole village committed to making this successful. Not only the surgeons and the hepatologists, but also your coordinators, social workers, counselors, advocates, to even the people who are speaking about it to individuals, marketing, et cetera that really spread the word.

Because one of the very important things about doing a liver transplant, as I had said before, is the educational and the awareness of it. And that's one of the things that we've invested in highly is the campaign to make people aware about live donor liver transplants. And as I said, by people, I mean the patients and their caregivers, the physicians who are looking after these and the pairs.

And each of them require a slightly different targeted approach for education. And so for physicians, we have brochures that we send out. We do programs such as this. And we've gone out to individual centers doing rounds and speaking about live donor transplants. For patients, we again have various educational resources, including brochures, video series, and general campaigns including advertising campaigns. We really call them educational campaigns to educate the general public about live donor liver transplant and what it is.

And we utilize the power of social media as well as other things to create and help people find donors. So this is something called the champion program, which really teaches patients who need a transplant how to go about the process of finding donors for themselves. Because if you think about it, if you had to ask someone about how to find-- whether they would be willing to be a living donor for them, it can be a very difficult ask if you don't know. And this just this program teaches them about how to go about it, how to use social media, how to use people that are within their circle to help get the message out about their need.

So we feel strongly that it's time to change the paradigm of how we think about liver disease in the setting of a live donor liver transplant program. And remember, the current rules of allocation and MELD, well, these are very appropriate and good for utilization of a limited resource. Remember, these were really set in place for that limited resource-- that condition, or that situation, of deceased donor transplant where you have 14,000 recipients, potential recipients, but only 8,000 donors.

So that ratio of 14,000 to 8,000 makes you have these rules in place. But with a live donor liver transplant, that ratio is really not there. The ratio is very different. It's one donor and one recipient. The ratio is actually one to one. And therefore, these rules don't necessarily apply in the live donor transplant situation.

And really the criteria for a living donor transplant should be based on a survival advantage. It's how we base our criteria for offering any medical therapy to patients, whether it's a new drug or a new surgical procedure. Because it provides a survival advantage to the patient.

And if you do that, then live donor liver transplant becomes not a last resort, but rather the first and best resort for patients. And so the way we think about living donor liver transplant, and our selection criteria, are really very simple at our center.

If we feel that the patient will get a significant survival benefit with the liver transplant versus best of the therapy that's available out there, whether it's chemotherapy, whether it's surgical resection, whether it's anything else. If a liver transplant will provide them with a better outcome versus that, and they have a suitable willing living donor, then we think that is a suitable situation to do a living donor transplant on.

By utilizing this approach, we think that it's possible that we can actually eliminate the waiting list. Because there are so many donors potentially that are willing to be donors. But to do that, we really have to educate. We have to educate, as I said, the physicians. We had to have to educate the payors. And most importantly, we have to educate patients and their families about the value of this.

But I think it is possible, as I said, to eliminate the waiting list. So that patients don't have to be on a waiting list waiting to find out if they're going to get a lifesaving transplant, never knowing when that day is going to come. And it'll be our patients that will take us there. And we've seen many, many special situations of different types of donors that have come forward to help their loved ones or to help complete strangers. And all of these are very unique and very special stories.

So I'll stop there, and I think you'll have an opportunity to fill out a questionnaire and ask any questions that you may have regarding this. And we'd be happy to reach back out to you with answers to those questions.

So thank you for tuning in. And as I said, if you have any questions, please let us know. Thank you.