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Nicole Harr: Thank you everyone for joining, we're really glad to have you here for cardiovascular issues in ADPKD. My name is Nicole Harr, and I work at the PKD. Foundation, I'd like to welcome each and every one of you. And just remind you to stay muted. If you can during the session, we'd appreciate that it helps with audio quality for everyone. And also, along throughout the presentations, feel free to put your questions in the chat box. And we'll have a Q&A at the end of the session. So, I'd like to turn this over to Dr. Chebib. And Dr. Sabbagh. They're going to be our presenters today. And before I turn off my microphone, would you like a 10-minute warning when you're getting it when we're getting close to the Q&A time?

Fouhad Chebib: Sure, that'd be great. Thank you.

Nicole Harr: Okay, thank you.

Fouhad Chebib: Well, thank you, Nicole. And thank you everyone for attending this evening. My name is Chebib one of the nephrologist and kidney doctor at Mayo Clinic in the Jacksonville campus, and I'm joined by Dr. Sabbagh, our cardiologists also from Mayo Clinic, Jacksonville. We're very pleased to be here today. And thank you for being here. And thank you for the PKD foundation for your invitation. So, hopefully over the next 35 minutes or so, we'll go over some cardiovascular concerns or issues and polycystic kidney disease. And particularly, we're going to be focusing on the autosomal dominant form of polycystic kidney disease. And then towards the last 10 minutes, we'll take questions and then prior to that, we're going to run kind of a case and kind of go over the different phases that PKD patients go through and why it's important to look into the cardiovascular and heart issues in PKD.

So, just as a disclaimer, this is for educational purposes only. And then both of us as speakers don't have relevant financial relationships, except maybe one disclosure that I'm very invested in PKD. And this is what I do for him for daily living. So, this is kind of my disclosure, but not financial. Alright, so no need to introduce PKD to you as an audience. But as you know, it's one of the most common inherited kidney disease, kidney diseases, and particularly probably the most common inherited diseases in general, across

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all diseases. And it's leading to relentless development of Kidney cysts, which are fluid filled sacs that lead unfortunately, eventually to kidney failure. And it accounts for about 5% of patients who have kidney failure in the United States, and maybe about 10% in Europe, as the diabetes is a little bit less in Europe.

So, as a natural history of ADPKD. Typically, we have very enlarged kidneys, very distorted kidneys, that are filled with fluids and sacks. But then early on in life, the kidney function is relatively well preserved, and then later on it declines. So, to be able to understand who has more severe disease than mild disease, we need to have other biomarkers such as Total Kidney Volume, or TKV. And then later on, we use traditional biomarkers, which is the Creatinine, that gives us the GFR or the glomerular filtration rate, which is the percentage where the kidneys are filtering. And then we also use the combination kind of all the time but towards kind of the later stages, we use the combination of this biomarkers autosomal dominant polycystic kidney disease is not just kind of one fit one size fits all.

It's a highly variable disease, where some of the patients would reach kidney failure earlier in life, and about half of the patients may be in their 50s, about three quarters of the patients in their early 60s, but some are in their late 70s-80s. And some would never reach kidney failure. So, it's highly variable. In general, males would reach kidney failure a little bit earlier than females. And about 98% of males with autosomal dominant autosomal dominant polycystic kidney disease will reach kidney failure by age 80. And about 77% With reach kidney failure by age 77% of females. Now, as you know, it's an inherited disease. So, you might have inherited either the PKD-1 or PKD-2 gene. And then within the PKD-1, it might be, there might be more severe mutations than others.

So, those are the changes in the DNA code that leads to the protein to be not functional. So, PKD-1 is more severe disease, but here I would like to show you that even if someone inherited bad mutation, the big anyone truncating mutation, they might not have a very severe disease versus kind of similar mutation may lead to a more severe disease. So, there's a lot of variability

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and even within the same family, some patients might reach earlier than others. So, I always say each patient would have their own path. And the reason why it's such a complex kind of why there's a lot of variability is that it's interplay of a lot of things. So, it's really beyond what you inherited from your parent, or if you develop a new mutation by yourself. So, what we call de novo mutation, it's not only what you inherited as PKD-1 or PKD-2 gene, it's also what you inherited as modifier.

So those are other genes and other things that you inherited in general, that could affect how the how the mutation, how the proteins are interacting. It's also there's something called epigenetics. We're after kind of what the protein have changes, even after what you inherited. So even a twin might have different phenotypes, or different disease severity in PKD. And also, that's a big component that you might be able to control, which is what environmental factors can affect polycystic kidney disease, like low fluid intake, or drinking less fluid may might lead to worse disease. If you eat a lot of salt, if there's high caloric intake and obesity can affect the kidney function negatively, and PKD negatively. So, all these factors interact together to affect how big the kidney cysts and how many kidney cysts you have.

And then also the thirst hormone called vasopressin, which is a very important hormone in PKD. All these effects all these different mechanisms on the cell level. So, how the kidney are producing the fluids and how they're growing to form a cyst. And all those we can see them. When we see you as a patient, we see if you have early onset of kidney, high blood pressure, hypertension, or if you have a lot of cysts, bleeding blood of blood in the urine, or cysts bleeding or cyst infections. And also, we look how big the kidneys are on the CT scan or MRI. We have other additional novel biomarkers that that all the scientists and clinicians are looking at to look at the severity of the disease. So, what can you do yourself to help yourself in PKD? So mostly, you'd like to slow down the disease process.

So, although you inherited a mutation that you don't have control, but there's a lot of these environmental factors that you can try to slow the disease process. There's other things that you need to be aware of that come with

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PKD. So, you can screen and manage those accordingly and appropriately. And you also can make sure that you advocate to yourself to get the right screening with your providers. And then also incorporate a healthy lifestyle. So, whether you have PKD or not, mostly in your in your household, it's very important to incorporate a healthy lifestyle early on, especially with the kids being at risk of having PKD. And not knowing if they have it or not, it's good for everybody to be very healthy, and incorporate that on a daily on a daily basis.

So, PKD is a systemic disease, which means that although the main concern is the kidneys, where they become cystic or have a lot of kidney cysts and kidney failure, you're very well aware that the liver also can have liver cysts. And also, these policies in protein or the protein that are abnormal in PKD. They're also present in the blood vessels in the heart, and in many other organs. But we will focus on the blood vessels, particularly the brain, blood vessels and heart in this presentation. So, what are the cardiovascular or the heart manifestations in polycystic kidney disease. So high blood pressure is a very important factor. And we're going to focus quite a bit on that. There's the defects in the valve, sometimes not all the time. There's also a higher incidence of brain aneurysms that you would need to be aware of.

And then also the function and the structure of the heart chambers sometimes could be different in PKD. So, the focus on high blood pressure is because it's a very common symptom. That might be the early symptoms that leads to the diagnosis of polycystic kidney disease. In general, as human beings, we tend to have more high blood pressure when we're mostly in the 40s-50s. And that's when typically, it gets diagnosed.

But with PKD it's diagnosed earlier in the early ages of 30 to 34. Some patients even have high blood pressure as children, so 20 to 30% of kids with PKD might have high blood pressure. So, there's a recommendation to check patient where are kids who are who are at risk of PKD. So, they have family history of PKD so one of their parents have PKD the kids before they get screened for PKD they need to check their blood pressure with their paediatrician on a regular basis, just as recommended by any other child and

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then if they are hypertensive or having high blood pressure, they need to be treated accordingly. Furthermore, if blood pressure is not controlled, it can lead to worsening kidney function, and it might make that decline of kidney function faster.

So, it's really one of the most important, potentially treatable variable and PKD. And it's very important for you as a patient to advocate for yourself and make sure that your blood pressure is well controlled. Because if you see your provider once every few months or every year, they don't have that control to kind of make sure that the blood pressure is well controlled. So, it's up to you to make sure that you're checking your blood pressure on a regular basis, you're following a good diet, you're making sure that you're getting the right treatment for your blood pressure. Now with why does the blood pressure occur in PKD, and sometimes, and many times it occurs before the kidney function declines. So, very early on in life with PKD, we might have high blood pressure.

And that's because of a lot of complex interaction that the kidney cysts have been leading in the kidney. So, the blood pressure is controlled by different variables. And in general, it's controlled by the hormones that the kidneys secrete an interaction between the kidney and a very small gland called adrenal gland, which comes on top of the kidney. So, these between the kidney and adrenal gland, there's kind of an axis of hormones, mostly the renin angiotensin, and it's more released because of the expansion of the cyst in PKD, the compression on the blood vessels in the kidney, which leads to a lot of growth factors and other hormones that leads to mostly hormones that leads to the increase in the high blood pressure.

So, that led to a very large study that many of you probably have been in the study, or some of your family members have been in the hall a or how the study which looked at the effect of blood pressure control on the slowing of PKD. And also, the effect of combining two types of blood pressure medications, and then the effect of lowering the blood pressure to a lower level. So, this study showed it was a very large study.

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So, thank you, for everyone who participated about 558 patients in just that one arm of health a study. So, in the patients that were able to reach blood pressure in the 90s-110. So, the low target where their kidney volumes was, the kidneys were growing at a lower rate as compared to the normal target or the traditional target where we try to achieve 120 to 130 millimetres mercury. So, there's a potential benefit where you can slow down the disease process with lowering the blood pressure.

And the reason why we really like the blood pressure to be well controlled is we try to avoid the complications of high blood pressure. So, having high blood pressure can and if it doesn't get controlled, and if it's high for many years, then the blockchain the heart chambers and what we call the left ventricle, so one of the big chambers of the heart can get thickened. And that's what we call LVH or left ventricular hypertrophy. And in patients who have high blood pressure, and about half of them might have this LVH. But this is an old study. And now we see that it's much less. That's because we have better control and better awareness of high blood pressure. And we know that if we have thickening of the heart, that means the blood pressure was not controlled.

And we know that this is combined with a poor outcome on the kidney and overall survival. Other complications of high blood pressure include vision loss, if really the blood pressure is very high, and then 100 for many long time, for a long time, or brain stroke, or a heart attack, or blood vessel damage and leading to heart attacks and other blood vessel damage in addition to worsening kidney function. And that's the general complication of any one with high blood pressure, whether they have PKD or not. Now in PKD, again, we try to target a little bit of a lower blood pressure target as compared to anyone with high blood pressure. And particularly someone who's on the younger side and will have preserved kidney function with very big kidneys.

So, what we call the mayo imaging class one C-1D-1E. So, this is adjusted age adjusted kidney volume. So, the patients who are at risk of rapid progression, and then if someone has vascular or valvular disease, we'd like to have their blood pressure on the lower side. And everybody else would be

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at 130 over 80 as a target, and that's an average so the blood pressure can go up and down, but we like an average to be in that range.

And then we'd like to start with either an ACE inhibitor or an ARB. So those are classes of blood pressure medications, so like Lisinopril, Losartan, and others. So, either or without don't usually combine both because if we combine them, there might be a risk of higher potassium. And one of the whole study the whole B show that there is no benefit, we can do also a better blocker or then a diuretic or a calcium channel blocker. If you're on general Q, we try to leave the diuretic to the last resort. And sometimes when the kidney function declines further, when you have advanced chronic kidney disease like stage four, or five, you might need that to keep you from building up the flow, the fluids and also to control your blood pressure.

So, things that you can really adjust your risk factors for is when you have high blood pressure, it's important to look at if you have a lot of protein, look at the echocardiogram assess for how thick the left heart size is, and then also look at your cholesterol and make sure your that's well controlled. And having a cholesterol, the LDL or the bad cholesterol being less than 100.

So, if you need to be on a medication that's important to start, then if you're smoking, hopefully I can convince you today to stop smoking. And if you're not smoking, don't take up that habit. So, those are the risk factors that you have control over. And you can gift yourself the health by not by adjusting everything that you have control over. Now, if you happen to have diabetes, which could happen in PKD, as anyone in the general population, it's important to control your sugars. And that's because of all the so the high cholesterol, being obese, having extra weight, having the sugars having the high blood pressure, it's all going to affect your blood vessels, your heart, your heart health, and that might affect your ability to get a kidney transplant or have good dialysis later on.

So, you need to keep your, your heart health as strong as possible. Now one of the biggest things that you can control is salt. And I always tell my patients salt is your enemy. Do not eat salt and try to restrict it. So, salt is hidden. And

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I'll show you kind of how it's hidden. But mostly, there's a lot of studies that show that if we restrict salt, particularly in PKD, there's important that it's better. So, if we for patients who've been eating more salt, it has been shown in the crisp study. And many of you are in the end the crisp study that followed the patients for decades and looking at the risk factors and why they have more severe disease than others. The patients who eat more salt, they have bigger kidney growth, so their kidneys are going to grow.

And that's also effect associated with faster decline in the kidney function. And then reaching kidney failure faster and more often. So, every 400 milligrams of salt a day can increase your risk of reaching kidney failure by 8%. So that's for every 400 milligrams. So, we recommend to restrict to 2300 milligrams a day. Now there's a study in Netherland from the Deepak trial that that followed the patients, almost 600 patients for four years. And then they showed that the salt intake is associated with high blood pressure, of course, and lower kidney function. But here the new thing is that it's not. So, we always think of eating less salt is important to control your blood pressure. So that's very important. But what's also more important in PKD, it affects your thirst hormone vasopressin.

So, there's a test called copeptin that we don't typically check except in trials, and for particular reasons, but mostly in kidney in clinical trials. And this trial showed that the salt intake affects your thirst hormone. And that's why it's affecting the kidney function to get to progress faster. So, definitely restrict yourself, that's the home key message. Now high salt affects in addition to the blood vessel, the kidneys, the immune system, inflammation, the brain and the bone, it's important to know that it's not only the shaker that that's high in salt. So, that's about 10%. What you add at the table, the rest is all in the processed foods hidden. So, it's important for anything that has a label in the back to look how much salt sodium you're having in each of the of the servings and how many servings you're getting.

And be aware of these. So, when you're doing your grocery shopping, and if you have issues with or challenges trying to understand what's high and what's not. Or you're feeling like you're not able to eat much. It's important

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to meet with a dietitian and have you have them guide you through the process. Now the other thing that you can modify is how much you eat and how much you put on weight and that's a challenge for everybody. And we're not going to deny it's very challenging to be in a normal body mass index. But let me show you a little bit of the data. And hopefully, I can encourage you to lose a little bit of weight if you have excess weight on you. So, another kind of post hoc analysis. So, after the fact of the clinical trial, one of the groups has looked at the patients in halt.

And they looked at how fast on how fast the kidneys are growing and how fast the kidney function is declining. And they saw a big correlation association between the weight or the body mass index and how severe the diseases so for patients who have are overweight or obese, in comparison to someone with normal weight, their total kidney volume rate of growth, so how fast the kidneys are growing, it's much higher and overweight and obese, and the kidney function decline is faster. And, and, and overweight and obese patients. So, it's important to kind of try to achieve a body mass index of around 25 to 28 to 25. Preferably if you can. Now there's a lot of valvular connections between ADPKD and having the valve being a little bit abnormal.

So, there's two terms we talk about a stenosis where the valve is kind of scarred and it doesn't open properly. And then there's something called regurgitation or leaky valve. So, it is PKD is associated with both mostly in regurgitation, so the mitral valve here. So, with PKD patients, there's a high risk of mitral valve prolapse, which we mostly monitor. And then there's also a little bit higher risk of regurgitation. We also look at the tricuspid valves on the right side between the two chambers of the heart. And then also we look at the aortic valve, and there's a little bit higher risk of regurgitation, or leaky valve. And then also, our group has looked at all the PKD patients as compared to patients who have other kidney diseases like diabetes and other kidney diseases.

We looked at their echocardiogram within two years of their, of their kidney transplant. And we find, and we had about 271 patients in each of these

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groups. And we found that PKD actually have much better heart health as compared to someone with diabetes, or someone with kidney failure from not diabetes and not PKD. So, what I mentioned that LVH, or the thickening of the heart was only 40% in PKD patients as compared to other patients who are the same age and same gender. So, diabetic was unfortunately the worst group in this category, the mitral valve regurgitation and tricuspid regurgitation is also lower in this group. So, it's a little bit lower than what the other groups have shared.

And then also the survival of patients after transplant, it's much better for PKD patients as compared to diabetes or other kidney diseases. Then also patients with PKD had what we call maze free survival rates, so they had less strokes, or heart attacks as compared to diabetic diabetics and other kidney diseases. So, some good news for PKD patients is that they're, although we're talking about cardiovascular challenges, they're typically healthier than other kidney disease patients.

But that doesn't negate the fact that you need to keep your health, heart health as healthy as possible. Okay, and this is the same study just kind of showing you a little bit more details that PKD here and blue typically are much better than a time of transplantation, much better in terms of the heart valves and then as the heart function, so how the heart is pumping or relaxing also, it's much better at time of transplantation. And this is what I mentioned that after kidney transplant, this is in blue, the PKD patients, they do much better and they survive for longer and much longer as compared to other kidney disease patients. And then they survive without strokes or heart attacks, as well. And stroke free survival as compared to other kidney disease patients.

Now over the next few minutes, I'm going to show you a little bit about the brain aneurysms. So, in general population, we, a lot of us are kind of living with a brain aneurysm without knowing so about 1% of anyone in the world has that. And PKD, it's a little bit higher in a chance about 9% overall. And then for someone who has a family history of brain aneurysm, so if one of your family members has an aneurysm, then you're a little bit at higher chance that you might have it as well. So, it's important to get screened. So,

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I'll show you who is screen usually. And unfortunately, it's associated with little bit of higher death and PKD patients. So, it's important to have that screen and taken care of.

So, when do we screen for aneurysms, so someone, so there's no clear guidelines, this is kind of an expert opinion, is age 20 to 65 would like to screen if they have someone in the family have themselves had the brain bleed, if they're going for a big surgery, like removing part of the liver or going for a kidney transplant, you want to be screened, because you don't want to have kind of bad event after a big surgery. So, it's important to kind of take care of that. And also, if you like to know, it's, it's your right to know. And then also, if you have a high risk of occupation, like a pilot, or other high-risk occupation, it's, you owe it to others that you need to be screened.

So, if you have, then you get screened, if it's negative, you repeat every five years, if you're at high risk, or every 10 years, if you're not at high risk. If you do find a brain aneurysm, it's not a completely negative, it's not a very bad news. The reason is, as we follow these patients serially, so when you get a brain aneurysm, it's important to have a follow up MRI more frequently, early on, so every six months, then every year, it's important to control the blood pressure, stop smoking, control your cholesterol. And then also if you have a very bad headache, the worst headache in your life, you need to head to the emergency department right away. But if you do that, we have shown in our institution at Mayo, we followed a lot of patients who had brain MRIs, about 800 patients, and then about 9.3% of them had an aneurysm.

And most of them, they were not that big of an aneurysm, so about four millimeters, and on average. And as we follow up these patients with the serial MRIs, none of them have ruptured, only five of them developed a new aneurysm. And only eight of these patients had the growth in their aneurysms, and seven required a pre-emptive clipping or coiling. So, there will be a procedure with a neurosurgeon to make sure that this aneurysm doesn't rupture. So, it's again that this is what I mentioned, it's good news that if you find it, there's a way to follow and not have a lot of issues from that. And now kind of finishing with a good note is we did a study in Minnesota

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and showed that PKD patients have exactly the same survival as the general population.

So, we've come I think, a long way in PKD world where even if you have PKD, your survival is similar to anyone else who doesn't have PKD, or kidney disease. And that's with the caveat that this is in Minnesota. So, trying to have a very good health. That's also important health care. Now, in general, what I like to show you quick, before we go to the journey with the patient, is if you have typical polycystic kidney disease, so both kidneys are big and have a lot of cysts, it's important to get a CT scan MRI, get your total kidney volume, assess if you have if you are at high risk of rapid progression or at low risk, because then you can get reassured if you have smaller kidneys, and you're not going to reach kidney failure. If you're at higher risk, then there's disease modifying treatments such as generic view that I'm sure you're aware of.

And then everybody would like to keep them as healthy as possible with the blood pressure control, drinking water throughout the day, keeping the cholesterol under good control and lowering your sodium and caloric intake. And with that I'm going to move to the journey with one of our patients and I'll invite Dr. Sabbagh also to join me. And so, let's start with Pete who's a 15-year-old A child, or teenager who has a family history of PKD has mother and grandfather. And so, he asks you if or the parents asked you ask me ask us if they'd like to, if it's important to screen. So, we typically don't recommend to screen yet because there's no changes in the management. But we recommend that they would, he would stay under very good healthy lifestyle and check the blood pressure on a regular basis.

And then hopefully, in the future, we have more treatments that could start early on in life. And at that point, we would like to screen more frequently and at younger age. But right now, if you're 18, and above, it's important to be screened. That's because there's new treatments, and you can slow the disease progression. Now he's 21. And he'd like to, he decided he wants to be screened. So, he got a kidney ultrasound, and he was found to have bilateral kidney cysts on both sides. And then the recommendation was to go to a CT

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scan or MRI to understand how severe the diseases and to understand what to expect in the future. And also, the recommendation was to keep his blood pressure low. And to work on his diet and body mass index. He unfortunately is smoking. So, we'll talk about that.

And then later on, he decided to be on Gen Q or tolvaptan. And then he continues to follow he's doing very well. He's thriving in life, he found that his mother has an intracranial aneurysm or a brain aneurysm. So, we recommended the brain. It's an MRI of the of the of the vessels. There was no aneurysm and then we repeat it in five years, and then every five years thereafter. Then on a follow up appointment, we heard we heard a heart murmur sorry for the typo. And then we recommended that he would go to Dr. Sabbagh, so Dr. Sabbagh ordered an echocardiogram. And please share with us kind of what you would look for usually an echocardiogram and what is an echocardiogram?

Dr. Sabbagh: Absolutely and thank you for the invitation. And hi, everyone. It's a pleasure to be here in discussing all this exciting, this excellent presentation, really an overview on cardiovascular implications of PKD. So, what first of all, what is a murmur? Because I see a lot of patients in my clinic saying I was diagnosed with a murmur. Really, a murmur is something that we hear on physical examination, it's not a disease in it by itself.

It is a physical exam finding meaning when we put the stethoscope, we hear a sound of gushing. And usually that signifies that blood is gushing through most commonly a regurgitant valve. So, the role of valves really is to basically open and allow blood to enter from one chamber to the other. And then when the heart squeezes, these valves either open or closed depending on their location, and it just allows a one-way directional blood to the blood doesn't go backwards, and it just moves from the heart to the body, etc, etc. So, there are different disease entities that would impact the competency of this valve causing blood to move backwards, instead of in the right direction, at high speeds, sometimes causing the murmur. This is what we'll hear.

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And so, when we hear that on physical examination, we order an echocardiogram or an ultrasound of the heart. And this is an examination where the cinematographer holds an ultrasound probe. And basically, that ultrasound probe shoots ultrasound waves that get reflected off the heart. And then we helps us identify the components several components of the heart, including the muscle of the heart. So, that's how we diagnose LVH, or left ventricular hypertrophy the doctor to be told you about. That's how we also diagnose valvular heart disease. So, problems with the valves, the opening and the closing of the valves, either inadequate opening or what we call stenosis or inadequate closing, causing leakiness. And that's what we call regurgitant valves.

It also helps us identify congenital heart diseases. So, problems in the structure of the hearts of people who are born with holes inside their heart or abnormal connections between cardiac chambers and non-cardiac chambers. And that's Dr. Chebib and the group showed that the PKD is associated with, please share with us that information, but the echocardiogram also helps us identify that and that's another source of murmurs.

Fouhad Chebib: Thank you. Thank you so much. And so, Pete has a mitral valve prolapse and we decided just to kind of follow up on that with making sure that if the symptoms occur other symptoms like feeling short of breath, or what have you, then to follow up with additional echocardiograms, and follow up with cardiology clinic, then he continues to kind of grow. So, Pete is now 43 Is kidney function is now 52. That's the GFR. So, we follow something called creatinine, which is a blood test that tells us how the kidneys are working. And he's executed chronic kidney disease stage three A. So, there's five stages of chronic kidney disease, one is normal, everyone with PKD has stage one because they have abnormal anatomy of the kidney. And then as the kidney function and the kidney reserve declines, they move down the stages and kidney five, stage five is kidney failure.

That's when you start thinking about either dialysis or kidney transplantation. So, he'd like to know if there's a way to predict when he's going to reach kidney failure. That's a very important information. And that's very sensitive

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and kind of emotional information to get but it's important to get that. So, then you decide to send him through the PKD platform or something that that we are working on at Mayo Clinic where anyone in the world can have an expert opinion from us, they can upload their clinical information, their CT scans, MRIs, and hopefully in the future, we can also have the urine and blood sample and genetic information. For now, we're mostly focusing on the clinical and imaging.

And then the hope is to have a bio registry and then for this particular patient, like Pete, to kind of get through the platform where we can look at their images, look at the clinical information, and provide back information, where we kind of tell them if they truly have ADPKD, how severe the disease is when to expect the kidney failure to be and the kidney failure onset. So, for him, we looked at the total kidney volume, and we adjusted that by their height and by his age. And we identified them as middle class, one C, so he's on the he is at risk of rapid progression. He's already progressing, where we see his kidney function low, so it's at 52% or ml per minute. And through the mayo imaging calculator, we were able to predict that he might reach kidney failure in 19 years.

And that's not the best magic ball or kind of prediction. So, there is some error to that, but at least gives you kind of good average or good prediction. So, he decided that he's going to have to take everything under control. So, he lost weight, you went into a good BMI, he stopped smoking, he was a little bit pre diabetic, to diabetic and he controlled his sugars. And he made sure that he's always compliant with his medication and medical plan, because it's important to take care of yourself. So, at the time, when you're going to need kidney transplant the team is confident that you're going to take good care of yourself and the gift of life that you're there to receive. So, it's important to really be truly compliant, not because of just compliance, but also because of that's the best outcome you're going to have and cherish the gift of life you're going to receive.

And also, he adjusted all his kind of financial and medical coverage plan. So, it kind of fits, where once he he's declining kidney function, he has good

support from his family, his business, his medical insurance, and what have you. Then he reached around 60, a GFR, of 20. And this is the time when you and your provider should consider going to a kidney transplant evaluation to be on the waitlist. And so usually what we what we do is upon referral, we usually do a stress test. And that's kind of a very common and very usual test that we do before getting on the waitlist, and Dr. Sabbagh will explain to us what, why we do a stress test. And I know we're running a little bit out of time, so we'll move a little bit faster, but we'll get kind of a good idea of what that is.

Dr. Sabbagh: Yes, absolutely. So, just two basic and important statistics. Coronary heart disease, or blockages in the blood vessels that feed the heart are one of the most common causes of morbidity and mortality in patients awaiting kidney transplantation. And it is the number one cause of death. And so, number one cause of death in patients who have received a kidney transplant, so aggressive screening for coronary heart disease, and risk factor mitigation, just like Dr. Attribute mentioned, is very, very important and the way we screened for Korea diseases first we meet the patient and discuss whether or not they have symptoms right. Common symptoms include chest pressure and shortness of breath. And depending on the risk factor profile and the symptoms, we then decide to proceed with stress testing.

And there are different types of stress test, but the basic principle is that we want to stress the heart meaning we want it to pump quickly or rapidly and, and work it so that it unmask these blockages that and declares itself on the stress test. So basically, the most common stress test is an exercise stress test, meaning that we asked the patient to stand on a treadmill and walk and then it ramps up gradually. And then we have hooked to their chest and ECG. So, an electrocardiogram to look at the electricity of the heart, which, again, if the heart, if there are blockages in the blood vessels that feed the heart, there are changes that we see in the electricity of the heart.

A lot of times, we also add an imaging modality to the stress test, in order to visualize changes in the heart with exercise that will also give us more information on whether or not there are any blockages indirectly, such as the

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nuclear stress test, or an echocardiogram ultrasound of the heart. And this is basically what we're looking for these blockages, which are plaques that form in the wall of the vessel. And they gradually grow, they can behave in two fashions, when they grow, they either keep growing, and then people start having chest pain with exertion, or they basically a rupture or burst. And you can see here, there's a clot that forms on top of it. And those are the people who have chest pain at rest. And that's what we call a heart attack, or myocardial infarction.

And so that's why we aggressively we aggressively screen for coronary disease. And if there are any concerning findings under stress test, or what we call high risk features that we identify on how far you want, the patient then on the stress test or not, we then take them to the cardiac catheterization laboratory and do what we call a coronary angiogram, where we take a catheter, which is that that slender structure and hook it to the blood vessels that feed the heart and inject contrast or dye into the blood vessels that feed the heart, and identify blockage. And in certain situations, we proceed with stenting, where we just here, put a wire across that blockage, balloon it a little bit to create space. And then here you can see it. Just see the ballooning part of it to create space.

And then we always put in a scaffold called a stent to push that blockage to the side. And just keep that artery open and improve the blood, the blood supply and real sample of a coronary.

Fouhad Chebib: Thank you. Thank you. Alrighty, so I know we're running out of time. So, I'm going to skip quick on those. But I'll just kind of to give you other ideas, and I'm sure you're aware of these things. So, it's important to try to get a pre preemptive kidney transplant. So, if you have someone who's able and willing to give you a kidney, that's the best way is to do a living donor kidney transplantation. And the best way is to do a pre preemptive kidney transplant, since you're being followed closely, you know exactly when your kidney function is going to decline down to the 10%. And then at that time, you kind of everybody's approved from the recipient, so the patient and the donor. And then they receive a kidney donor, the kidney donation and the transplantation.

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Now, if the donor is not a good match with the recipient, there's a way called kidney pet program, as long as there's someone willing and able to donate a kidney, then there will be a lot of swaps, it could be up to 10 pairs or even more with twin among many centers. And a lot of times it will happen where you will get a kidney transplant, even if you're incompatible or high-risk match type of things. And then so maybe we'll skip that just to allow to allow the couple of questions. And, again, as a providers, and as Mayo Clinic, we are in this journey together with you. And we appreciate your trust in us. And being in many clinical trials and seeing you all the time in the clinic. It's definitely an honor and a privilege. So, thank you. And with that, maybe we can take a few questions. Sorry, we ran a little bit out of time.

Nicole Harr: That's okay. I think we'll get a couple and thank you so much. That was a wonderful presentation. One question we have is does a family history of both PKD and heart issues imply an increased risk for heart issues?

Fouhad Chebib: So, having family history of heart issues? Does it increase risk of heart issues? Not necessarily.

Nicole Harr: In PKD patient's family history of PKD and heart issues?

Fouhad Chebib: Yeah, not necessarily. So, the studies have shown that anyone with mutation of PKD so having those policy systems being abnormal, then they are at high risk. There is no particular association except if there's like non dilated nonischemic, dilated cardiomyopathy. So those are rare things where the heart is more kind of dilated and it's not because of a heart attacks and heart disease. Those are some somehow inherited. So, there might be connection but not in the general sense.

Nicole Harr: Are PKD patients are at higher risk of needing valve replacement?

Fouhad Chebib: So, given that they're at high risk of having aortic valve regurgitation, mitral valve prolapses and tricuspid valve regurgitation, I would say yes. And Dr. Sabbagh, would you agree?

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Dr. Sabbagh: Yeah, absolutely. It's a risk factor for valve degeneration. And, and so now, I'll tell you that disease progression is very well, even with the risk factors, but it does predispose for valvular heart disease. And with that comes that associated increased risk of, of needing valve replacement down the road.

Nicole Harr: Okay, I'd like to squeeze this one in. Looks like we have about a minute, we had a couple of questions about salt intake. So, what is your recommended daily amount of sodium for PKD patients and also, if you're on tolvaptan, and your bloodwork is showing that your sodium levels are low? Do you still recommend a low sodium diet?

Fouhad Chebib: Excellent question. So, those are two separate things. So, in general, we recommend 2300 milligrams of sodium intake per day. So, that's kind of a target, not a target, but kind of staying below that. Now, if everything in life, if you go to the two extremes, where you really restrict extremely low, then there might be an issue. So, it's like a J curve. So, but it's important, it's very hard to restrict salt.

So, when we say less than 2300 milligrams, typically, it is challenging to reach that. So, we say 2300 milligrams. Now I was told that and a different story. So, when we do see the serum, the blood sodium low in the, in the in the blood on the blood test, that's not related to how much salt we're eating, although there is some connection. But for the most part, low sodium in the blood means that you have excess fluids in your system, and a way that you're drinking more than you should. So, sometimes patients, so many of our PKD patients, we've been always recommending drink a lot of fluids, so they've got into that habit. So, when you drink a little bit more than what your kidneys can handle. So, if you have a lot of water that you're drinking, the sodium levels is going to drop.

So, you just need to readjust a little bit by drinking a little bit less, and tolvaptan. And in general, makes the sodium go up. So, that's why we tell our patients to drink more, because they need to make sure they respond to their thirst sensation, but sometimes they drink a little bit more, and that's why the

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soldier drops. So basically, for that second question, and just need to back off a little bit on how much fluids you're drinking.

Nicole Harr: Okay, I know that we're at time, I'd like to squeeze one more question in. And if you need to go, that's okay. There's a 15-minute break between this one and the next session. We have a question about LDL. So, when you're looking at LDL, what are your recommendations before starting a statin?

Fouhad Chebib: So, our goal is 100, less than 100. But I will defer to X above also his he's an expert in that too, when would you recommend to start?

Dr. Sabbagh: Yes, absolutely. So, when I see patients, they usually have coronary disease or blockages in the blood vessels that feed the heart, the recommendation currently is less than 70, actually. So, it goes from 100 to less than 70. And then the Europeans are lowering the number more and more. So, we're becoming a little bit more and more aggressive to that and they're almost at 40. So, we're very aggressive. To summarize, we're very aggressive about lowering the statin if there's coronary disease, or evidence of chronic disease, using risk factors, risk factor scores, or the coronary calcium CT scan that we sometimes use in patients who have intermediate risk. If there's evidence of coronary disease, then we just go less than seven.

Nicole Harr: Okay. And can you clarify really quickly, what did you say the LDL cholesterol number should be?

Dr. Sabbagh: Less than 70 for coronary heart disease and 100 for those who don't have chronic disease?

Fouhad Chebib: Yeah, there's some clinical trials showing, especially in kids that if you start to start in the kidney growth might be a little bit slower. But if someone has heart disease, it's important to be more aggressive as doctors abovementioned. So, if you have higher than that, let's say 110 120, 130. And you're not able to bring that down just by avoiding the dietary. So, trying to do lifestyle modification then we would be we have low threshold and in other words, we'll be aggressive to start astatine.

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Nicole Harr: Okay, thank you so much. Please also we just put the link to our survey in the chat. So, if you would complete our survey, we would really appreciate it. I'm sorry, I didn't get to all the questions, but hang on to those because there was a Q&A session on Saturday. So, you can ask those questions at that session as well. There is a 15-minute break slightly less than that now. And then the next breakout start at five o'clock central time. Thank you so much to both of our presenters. We really appreciate this information. It was a great session. So, thanks, everyone. Enjoy the rest of the conference. And thanks for kicking it off with us.

Fouhad Chebib: Thank you, everyone.

Nicole Harr: Bye everyone. Take care.

[Audio Ends] [01:25:52]