Vlad Zaha, MD (00:17):

Welcome to the Hypertrophic Cardiomyopathy podcast, titled Hypertrophic Cardiomyopathy, Genetic Counseling, and Family Screening. This is one of the series of podcasts from the American Heart Association HCM Initiative, sponsored by Bristol Myers Squibb. My name is Vlad Zaha. I'm an assistant professor of internal medicine, I'm Medical Director of the Cardio-Oncology program at Simmons Cancer Center and multimodality cardiovascular imaging specialist in the HCM Center of Excellence at UT Southwestern Medical Center. And I have with me today, three guests. Jessica Chowns is a genetic counselor who works in the Inherited Cardiovascular Disease program at Penn Medicine in Philadelphia, Pennsylvania. She has been working in the center for over five years and sees patients with cardiomyopathies like HCM, as well as those with other genetic cardiovascular diseases. Dr. Jose Jolgar is Professor of Internal Medicine, Director of Cardiac Electrophysiology Fellowship program at UT Southwestern Medical Center in Dallas and serves on the writing committee for the 2020 AHA ACC Guidelines on Diagnosis and Treatment of Hypertrophic Cardiomyopathy. And Paul McDermott, our patient representative, who is a heart transplant recipient that had HCM.

Vlad Zaha, MD (01:37):

So, thank you all for joining us today, and I would like to begin our discussion here with a perspective from Paul. Would you like to share with us what is your and your family experience with HCM?

Paul McDermott (0:00):

My journey began about 40 years ago within one family of my first cousins. Four of them had experienced sudden death, and we didn't know why. Back then, they didn't know what HCM was. And it was 40 years ago during one of the deaths and the autopsy had revealed that he had IHSS. They called it back then. He had HCM. When they found that out, they said it's familial, so they asked and they notified all the close relatives who want to get tested. So, I'm one of 15 children. And at the time, my mother and father were still alive, so we all went out and got echocardiograms. The EKG alone would not have necessarily revealed it, so we had echocardiograms. After those were completed, it turned out that seven of the 15 children had HCM, and my mother was the carrier.

Paul McDermott (02:52):

So, after that happened, our doctors gave us some advice and it's important to mention here, we were not sentenced to a life in a rocking chair. We were told, "No, no. We're going to put some limitations on you, but you can still have a pretty full life." So, using me as an example, I was still able to be extremely active in sports. I played competitive sports till I was 42. It's just that I wasn't allowed to do certain things like sudden starting and stopping. So, I went from being a center fielder, playing hardball to being a pitcher because it was more consistent. I was able to still jog, I just couldn't sprint. So, I was able to have a pretty full life living with HCM.

Paul McDermott (03:34):

Now, at the time there was no medication for HCM other than do things like a beta-blocker. So, my heart wouldn't work as hard, and my pulse rate was kept down and my blood pressure was kept down. But that was where the journey was going. And then about 10 years after that, I was reading an article in the paper on a Sunday morning, a local paper, to fill out the inquire. And I read where a Dr. Simon at Harvard Medical School had identified the genetic marker for this condition. So, I reached out to her and said, "I'm one of 15 kids. We're all alive, and we have this condition. And my mom who gave it to us is alive, and I thought you might find that of interest."

Vlad Zaha, MD (04:16):

So, Paul, let me just interrupt maybe for one moment here. And I really thank you for sharing your family's experience with this. And maybe at this stage, can you tell us how did this HCM impact your siblings and the rest of the family as well?

Paul McDermott (04:34):

Yes. And since we're all different people even though brothers and sisters, we're all very different personalities. Some took it, not depression, but certainly in a melancholy manner. They were really upset about it. Me being an optimist, I felt like from this day forward, they're going to watch my heart so closely. I will not be that guy riding a bike dropping dead. So, I was actually not sad about it. I thought they're going to... The Grim Reaper's got to find another way to get me because it's not going to be my heart because they're going to watch and poke and prod me so closely. But others were really upset about it, and it took them time to make peace with it.

Paul McDermott (05:12):

For example, when they came up with the genetic testing, my one sister did not want her children tested because she was afraid how it would impact them because it impacted her in a negative way for years until she made peace with it. And I talked to her and said, "Well, you can find it out by genetic testing or you can experience them having sudden death and then spend the rest of your life going. "Oh, if only I had known," because her children were very active in sports. The one was the Catholic League MVP for basketball. So they were playing extremely high level of competitive sports, and I said, "I would rather find it out by a test than finding it out by going to a funeral."

Vlad Zaha, MD (05:55):

I think that is a very good example. So, if you would like to share with us now, what was your experience as probably one in the first in your family having had the genetic testing?

Paul McDermott (06:07):

With the genetic testing, it was important because now we had a way of testing because my family, at the time with 15 kids, but then we got married and we had children and now we have grandchildren. And thanks to the genetic testing, which also thankfully since it came down in price so dramatically. So, it's not something that's expensive. We're able to get all the children tested and the grandchildren tested. So, we were able to identify them at a very, very, very early stage. And as you would imagine, some of them became very symptomatic, but thanks to the genetic testing, they're already leading a smarter lifestyle that was consistent with HCM.

Vlad Zaha, MD (06:50):

Excellent. Well, thank you so much. I would like to turn to Jessica now and ask you to outline for our audience what is genetic counseling?

Jessica Chowns (06):

Yeah. Certainly, genetic counseling, something that can be done either by someone like me and genetic counselors trained in doing genetic counseling specifically or certainly any of the medical professionals who do this regularly. And it's really a process that involves oftentimes genetic testing, helping to interpret genetic test results, communicate that information to families, to their healthcare providers,

and trying to really break it down in an understandable and meaningful way so that patients can use genetic testing when we can just like Paul's family has and try to prevent the bad things that can happen when you've got this heart condition running in the family. And so, we certainly act kind of in that process of helping people to cope with the information of learning that this is something that they're dealing with in their family and explain all the complex genetic information that goes along with it.

Vlad Zaha, MD (07:51):

Thank you. And Dr. Joglar from a medical perspective, when is a genetic test recommended? Who is the best candidate for genetic testing?

Jose Joglar, MD (08:06):

Certainly, it's interesting listening to Paul because Paul is essentially describing his own personal experience, also describing the utility of genetic testing. But ideally, patients who get diagnosed with hypertrophic cardiomyopathy in the guidelines we gave a Class 1 recommendation to genetic testing. And the advantage is once you identify a likely pathogenic mutation, then you can do what Paul described, which is cascade testing of family members. And the importance of doing that is, like Paul mentioned, those family members who are identified as having the mutation, then they can be surveilled closely. The opposite is true. Those who do not have the mutation can essentially move on with their lives and have a normal... Don't have to be afraid, can be reassured, have normal sports experiences, et cetera.

Jose Joglar, MD (08:56):

The patients with familial HCM tends to have a higher yield, and I can let Jessica comment more on that. Some elderly patients present with spontaneous HCM. The yield is lower, but again, we gave a class recommendation to essentially any new patient who presents with HCM as a way also to rule out the possibility of other conditions that can mimic HCM. it's a small percentage, but it's also very important that we can also rule out other conditions. So, I think Paul described very well in his own personal experience the Class 1 recommendation that we gave in the guidelines.

Vlad Zaha, MD (9:37):

Paul, I would like to ask you, what was your impression about the genetic testing report? How did you feel when you received that?

Paul McDermott (9:50):

Well, for my case personally, I have three sons, and one did test positive. But as I said, he's now 32, and he is not symptomatic, so that's great news. But when he tested positive, I wasn't happy about it, but I did know he was in good hands at Penn, that he was going to be monitored so closely. As I said earlier, he was not going to die from a heart condition because he made a few adjustments in his lifestyle. Again, not dramatic. He just made a few adjustments. And so for my case, it was nice. Knowing two could have a full and happy life and do crazy stuff. And the one could do 90% of that, but we knew that one was, and he knew who he was. And so he was able to adjust accordingly. The great news though is for about 35 in these 40 years, the counseling we got initially, doctor, was a little bit later than that.

Paul McDermott (10:45):

Here's how your journey's going to look. And it will end with a heart transplant or will end with a death earlier than you might have otherwise experienced, maybe at 65 or 70, like my aunts and my mother

did. But the good news that's happened now is my sister Regina is currently in a clinical trial. And she went from not being able to walk one block without stopping four times for a rest, and I'm not exaggerating or embellishing, to with this new drug that now is actually Dr. Simon kept her promise. They came up with a new drug that helps the condition, improved her condition, so she is now on a treadmill 30 minutes a day at 70 years old. I mean, look at it, look at the contrast. Three years ago can't walk one block without four rests. Today, older, and she can be on a treadmill for 30 minutes.

Paul McDermott (11:39):

So now, when you go to a Jessica and you're getting counseled, instead the end of the story being you got to get a heart transplant like myself or my older sister, who had to get a heart transplant, you can now take a pill. It's just a wonderful story that now has a much, much better ending instead of the way it was presented for 35 years.

Vlad Zaha, MD (12:01):

Thank you for sharing this very interesting transition of the counseling process between the older times with the progression of science and medicine today. So Jessica, I would like to turn to you to ask about the current genetic reports that sometimes can be quite cryptic. And what are your thoughts about their meaning and how to translate that for the patients?

Jessica Chowns (12:26):

Yeah, and I think Paul's experience was maybe a little bit different than some of the patients that get diagnosed now, because back then he was part of a research study that was looking for genetic markers for HCM, and they were able to identify that genetic cause back then. I think his experience was maybe a little bit different than some people who get diagnosed more recently, but certainly a large number of genes are looked at now at least 30 to 40 genes typically on most genetic testing panels or HCM specifically. And the results aren't always clear cut. We don't always find that pathogenic mutation that explains the family history if there is one.

Jessica Chowns (13:01):

As Dr. Joglar was mentioning earlier, the yield of genetic testing or likelihood of finding that pathogenic mutation increases when someone has a family history or when they're diagnosed at a younger age. It's maybe upwards of 60% or so of families that have a family history of HCM, where we can find that genetic cause and use it as we have in Paul's family, which is really helpful. Of course, the biggest kind of scourge perhaps in genetics is understanding what all variation means in our genes, and we certainly don't know it all. A lot of times we get these inconclusive results from genetic testing.

Jessica Chowns (13:31):

By definition, there are changes in the way genes are spelled but no one can interpret yet. They could be the cause of HCM in that person or they could be benign and harmless because we all have a lot of benign genetic variation in us. So usually, it takes years to figure out what an uncertain result means. And it's something that should be watched and checked on periodically to see if that interpretation changes over time. But those variants of uncertain significance are what makes interpreting a genetic test result particularly tricky, but certainly even a negative test result can't fully rule out a genetic predisposition to HCM because we know a lot more than we did 40 years ago about the genetics of HCM, but we certainly don't know it all. And so, certainly we still follow quite a few families who got

multiple people in the family affected who have negative genetic testing. So, in those families, we can't use genetic testing to help their family members out.

Jose Joglar, MD (14:24):

Let me comment on the cryptic nature of the report. That's why we need genetic counselors or clinicians who are specially trained in genetic counseling. Because when I started reading these reports as a clinician, I had no idea what those things were saying. And these are very important to understand. We have come a long way, not only in the quality of the genetic testing, the number of mutations, but also in reporting them accurately. So, it's very important that they understand that the idea I used to identify pathogenic mutations, and also we've been calling for the societies to reduce variants of unknown significance. What Jessica said that we don't know what they mean to keep monitoring those gene defects and see whether they come up in the future. So genetic testing is also an ongoing process. It's not a one-and-done. It's important that we continue to monitor those variants that we don't know what they mean now because they can then change in the future, and then you can contact the patient and act accordingly.

Vlad Zaha, MD (15:27):

So from your experience, Dr. Joglar, at what stage in your interaction with patients or generally clinicians should refer the patient to a genetic counselor?

Jose Joglar, MD (15:40):

I think that every possibility, every time you have a genetic disease, you should refer to genetic counseling because what happens is a lot of people don't have the expertise. We're frontline clinicians, and we just don't have the expertise to explain these in way that the patient can understand. And that's why genetic counselors have so much value in my mind. So essentially, it's a team approach to genetic counseling. It should be a team approach. And then accordingly, we can then make clinical decisions. But I certainly know that a lot of HCM clinicians have great experience and have been already trained in genetic counseling. But across the board, it's better if you have a specialized trained, well-trained expert that can provide accurate information to the patient.

Vlad Zaha, MD (16:33):

Thank you. Paul, from your experience, how do you feel this really sophisticated, scientific information was transmitted to you? How was your experience with your genetic counseling? Do you feel you had a good understanding of what was going on?

Paul McDermott (16:54):

Yes. What I thought they were frankly in communication; I give them an A plus. As you would imagine in something that they didn't know much about 40 years ago, every time they talked to me, as they became aware of more information from the research, they relayed that to me. As a specific example, I had a sister who presents not at all symptomatic. She didn't think she had to have her kids tested then for the genetic marker. "I'm not symptomatic, then my kids are going to be okay even if they get it." Well, the genetic counselor said, "No, no, it's not a recessive gene. It's important they still get tested." And as it turns out, one of her children has become symptomatic.

Paul McDermott (17:06):

So, as they learned more, they kept us informed instead of us making the stupid mistake of going to the Internet and believe what we read on the Internet and maybe doing something that literally could cause our death. And so, they just do a great job keeping us abreast of the newest and the latest of what's going on in that field.

Vlad Zaha, MD (18:20):

Thank you. Dr. Joglar, now that we have received the genetic report and placing ourselves in the position of a patient, what would be your summary of interventions and what does the genetic report influencing the decisions for our clinician?

Jose Joglar, MD (18:58):

Well, the most important benefit is cascade testing, meaning that you can then test once the mutation has been identified in the affected individual, we call that a proband. Then, you can do genetic testing on family members. And like I said, those who have the gene can be surveilled more diligently. And those who don't then have peace of mind and can move on with their life and can go on competitive sports and things like that. Having said that, what we're not doing yet is making clinical decisions based on genetics.

Jose Joglar, MD (18:54):

There's some data suggesting that some specific mutations are more lethal or more severe than others, but because the disease expresses differently, the same gene defect can express differently in different patients. What the guidelines made clear is that we're not making clinical decisions on the genetics alone. So that's very important to emphasize, but in the future that might change since we're learning more and more and more. We're getting better at this. It is possible that in the future, we can make decisions based on genetic information.

Vlad Zaha, MD (19:33):

Excellent. I think that's is very helpful. So Jessica, genetic testing sometimes can be very costly. And one important question that comes in our practice today is what is the accessibility. And sometimes there is a financial toxicity of testing and what to do when cost is a barrier.

Jessica Chowns (19:57):

I'd say this is something that has changed greatly in the last probably 10 years or so. The cost of genetic testing has come down a lot. And in our clinic, it is pretty rare for us to not be able to get testing accomplished when it's desired due to cost. Certainly, the biggest costs associated are often for the program for that person who's doing that big panel looking for a genetic cause. But even those can be done for a few hundred dollars out of pocket. I realized that's certainly still unapproachable for some patients, but there are some free testing options available as well. So, it's really become something that is accessible for most patients who want to do it.

Jessica Chowns (20:36):

And then of course, once you find that mutation in the proband of testing of other family members for cascade screening or cascade testing is often cheaper than doing a full panel because you're really just looking for that specific mutation and that person as opposed to doing the whole panel. So, cost has really become something that we're certainly very careful with. And we certainly try to get estimates for

patients ahead of time as to what their costs will be for the genetic testing, but it's something that's becoming less of an issue in more recent years.

Vlad Zaha, MD (21:08):

That's very encouraging. So, I would like to have your final thoughts now as we are coming towards the end of this podcast. So, we'll start with Paul. Anything you would like to share as final thoughts?

Paul McDermott (21:24):

I just have two comments, doctor. One is as they help us and Dr. Owens, frankly, her team are brilliant at this. They realized when they take care of Regina and not just taken care of, as an example, my sister Regina. Regina has about a hundred... My immediate family now is 150. We all love Regina a whole, whole, whole, whole lot. So, when you're helping Regina, you really are literally making 150 people happy. And I'm stating a fact, it's not that's... That is true. What's nice now, as I mentioned the journey story is now a different ending story. Regina has a large family. She has a number of children and number of grandchildren. And because of this new medication that hopefully will be approved by FDA in the near future, she said for the first time in 40 years, when she saw her children and now her grandchildren on Mother's Day, she was able to look at them and not feel guilty and say, she goes... And wasn't conscious, she goes, "I realized I was at peace because I knew their journey would not end with a heart transplant or sudden death."

Vlad Zaha, MD (22:35):

Okay. Excellent. Thank you. Jessica, any thoughts that you would like to share with our listeners?

Jessica Chowns (22:45):

I think that HCM is clearly a genetic condition that can really impact families, as Paul so kindly shared with all of us, that the process of undergoing genetic testing, having genetic counseling, coping with the diagnosis and what it means for the family can be tricky. And certainly, there's lots of complex feelings. As Paul just mentioned, guilt is really common in a lot of the families that we see. And so certainly, it can take years for families to really come around to this information, to process it, to deal with it. And so genetic testing, just one piece of that, but certainly keeping in mind the whole family, as Paul said, and treating the whole family as much as possible is always a good way to go with this.

Vlad Zaha, MD (23:28):

Thank you, Jessica. And Dr. Joglar, you shared with us a lot of important highlights and emphasis on how our practitioners are viewing genetic testing. Would you have any final thoughts to share?

Jose Joglar, MD (23:40):

Yeah. As genetic testing has gotten cheaper, more accessible, technology has gotten much better, we need to do a better effort in the clinical frontlines to enhance our accessibility to genetic counseling either by getting more people that Jessica trained to specialize in how to counsel patients, but also for clinical frontline workers, we need to get better at this. It used to be that genetic was something very specialized, very esoteric. And as it's getting more common, it's getting better. As clinical frontline physicians, we need to be able to understand these better, be able to explain it better, be able to adopt it in a more seamless fashion, do a better job at embracing this genetic testing process.

Vlad Zaha, MD (24:32):

Thank you.

Paul McDermott (24:33):

Can I make one more comment, please?

Vlad Zaha, MD (24:35):

Yes, please.

Paul McDermott (24:36):

About the genetic testing. You would ask Jessica about the cost of it and how it's come down, but when I've talked, and sometimes Dr. Owens has had me speak with families about getting genetic testing, it wasn't the money that, from a patient perspective, that they're reluctant to do it. They don't want to know. They're afraid of knowing. And so, I had to talk because they think they're going to get sentenced to a life in a rocking chair. And so, I let them know the hardest step is get them to the cardiologist, let them do a blood draw. As I said earlier about my sister, they rather not know to know, and I had to explain to them the benefits of knowing. And that it's not as harsh as they might think it is where you don't have a good life anymore.

Jessica Chowns (25:25):

I've just said best-case scenario, we've turned you into a genetic counselor for your family, right? Is that you've now become someone who can help your family in the same way that we can and see them more often.

Vlad Zaha, MD (25:36):

There you go. That is an excellent point.

Jose Joglar, MD (25:40):

It's important that we be able to translate this complex information into very simple terms, language that patients can understand. That's what I'm talking about, and that's what we need expertise. We need to train more physicians and also as specialized people like Jessica to be more available across the country to do that.

Vlad Zaha, MD (26:00):

Excellent. So, thank you, really. Thank you all for participating in this podcast with me today. This was a lot of important information with points about genetic counseling and family screening. This podcast is a part of the American Heart Association HCM Initiative, sponsored by Bristol Myers Squibb. And in closing, I'd like to remind everyone, listening, to encourage your patients to play an active role in their medical care by advocating for themselves and their family members, just as Paul demonstrated while sharing his personal journey with us today. They can also go to AHA hypertrophic cardiomyopathy patient website for more education. Thank you.