Miguel Leal, MD (00:04):

Hello everyone, and welcome to the Hypertrophic Cardiomyopathy Podcast titled Needle in the Haystack: Screening Large Populations for Hypertrophic Cardiomyopathy. This is one of a series of podcasts from the American Heart Association HCM Initiative, which is a sponsored by Bristol Myers Squibb. I am Miguel Leal and I'm an associate professor at Emory University in Atlanta with the clinical cardiac electrophysiologist section, and it is my pleasure and my honor to introduce my two colleagues and our patient representative who will be joining us for this podcast today. We will have with us today Dr. Judy Hung, who is the director of the division of clinical research as well as the echocardiography section at Massachusetts General Hospital and a professor at Harvard Medical School.

Miguel Leal, MD (00:47):

And we also have directly from Europe Dr. Antonio Pelliccia, who is a cardiologist and a scientist with specific expertise in exercise, sport and cardiovascular disease. Dr. Pelliccia is currently the chief of cardiology at the Institute of Sport Medicine in Rome, a place where Italian Olympic athletes are periodically evaluated. So, we're very fortunate to count on the expertise of Dr. Hung and Dr. Pelliccia here today. And to add to that we also bring the unique patient perspective, and to that extent we have Ava Van der Meer join us today. So, I thought I would let Ava introduce herself. Ava, welcome to our podcast.

Ava Van der Meer (01:23):

Thanks for having me. I am a 27-year-old patient with HCM. I'm also an avid runner, biker and outdoor enthusiast. I was first diagnosed with a heart murmur when I was 16 by just a general pediatrics practitioner and was later diagnosed with HCM at the age of 23. And a year after that, I received an ICD.

Miguel Leal, MD (01:44):

Well, Ava, it's great to have you here, and I'm sure you'll contribute enormously to our discussion today. And I'll start right off the bat with Dr. Hung. Dr. Hung, hypertrophy cardiomyopathy is this fascinating condition, something we see in practice in one way or another in multiple specialties and subspecialties. So, I was wondering if you could give us a brief overview, including its definition and a little bit about its prevalence in the general population.

Judy Hung, MD (02:08):

Sure, Miguel. Thank you again for inviting me. So, hypertrophic cardiomyopathy is a common heart condition with a genetic basis. It's prevalence has been estimated to be one in 200 to one in 500 based on imaging criteria. And it's diagnosed predominantly by imaging, initially by echocardiography. And it's defined as the presence of LV hypertrophy in the absence of another cardiac or systemic disease that could explain the degree of LVH. The hypertrophy criteria that is used is a maximal end diastolic wall thickness of greater or equal than 15 millimeters. And it's most commonly the hypertrophy is seen in the anterior septum extending to the anterior wall, but there are a number of morphologic variants observed, including hypertrophy just localized to the apical region. So, that's the prevalence and the definition. It does have a genetic basis. About 30 to 60% have an identifiable genetic variant and it's inherited in an autosomal dominant pattern.

Miguel Leal, MD (03:18):

Thank you, Dr. Hung. This is certainly a disease condition about which we have learned a lot over the last decade or two, including the genetic inheritance patterns that you described. And now I'm going to

bring Dr. Pelliccia to the conversation. Dr. Pelliccia, you have been devoting a lot of your professional career to the art of screening, and today we're discussing how relevant it is to screen populations for this important condition that Dr. Hung just presented us to. So, tell us a little bit about screening, Dr. Pelliccia. Why is it such an important tool for certain disease conditions?

Antonio Pelliccia, MD (03:52):

Hello. It's a real pleasure to be invited here, and it's an honor. It's a privilege for me in consideration that I'm just an expert from the other side of ocean. And I will give you some clues from our experiences here in Italy. Let's start from this because this is very relevant and different from your scenario. In Italy we have a screening for athletes, not for general population, for athletes, including electrocardiogram. This screening has been implemented by legislation. So, it's a federal obligation and is performed by specialists in sports medicine, which are internists with a specific expertise in cardiology, nutrition, exercise, physiology, et cetera. Well, why this? Because the hypertrophic cardiomyopathy has been one of our target for decades. Because in the physician's mind, hypertrophic cardiomyopathy for decades was the number one killer for athletes.

Antonio Pelliccia, MD (05:14):

So, we spent a lot of care and attention to look for early diagnosis of hypertrophic cardiomyopathy. And from this experience actually derived the concept that electrocardiogram is particularly efficient and suitable for screening purpose. Because there are a number of electrocardiographic abnormality. And I want to be clear, just one electrocardiographic abnormality does not make any diagnosis. Because diagnosis, as exactly say our colleague Dr. Hung, is based today, still today, is based on the imaging technique. However, electrocardiogram is easy. In our screening program it is implemented for everyone and actually was one of the main reasons to raise suspicion for hypertrophic cardiomyopathy.

Antonio Pelliccia, MD (06:16):

In other terms, we were able through the screening process to identify those hypertrophic cardiomyopathy that are just mild or milder or even more marked electrocardiographic abnormality but not any specific limitation, specifically during sport, and not any specific symptoms. So, in other terms, these individuals, if not screening, probably would never diagnosis until maybe late in age. So, the screening purpose for hypertrophic cardiomyopathy is particularly relevant because it is feasible and efficient by EKG. Obviously what I'm saying is based on the assumption that the physician reading the electrocardiogram is able to identify the changes compatible with the presence of hypertrophic cardiomyopathy, and then have a suspicion for hypertrophic cardiomyopathy and then require for imaging testing. As I said before, just the EKG is not sufficient for confirm the diagnosis.

Miguel Leal, MD (07:32):

Thank you, Dr. Pelliccia. Dr. Hung, bringing it back to you. We learned from Dr. Pelliccia that the EKG or the electrocardiogram has a fundamental role in identifying individuals who might present with this disease condition. Do you have similar thoughts regarding other imaging techniques such as, for instance, echocardiography or cardiac MRI, or is it not really a suitable test for screening purposes?

Judy Hung, MD (07:55):

Yeah. No, I think the subject of screening for hypertrophic cardiomyopathy is, there's been a lot of discussion about how best to do that. And at least the practice patterns here in the United States, and also as advocated in the recent AHA and ACC guidelines from 2020, they do not recommend a screening

of the general population. And that the screening should really be guided, which is what everyone does. I mean, guided by clinical and family history. I think the subject about athletes are a special population in which it doesn't probably really apply because professional athletes, it's based on what the organization wants to do. But screening should be based if there's a family history that's positive. And you should go back three generations.

Judy Hung, MD (08:46):

Obviously an abnormal ECG, of which I know Dr. Pelliccia has a lot of publications on that. And symptoms, especially exertional symptoms. And then the classic exam. It's classic systolic murmur with a provocative maneuver, such as Valsalva or standing from squatting, if that increases. So, those are the basic clinical and family history parameters that should tip you off that this could be hypertrophic cardiomyopathy. And then following that, the screening for us is really, the diagnostic test is imaging, and predominantly echocardiography as the initial one.

Miguel Leal, MD (09:24):

Thank you both, because it really helps us situate where this disease stands in the world of screening. Clearly not a condition that we can simply screen everyone for, nor should we, but at the same time Dr. Hung just brought a very important point. History and physical examination continue to be remarkably important tools when trying to identify which individual may or may not be at risk for this condition. And specifically including the family history which, as Dr. Hung said, is not just asking about mom and dad, but going up a few generations, going to the siblings, going to the offspring and trying to detect any signal towards a problem. So, that's a perfect segue to bring here Ava to our conversation. As we discussed earlier in this podcast, we have the privilege of counting with a patient representative, Ava Van der Meer. Ava, tell us a little bit about your view on this discussion Dr. Pelliccia and Dr. Hung have started in terms of screening patients, trying to find this disease condition, trying to dig deep into the symptoms and the clinical presentation of a patient in order to make the right diagnosis.

Ava Van der Meer (10:26):

Yeah, definitely. I mean, talking from my own experience, I think screening is absolutely essential to really just prolonging the lives and lifestyles of people living with a heart condition like HCM. As with many of these HCM diagnoses, mine wasn't really a streamlined process. So, I didn't immediately find out that I have HCM in a general use screening or a sports screening because my instance of HCM developed over time. So, when I was about 16, a general screening did discover that I had a heart murmur. And because of that, I was referred to a cardiologist every two to three years following. So, by the time I was 23 and I was living in Chicago at the time, I went to a new cardiologist there and HCM was immediately apparent.

Ava Van der Meer (11:09):

This was quite a shock to me because I didn't have any family history of cardiac arrest or HCM that I knew of. I just run a marathon a few months prior. So, I was in complete denial that I had any sort of heart condition. But I ended up going to a center of excellence in San Francisco where I'm from, and they found the muscle scarring in an MRI. They found the gene variant and they also found an episode of ventricular tachycardia. So, they essentially explained to me that sudden cardiac arrest was a very real possibility for me, and I needed to make changes to my activities and get a defibrillator and really cut back on what I'd been doing. So, it was a hard diagnosis to come to terms with, especially since I live such an active lifestyle and I felt relatively good.

Ava Van der Meer (12:01):

I didn't feel sick or bad like I was expecting somebody with a heart condition to feel. But with the knowledge and with the screening, I've been able to really make more informed decisions about the risks I was willing to take and take preventative measures such as getting an ICD to really protect my life and my passions rather than leaving my fate up to chance. So, I'm very grateful for my screening and for the process that I went through. And I'm still able to do everything I love just in a more moderated way, I guess I would say.

Miguel Leal, MD (12:36):

Ava, we're all very glad that the course of your care has been so successful because as we all know, sometimes unfortunately the first presentation of a disease like HCM could be a fatal arrhythmia or a near fatal cardiac arrhythmia. Ava, let me ask you a follow-up question. During the process of having the disease diagnosed and all the testing that followed, were you able to benefit from a scenario where there was shared decision-making between you and your multiple clinicians?

Ava Van der Meer (13:01):

Mm-hmm.

Miguel Leal, MD (13:01):

I ask you that because we live in an area of empowering our patients and their advocates, family members, their significant others to have not only a full understanding of the disease condition, but also participate in an active way in the care of our patients. So, how was that in your specific journey?

Ava Van der Meer (13:19):

Absolutely. I mean, I think going into the diagnosis and talking to my clinical team, something that I made clear from the beginning is that being active and running and biking and swimming and doing everything that I loved was critical to my wellbeing. And I think they were able to hear that and help me adapt the decisions we make to essentially meet my expectations for what I wanted from my life. So, I think getting the ICD was a big part of that. My doctors were willing to let me keep doing what I love to do as long as I had that safety measure in place. I'm in current conversations with my team about beta blockers, and that's something that I haven't been willing to get on yet so that I can keep exercising and engaging in activities at the level that I want to. But that is something that they've been very patient with me about, and we're feeling out whether that's something that I need to do or whether that's something that I can put off until symptoms start catching up to me.

Miguel Leal, MD (14:25):

Thank you, Ava. Dr. Pelliccia, Italy is the few places in the world that is able to maintain a very organized screening infrastructure for HCM utilizing the ECG, the electrocardiogram, as you mentioned, as the pillar of that process. Were there any barriers to implementing this well-organized screening system and was cost or cost-effectiveness ever an issue for Italy?

Antonio Pelliccia, MD (14:51):

Well, this is a usual question that my colleague and your country colleagues, US colleague, usually rise about the cost efficiency of the screening for hypertrophic cardiomyopathy. In reality, the screening has been implemented by law, not just the first screening of hypertrophic cardiomyopathy. Screening of

hypertrophic cardiomyopathy was good results of our, let's say, activity. But originally the screening has been implemented as a social problem, as a preventive medical program. Because in our society, we have a number of social initiative. Our society has a number of, let's say, benefit for the lower classes. So, the individuals that are considered to be in need. For instance, this screening for athletes is totally free of charge for all individuals up to 18 years. And it's not just for hypertrophic cardiomyopathy, as I say. Just for global health. It's the occasion to advise an individual about nutrition, body composition, fitness, all the issues that rise to the attention of the physician. Then it's much more relevant what we cardiology did because we actually by EKG.

Antonio Pelliccia, MD (16:34):

Just want to remind that electrocardiogram is abnormal in 90% of hypertrophic cardiomyopathy patients. So, nine out of 10. Symptoms may be present in 20%. The limitation of the performance, never present. Murmur, 20, 30%. So, electrocardiogram is the key issue for rising suspicion for hypertrophic cardiomyopathy. That's exactly what we did. And that's what actually, let's say, arrived to the scientific paper, to the recognition of the scientific community. But the screening cannot be, should not be cost-efficient just for hypertrophic cardiomyopathy. Because if you consider how many diagnosis of hypertrophic we can do, let's say 100, how many of these people will die? One. So, should be not cost-efficient in terms of, let's say, identify one individual. The screening in our society is, as I said before, is a benefit, a program for all the society. And the cost, relatively less. Because all the physical examination by the specialists in sports medicine, the electrocardiogram, et cetera, the remaining issue or the physical examination costs the equivalent of $60. 6-0 dollars, all included.

Antonio Pelliccia, MD (18:15):

It's obvious that such a kind of cost is totally affordable from all the family. If you consider that, let's say, a pair of shoes, Adidas, Nike, et cetera, costs double. So, the physical examination and the, let's say, the certification of eligibility by the physician is not considered an economic burden and is considered by the family such a, let's say, good initiative. It's totally acceptable because it's considered some kind of care spent for the, particularly, the young generations. So, there is no discrimination issue. In our society, the screening is not an issue of discrimination. On the contrary, it is considered something, let's say ,good for all, particularly for the lower classes. And so to address your question, cost efficiency, probably not, but this is not the question that will arise.

Miguel Leal, MD (19:21):

Well, I really appreciate this perspective you just gave us. It's something that is, as you said, very specific to the reality in Italy, but there are many positive aspects of the care, the way it is delivered in Italy, that many places, including the United States, could certainly try and mirror adapting to our local geopolitical reality. Dr. Hung, let me hear your perspective now, as somebody who works across the pond, on the other side of the Atlantic in relation to Dr. Pelliccia. What could the barriers be to implementation of a population-wide screening initiative such as the one that we have in Italy right now?

Judy Hung, MD (19:55):

Yeah. I mean, I wish we could recreate the Italian health system in the US. A very different system in many respects. And the issues for us are indeed cost-effectiveness and efficient use of really limited resources that we have. And in addition to the cost-effectiveness, it's also the issue about the false positive findings and the downstream effects of that that has also been raised, where likely it leads to probably minor abnormalities being detected, but then the effects on the patients of finding an

abnormality, then following up on that. And so I think that's also to be considered as well. I think the standard is not to do generalized ECG screening, but again, to guide it by clinical history and family history for moving on to diagnostic testing.

Miguel Leal, MD (21:00):

Thank you very much. Ava, let me ask you another question on the same topic here. As the screening process went on in your case, driven by clinical symptoms, and then as you mentioned you specifically didn't have any family history at the time of your diagnosis, give us a little insight on the burden of the anxiety that the screening process brought to you from the beginning to the completion, until you had the diagnosis in your hand and a plan in place.

Ava Van der Meer (21:25):

Oh, man. Yeah. I mean, I think the anxiety doesn't ever entirely go away. I think when I first found out that there might be something wrong with my heart, there was no anxiety because I was just in denial. I just didn't feel bad, and I didn't want to accept that my normal may not be what others consider normal. But obviously my heart was doing things that could put me in jeopardy and that's what the doctors were finding out. So, once I did have that set diagnosis, I think that's when the anxiety started kicking in more just in terms of, will it get worse and how is my HDM going to progress over time and will my ICD go off. And I think those are very real anxieties that stick with me to this day.

Ava Van der Meer (22:10):

But I also think that having the knowledge about HCM has really armed me with the ability to evaluate the options I have in front of me. And having options for how I want to progress in my journey has definitely helped me come to terms with my new reality. So, whether that's down the line, if I do need to go on beta blockers or if I need to get open heart surgery or whatever else may come my way, I know that there are options that will help me thrive with HCM and hopefully keep doing what I love and keep being an amateur athlete.

Miguel Leal, MD (22:49):

Thank you very much, Ava. We appreciate your perspective once again. And as we approach our closing remarks, let me ask Dr. Pelliccia, what's your suggestion, sir, your recommendation regarding sports participation and hypertrophic cardiomyopathy, which is such an important patient population with so many implications to their personal and sometimes professional lives? So, once a patient that participates in sports activities is diagnosed with HCM, what is the overall gestalt of the recommendations and how much will their lives be likely to change?

Antonio Pelliccia, MD (23:21):

Miguel, this is a very challenging question. A very challenging question. Let's say, according to the most recent guidelines, there is a much more liberal approach. Because as I mentioned before, for decades we were scared about hypertrophic cardiomyopathy as one of the most common cause of sudden cardiac death in athletic field. And we were very scared. Anytime that we recognized hypertrophic cardiomyopathy there, immediately we were, let's say, proclived to say, "Please, avoid sport participation." However, during the last decades, there are number of, few, very, very few, observation on a selected group of hypertrophic cardiomyopathy patient that actually are reassuring in other things. Just because we, by screening, identify a very large spectrum of this disease, not only the people with

the symptoms, with ICD, et cetera, but very large proportion of the people that have just, let's say, electrocardiographic abnormality, very mild, no obstruction, no limitation in their performance.

Antonio Pelliccia, MD (24:35):

So, now we are approaching the disease with more, let's say, unbiased and more relaxed pattern. And obviously we try to stratify the risk for patients with hypertrophic cardiomyopathy and the criteria for risk, not only the five major criteria, sudden death, syncope, left ventricular hypertrophy, ventricular arrhythmia, et cetera, but also the presence of scar on CMR, the presence of arrhythmias on exercise testing or Holter monitoring, et cetera. And eventually there are a number of these young or adult hypertrophic cardiomyopathy patient that have a very low risk profile. Very low risk profile. According to the European Society of Cardiology score, the larger proportion of the people that we saw participating in sport has a risk profile one or two. Less than four. So, no indication to ICD. There are probably no indications to any drugs. For these individuals now we have a much more relaxed approach. And we suggest that selectively, after careful evaluation and risk certification, we can advise and allow sport participation.

Antonio Pelliccia, MD (26:05):

In this regard, we should mention what the guidelines says. That is, shared decision-making. Well, shared decision-making is very big issue. I think that at the moment is more a wish than a reality. Why I'm saying more a wish a than reality? Because it's relatively easy to implement a shared decision-making when you have a patient who is adult, relatively accultured, that really understand what you are explaining about the disease, who is really concerned about the health.

Antonio Pelliccia, MD (27:17):

I'm lucky in Italy because in Italy the final decision about eligibility belongs to the physician. So, after discussing, explaining, the final decision-making is the physician. But this is just in Italy because we are responsible in front of the law of the eligibility. In your country it's a totally different scenario, much more challenging. And in my personal view, the physicians actually risk to have a lower impact than what should be. Because the physician is the physician in terms of knowledge, in terms of care, in terms of perspective for life. There are issue that eventually in the individual case can be missed by the patient. What is your experience if you have experience in this issue?

Miguel Leal, MD (28:42):

Dr. Hung, what are your thoughts on this? This is a very provocative thought that Dr. Pelliccia is going to leave us with. What are your thoughts?

Judy Hung, MD (28:49):

It's increasingly recognized the importance of. Before, I think, our approach was very paternalistic, if that's the term, but increasingly we are recognizing the importance of having the patient perspective and the fact that it's not necessarily just about outcomes but it's also about quality of life. And that incorporates the shared decision-making as well. So, as with the recent guidelines from AHA ACC in 2020, there are actual parts that directly discuss shared decision-making. So, I would just like to potentially conclude first by thanking the AHA for doing this podcast and sponsoring this podcast, one because I think the message here is that hypertrophic cardiomyopathy is a common disorder. It is a common heart condition. And it's increasingly important to diagnose it, especially early, because we have increasing therapies for it. More recently, a pharmacologic therapy that's been improved by the

FDA. So, again, I want to raise awareness of the importance of diagnosing it and doing that careful history and physical exam and having a low threshold for the possibility of hypertrophic cardiomyopathy.

Miguel Leal, MD (30:15):

Well, I would like to close by thanking Dr. Hung from Harvard Medical School, Dr. Pelliccia from the Institute of Sports Medicine in Rome, Italy, and our patient representative, Ava Van der Meer, for a great discussion. We covered a number of topics today, from a brief overview and definition and prevalence of hypertrophic cardiomyopathy to the importance of screening, to how it can and cannot be done, to how it should, and perhaps should not be done, and the different tools that we have in our hands, including history and physical examination, diagnostic tests, and a very important component, which is this shared decision-making with our patients as you navigate through screening, diagnosis and treatment.

Miguel Leal, MD (30:53):

I would like to thank everybody for participating in this podcast with me today, which is a part of the American Heart Association HCM Initiative, sponsored by Bristol Myers Squibb. In closing, I would like to remind everyone who is listening to us to encourage your patients to play an active role in their medical care by advocating for themselves and for their family members. To get any additional information, please visit the American Heart Association's hypertrophic cardiomyopathy website for more education. Thank you very much.