Anjali Owens: 00:00 Welcome to the hypertrophic cardiomyopathy podcast titled Defibrillator (ICD) Therapy; Selecting The Appropriate Patients. This is one of a series of podcasts from the American Heart Association HCM initiative, sponsored by MyoKardia. I'm Anjali Owens, Director of the Center for Inherited Cardiovascular Disease at the University of Pennsylvania. I'm joined today by Dr. Miguel Leal, Director of the Arrhythmia and Electrophysiology Service and Director of the Cardiovascular Medicine and Electrophysiology Fellowship Program at the University of Wisconsin-Madison. And Dr. Rakesh Gopinathannair, Director of the Cardiac Electrophysiology Laboratories at the Kansas City Heart Rhythm Institute, as well as the Electrophysiology Medical Director at Research Medical Center. We are excited to have a patient representative with us today as well. Ms. Kristin Chris. We will discuss the risk of sudden cardiac death in patients with hypertrophic cardiomyopathy and the role of implantable cardioverter defibrillators or ICDs over the next 20 to 30 minutes. Dr. Leal, can you start us off with a little background regarding the pro-arrhythmic potential of HCM?

Dr. Miguel Leal: 01:21 Thank you Dr. Owens. It is a pleasure to be here discussing this very important topic. And as you pointed out, hypertrophic cardiomyopathy does have the potential to be pro-arrhythmic, to cause arrhythmias that can be relatively subtle and become more of a nuisance to the patient, but also to the extreme of comprising a spectrum of life-threatening arrhythmias that may affect essentially every single area of the cardiac muscle. The disease itself, hypertrophic cardiomyopathy, involves abnormal growth of myocardial cells which essentially become larger than they should be. And as a consequence, that is more muscle altogether involving all chambers of the heart but notably the lower chambers also known as the ventricles. Both right and left ventricles can be unequally affected. And the consequence is that we evolve from a histology, from a tissue level of organized and well-distributed longitudinal myocardial fibers to what we usually call them myocardial disarray of cardiac fibers, of cardiomyocytes.

When now you have this unplanned and completely out of control growth of cardiac cells in many directions resulting in a very disorganized scaffolding of cells, which no longer follows the typical rules by which cardiac cells follow electrical impulses in order to beat, in order to generate that electrical mechanical coupling that the heart is known for. As a consequence of that, there are areas of the heart they may be perfect substrates for the development of arrhythmias. And we particularly worry
about the lower chamber arrhythmias, the ventricular tachyarrhythmias, both ventricular tachycardia and ventricular fibrillation. In addition, as patients with hypertrophic cardiomyopathy grow older, some of those cells do not receive adequate blood supply from the coronary circulation that is simply too much demand and not enough supply to feed all of that tissue, so you may have regressive cell loss in pockets within the hearts in areas that can comprise all layers of the endocardium, mid myocardium and epicardium strata of the heart.

Those areas of scar may serve as perfect reentry circuits that essentially will generate ventricular tachy-arrhythmias following that mechanism. So, you have a condition that has this inherent potential, and unfortunately it's hard to predict when it will happen. In fact, one of the main reasons for our conversation today is to try and select the patients who would benefit from additional therapies because it is well-known that this type of arrhythmia can occur early at the middle of the patient's lifespan or quite late in presentation. And there is still a lot of uncertainty regarding what patients will suffer those arrhythmias and who is at higher or lower risk within that spectrum.

Anjali Owens: 04:08 Thank you. Let's talk about the defibrillators and how they work to prevent or treat these episodes of arrhythmia. Dr. Gopinathannair can you discuss the basic concepts of ICD therapy?

Dr. Rakesh Gopi....: 04:22 Thank you, Dr. RobinsonOwens. Pleasure to be part of this podcast. Implantable defibrillators have been around since the mid '80s and has been regularly used in mostly in patients who are at higher risk for what we call as cardiac arrest or sudden cardiac death, which is primarily due to life-threatening ventricular arrhythmia as Dr. Leal pointed out. Current generation defibrillators involve a defibrillator device that typically goes into the left upper chest or right upper chest region of the patient where it's placed under the skin and the fat tissue there. And then typically they have a lead or a wire that goes through a vein that runs under the clavicle or the collarbone, and goes all the way to the inside portion of the right bottom chamber or right ventricle of the heart where they are typically attached to the heart muscle using a tiny screw. This particular type of device is called a transvenous or defibrillator meaning that there is a wire that actually inside the vascular space or inside the vein around which there is blood flow.
This is one type of the different blood and then defibrillators can have one or two wires typically. And then you need a second wire that one goes into the right upper chamber or the right atrium. This is usually used in people who have very slow heart rate or has, for them disturbances such as atrial fibrillation and irregular heart rhythm coming from the upper chambers. But the primary lead or the wire that is responsible for the shock function of the defibrillator is the one in the right bottom chamber. Over the past several years, we now have another option in terms of defibrillators. And this may be especially important in the hypertrophic cardiomyopathy population. This is the so-called subcutaneous defibrillator. Dr. Leal is going to discuss the pros and cons of ICD therapy. What the subcutaneous defibrillator does is that it's completely outside the blood flow system, it's not inside. There's nothing that goes inside the heart.

The device is situated in the side portion of the left chest region, somewhat below your left armpit. And there is a wire that is placed underneath your skin and alongside the sternum or the breastbone on the left portion of it. And this particular device works equally well for studies in terms of rescuing a patient who is having life-threatening ventricular arrhythmias. So, the defibrillators have become much more sophisticated, smaller, and has longer battery life. So to give you an example, the transvenous one or the one where the wire goes into the heart nowadays have almost 12, 13 years of battery life whereas the subcutaneous device has lesser battery life, but again this is a newer technology and this is going to continue to improve as time goes.

Anjali Owens: 07:33 Dr. Leal, there are certainly risks and benefits of all therapies, especially in basic procedures and lifelong implantable devices. Can you share your opinion on the risks and benefits of having an ICD?

Dr. Miguel Leal: 07:47 Certainly Dr. Owens and I couldn't agree more with Dr. Gopinathannair just said. Essentially these devices they are here to stay. They were launched in the early to mid '80s, and they have saved a number of lives over the last few decades. But as you indicated, it's not just all glossy and perfect there are scenarios that we have to always ponder if it is the right call to be made to have a patient receive a defibrillator implant, be it the transvenous type, the type that goes through the collarbone vein, the subclavian vein, or the axillary vein, or the cephalic vein as Dr. Gopinathannair just explained, or this newly available subcutaneous defibrillator which has been around for
a little over half a decade now in the United States. And it certainly is a device that serves as a viable alternative, especially if one wants to take a slightly less invasive route and not necessarily commit the patients endovascular space to implant that hardware.

So, the first consideration here is that the benefit is sudden cardiac death prevention. What these devices do is they will watch the ventricular rhythm pretty much 24/7 uninterruptedly. And if the patient engages into a life-threatening arrhythmia that could cause collapse, syncope or even sudden death, the device is programmed to respond to it. If it's a transvenous device initially tries to outpace the arrhythmia delivering a rapid sequence of pacing beats that we call anti-tachycardia pacing sequences or ATP. And if those fail, the device will simply shock the heart, trying to cardiovert the VT or defibrillate the VF back into a regular, viable, perfusing rhythm such as sinus rhythm for instance.

The subcutaneous device, because it is external to the chest. The lead is located between the skin and the rib cage to the very left side of the breast-bone on the sternum. That device does not have the ability to pace the heart, but it can shock. And the shock is as Dr. Gopinathannair just stated, equally effective. The many studies have demonstrated that those devices are truly effective in saving lives and preventing sudden cardiac death. So, the benefit is clear. And again, the difficulty is in terms of selecting the right patient, and we'll be covering that later in this podcast today, but the risks are also real. Every time a defibrillator is implanted, one has to agree and accept that this is a lifetime commitment to permanently implant the hardware, be it the transvenous system, which brings the additional relevance of endovascular hardware, or the subcutaneous system which is still hardware that is implanted in the body. So, it's not a procedure that you can simply have the patient receive in a couple of weeks later, a few months later then let's get it out, and a few years later let's put it on.

Again, all these patients can always change their mind. It is absolutely their right and sometimes indications change too. But one ideally wants to minimize the amount of procedures a patient goes through throughout his or her lifetime because each of these procedures carries an increased risk of infection and bleeding. In addition, these are artificially placed hardware, equipment type things so they can fail. Leads may break, they may fracture, the insulation around the leads may also suffer from abrasion over time. And there are concerns about what we
call inappropriate shocks. If there is any noise oversensing by the device, or if there is any electromagnetic interference from the outside that the defibrillator picks up as if they were true ventricular arrhythmia potentials that could result in the device wrongfully assuming the patient is having an arrhythmia and delivering a shock or two or more that the patient never needed.

So it only makes sense to implant a device whose appropriate shock rate far exceeds the likelihood of inappropriate shocks, and fortunately, we’ve come a long way. These devices have evolved from inappropriate shock rates as high as 10 to 20% to now less than 5%. And this is something that is reassuring. It is still not at perfect, and we have to always make sure that our patients know about those risks when they provide informed consent to undergo any implant of any kind. But that is something that we always highlight to them, that is the risk of lead failure, either by fracture, by insulation failure or other mechanisms, the risk of infection and bleeding typically during the perioperative period, there is the risk of inappropriate shocks that I just mentioned.

And there are other features that are nowadays not as concerning, such as for instance, the compatibility with MRIs. In the past, having a defibrillator meant you could never go through an MRI machine, but that is not necessarily true anymore. And several devices in fact, most of the modernly available devices do offer the ability to have the patient go through an MRI scanner although certain safety conditions have to be met and this is still not routinely offered in every center in the United States and beyond. But these are just a few of the risks and benefits that we discuss with patients. We could go on for longer but I think those summarize some of the main topics that we always want to highlight when we talk to a patient and to a family member about ICD therapy.

Anjali Owens: 12:49 Thank you, Dr. Leal, one of the ongoing challenges in caring for patients with HCM is appropriately identifying high risk patients who would benefit from an ICD. Ideally, we'd have a way to accurately risk stratify patients so that we don't over-utilize or under utilize this important therapy. Dr. Gopinathannair, how do you approach the challenges of patient selection in this population?

Dr. Rakesh Gopi...: 13:15 Thank you, Dr. RobinsonOwens. This is a great question. And one that can be very challenging at times. Let me start by listing some potential risk factors that portend higher risk of
ventricular arrhythmia or risk for what we call a sudden cardiac arrest. And I'll rank them in the order of severity being high to low. The say one would be somebody who already survived a sudden cardiac arrest, and that'd be the highest priority for an ICD because they already had a ventricular arrhythmia episode that was life threatening. The second would be someone with a significant family history. What does that mean? So either a first degree relative who suddenly died before 50 years of age, or you had two first degree relatives that had sudden deaths at various times in their lives, the third one would be unexplained passing out.

So there are various reasons for passing out in patients with hypertrophic cardiomyopathy and not all of them are dangerous, but again, if somebody had an unexplained completely unexplained passing out, either not doing anything that would have caused that and within the previous six months, and that actually indicates a higher risk for, or raises suspicion about ventricular arrhythmias. Number four would be how thick your heart muscle is. There are various numbers, I think the accepted number is that if your heart muscle is more than three centimeter in thickness, that actually indicates a higher risk for sudden cardiac arrest.

Then there are a couple of other factors. One is that when you have a non-sustained ventricular arrhythmias, meaning that either three beats or more of rhythm disturbance is coming from one of the bottom chambers, and as Dr. Leal has mentioned, there is sometimes these thick muscles can harbor a scar or the cells are not all the way right, so that can result in some of these ventricular arrhythmias. But if you tend to see a lot of them or multiple salvos of them, that makes you concerned. If that particular one is combined with another one of the other risk factors, for example, somebody passed out unexplained and then you're seeing a lot of these ventricular arrhythmias that combined together can make a stronger case to offer an ICD to that particular patient.

Another one is that as we all know when the muscle is thick, it prevents blood flow from out of the heart. So if you were to run this patient on a treadmill and the blood pressure, typically when you all run, the blood pressure tends to go up but in some people with hypertrophic cardiomyopathy, blood pressure tends to drop or they do not even go up at all. Those are considered more of a higher risk. But again, with that particular finding, you want to try to have something more to offer them a nice, for example, with this treadmill test results along with
somebody who has a family history so that makes your case much more stronger.

We also have newer markers that portend a higher risk one is, doing a cardiac MRI and finding that there is evidence for significant amount of scar within the heart muscle, especially in that thicker segment, that actually has been shown to have a higher risk of developing ventricular arrhythmias. Genetic testing, this is not a forum to discuss that, that in itself is a big topic. And there are certain types of mutations that are considered to have a higher risk, and then you have marked obstruction to flow of blood from the heart. Those are also considerations in terms of offering an ICD. So I want to summarize by saying that more risk factors you have, the more confident you can be in your diagnosis, if you already had an aborted sudden cardiac arrest, or if you had very strong family history, and if you have extremely thick heart muscle, and you're very clear that there's no other reason for a passing unexplained passing out but other than ventricular arrhythmias, then those are very reasonable to offer ICDs.

The problem with all these risk factors are that they all have great negative predictive value, meaning that if you have a negative test, you can be very reassured that your risk is low. But on the other hand, they do not have a great positive predictive value meaning they, by themselves, we cannot say it's certain that this patient is going to get an ICD defibrillator shock in a couple of years from now. So, this is an evolving field, more and more markers are being identified. If you can work through these risk factors and try to risk stratify the patient that you are making a very informed decision to protect this patient.

Anjali Owens: 18:10 Turning into Ms. Chris, one of the most important things we can do as cardiologists is to include our patients in decision-making and to tailor medical care to each patient as an individual, in the context of population-based medical guidelines. Tell us your viewpoint on defibrillators and how a defibrillator may have impacted your life.

Ms. Chris: 18:32 Thank you, Dr. Owens. I do believe that ICD is an amazing thing. I do believe that by the age of 25, I should have had one. Dr. Gopinathannair was saying is that I had pretty much all of those factors that he listed. I do have a mother and a sister that both suddenly passed, one was 40 and one was 33. Both of them I believe that if they may have had an ICD could have been saved. My mom did have a pacemaker, but she only had one of the wires and that was back in the '90s.
So I know that technology has gotten a lot different and we have come a long way so I know that if it would have been different back then, I think that both of them probably could have been saved. It has also taken a long time for me to be an advocate I should say for myself, to show various doctors that I should be having an ICD with that family hereditary and also with my symptoms because I’m very symptomatic. I have atrial fibrillation and I also have bradycardia so I also go very low. My normal heart rate without an ICD is around 35 beats per minute. Normal is around 60 to 80 and I have a lot of symptoms. I also have passed out and for no reason. There was a lot of factors that went into play, and I fought very hard knowing that it seems as though this is what I need to protect myself.

And I’m now having children protecting myself so I can be around a lot longer than my mom and my sister were able to. So it was definitely a hard decision to make, but it was also a no-brainer. I always call it my insurance policy because it definitely makes me a lot more safe knowing that if something were to happen, that I know that it would shock me and one day save my life. I have not to date been shocked, thankfully. I have had my pacemaker in since February 2018, but I do know that if anything, push come to shove, if anything were to happen then I know that I am safe.

I also found out that I had the hypertrophic cardiomyopathy through genetic testing and then with everything, with all my symptoms and everything else that I've been through over the last 14 years, it all made sense. And my genetic testing came out with a mutation of me having the hypertrophic cardiomyopathy as long as well as all my echo-cardiograms have all showed my muscle mass is bigger than normal and so everything just made sense. I also had my children checked out in the event that if something were passed down to them and they actually have no mutation of hypertrophic cardiomyopathy at all, and none of them have had any symptom of any other cardiac issues. But if that were the case and I had to make that decision for my children and thankfully I don't, but if I were, I would be a lot more proactive also knowing all the knowledge that I have and the experience that I have where I’ve been, that I would have no doubt in putting an ICD in them.

I know for a long time a lot of doctors said the risk of putting in an ICD was not worth it because I was so young and I guess technology wasn’t as good 14 years ago so they were always so nervous. But I can say today that I definitely would, without a doubt, do it all over again and wish that I could have had it a lot
sooner but thankful that nothing has gone wrong, and with
prior to my ICD. And if anything were to ever happen that I feel
good about having it there and knowing that I'll be okay.

Anjali Owens: 22:23 Thank you Ms. Chris, for sharing your story, which is clearly one
of both amazing self-advocacy on your part and also
unfortunate tragedy for your mom and your sister, thank you
again for sharing that. In the last few minutes, I have a couple of
questions about long-term device care, starting with you maybe
Dr. Leal, can you tell us what is appropriate regarding
longitudinal follow up for patients with ICDs and also for
patients who have HCM but do not currently meet criteria for
needing a defibrillator.

Dr. Miguel Leal: 22:57 Thank you, Dr. Owen. I think this is a very important point. And
just listening to Ms. Chris, we appreciate how important and
life-changing events a defibrillator implant or remove for
instance can be in a patient's journey. And that is why the
decision to implant is so important and selecting the right
patient is so important. And once that decision is made and the
device is implanted, the worst thing that could happen to a
patient is to be lost to follow up because there are electrical
parameters, they need to be measured and followed over time
to make sure that the battery is working well, that the cables
are in great shape, there are many numbers that we look into
such as sensing pacing thresholds, pacing impedances, trends
that we follow over time to make sure the devices are doing
their job and doing it well.

It is as Ms. Chris said I think insurance policy and so it has to be
working every single time it is required to work. Anywhere
between zero and ten times, it doesn't really matter, we want
the device to be perfectly operational condition and follow up is
important. Most places will see these patients somewhere
between one and two or three times a year. At least one annual
follow up visit is highly recommended, a face-to-face visit, but
we have the benefit of remote following or remote monitoring
as well. Patients nowadays receive a transmitter box that it can
be placed by their bedside table, which will promote this nice
exchange of data between the remote transmitter and the
device so that the device clinic where the patient is enrolled can
receive real-time information. And if that is any yellow alert, a
red alert that can be immediately acted upon without delay.

If a patient does not yet merit criteria for a defibrillator implant,
a lot of the conditions Dr. Gopinathannair mentioned can
change over time. So if somebody has none of those risk factors
or is not quite ready to make that decision, that patient should be seen in longitudinal follow up again, at least once a year, and some sites will do it slightly differently, simply in order to make sure that the situation does not change because a patient could go through a syncopal event, a passing out event which sometimes it's even hard to remember if it's a one or two times a year situation; and those things may make a difference between a patient not having any indication from an ICD implant now and developing the indication of or a meeting criteria for an indication in five or 10 years.

So not needing an ICD at a certain point in time does not mean that a patient will never need one. And once the decision is made, if it's important to go ahead and do it as it was in Ms. Chris’ case for instance, that follow up is really important so that any issues related to long-term ICD maintenance and monitoring can be addressed immediately as they occur.

Anjali Owens: 25:30

As our last question, Dr. Gopinathannair, can you share insights regarding ICD therapy discontinuation and in what settings this may be considered?

Dr. Rakesh Gopi...: 25:41

Yeah. This is always where shared decision making becomes very important. And in a condition like hypertrophic cardiomyopathy and the fact that many of the patients get their ICDs while they are young, they tend to have this device for a long, long time and they go through multiple generator changes, fortunately, our battery lives are getting better. Typically, since this underlying situation is there and the risk is there, although it varies between different individuals, I would have a really hard threshold of turning off a defibrillator given the uncertainties of what we don't know long-term. And only a small proportion of hypertrophic cardiomyopathy patients, which is in the single digits, tend to get ICD shocks every year. So some situations you can think of where you would consider this one is obviously end of life situations or any other type of illnesses that the chance of surviving or living beyond a certain period is very minimal.

And there are also situations where you are having so much of arrhythmias and having numerous shocks, and then despite everything you can throw at that arrhythmia it's not controllable. And you're thinking about more comfort palliative measures and that would be another situation where you have the discussion. So obviously as Dr. Leal mentioned, we would provide the patient with the risk and the benefit, and in an appropriately selected patient it's been shown that the benefits
outweigh the long-term risk, although there are lead issues, other things could happen. So this is always a continuing conversation and a patient's status changes, device related issues can develop and we always try to keep that balance between risk and benefit if it shifts in a way that requires this conversation to be had again, and that's where you sit down with the patient and make a shared decision.

Anjali Owens: 27:49 Thank you all for participating in this podcast with me today, a lot of important points about defibrillator therapy and selecting the appropriate patients. This podcast is a part of the American Heart Association HCM initiative, sponsored by MyoKardia. 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 Ms. Chris demonstrated while sharing her personal journey with us today. They can also go to AHA hypertrophic cardiomyopathy patient website for more education. Thank you.