HCM Around the Globe: Not an Isolated Issue

CMEO Podcast Transcript

Martin S. Maron, MD:

Hello, I'm Dr. Martin Maron on behalf of CME Outfitters. Thank you for joining us for a new CMEO Snack series, titled A Global Response to Hypertrophic Cardiomyopathy: Sharing Experience, Sharing Resources. This activity is supported by an educational grant from Bristol Myers Squibb. This is the first of three CMEO Snacks, and we'll cover screening for HCM Around the Globe. Again, I'm Martin Maron. I'm the Director for the Hypertrophic Cardiomyopathy Center at Tufts Medical Center in Boston, Massachusetts. Thank you again for joining us, and I am very pleased to be joined today by Dr. Marco Torres from Porto Alegre, Brazil, who I will first ask to go ahead and introduce himself. Welcome Dr. Torres.

Marco Torres, MD, PhD:

Thank you very much, Dr. Martin Maron. I'm a retired professor responsible for our hypertrophic cardiomyopathy unit in my city. That is about a 1 million person city. But I have many connections all over the world and also in Latin America, mainly with people from Colombia and Argentina. So it's my pleasure to be here.

Martin Maron:

Well, thank you very much. Here, first, is our learning objectives for today's activity. After participating in this activity, learners should be better able to screen appropriate patients for HCM using evidence-based diagnostic strategies. Okay, so let's get started. And again, we're just going to have a conversation about hypertrophic cardiomyopathy. Dr. Torres, you're in Brazil, one of my favorite countries, by the way. It's a beautiful place. Beautiful people. Great energy. I love Brazil. So you're in Latin America, in Brazil. Tell us first a little bit about, sort of, your approach to how you, when you get referred patients, diagnose hypertrophic cardiomyopathy. What's your approach to making that clinical diagnosis? What do you rely on? How do you do it? And maybe take the listeners through that first for a second.

Marco Torres:

Okay. The patients come usually with three presentations that all, then, are related with the histopathology of this genetic disease. Or they come with a familial history of sudden death, more commonly seen in adolescents and the younger age guys, or else they come with a complaint of arrhythmias or syncope. Or sometimes they come because they have a cardiac murmur that was found by a clinician. Or sometimes they come because they have breathlessness. So, this is the basis. The basis of the presentation of this is important.

Martin Maron:

Right. So patients come to you, usually referred to you, with symptoms or an event. Sometimes, perhaps, also they get identified as having an abnormal electrocardiogram or heard a murmur on exam. What do you use? What tools do you use at your fingertips to make that definitive diagnosis in that patient then? How do you go about that?

Marco Torres:

They always go for an EKG, an electrocardiogram. If we find LVH, left ventricular hypertrophy, or if we find large, broad, and deep Q waves in the precordial leads, mainly if they have a history of a sudden death patient in the family, they are highly possibly, and possibly compromised by the disease. The second test that they always do, it's important to say that also not only in Brazil, but in many European countries, an echocardiographic study is done by the physician during the visit, during the office outpatient visit. In the U.S., it's not much difference because, when they come into an outpatient clinic or a hospital, the sonographer will do immediately if we asked. But as soon as an echo study, echocardiographic study, a comprehensive echocardiographic study has found in any region, in the absence of LV cavity, left ventricular cavity enlargement, if we find one or more segments that are hypertrophic, and bigger than 13 millimeters, then we already have the basis for the diagnosis.

Martin Maron:

Gotcha. Okay. So you have to identify 13 millimeters or more anywhere in the left ventricle. You're usually using echocardiography to do that.

Marco Torres:

Yes.

Martin Maron:

That's the primary basis for diagnosis, correct?

Marco Torres:

Yes. Correct.

Martin Maron:

Just to expand on that for one second, the recent 2020 North American guidelines, ACC, AHA, and HCM, really elevated the importance of magnetic resonance imaging in HCM in two ways. Both in patients where the diagnosis may be ambiguous, borderline wall thicknesses by echo, or you can't see parts of the LV chamber well enough by echo. So using MRI to help confirm that the wall thickness is increased or not. And also, for the identification of high-risk features like a lot of scar, late gadolinium enhancement, or apical aneurysms. Tell us a little bit about your experience with MRI in Brazil and Latin America. Are you using it? Are there access problems at all to get an MRI? Tell us about that, given its importance in the contemporary evaluation now for HCM.

Marco Torres:

It's very important to use MRI. And we have it, actually, all over the country. We have many, many groups that are doing these, even in my 1 million population city. But you are absolutely right that it's a very important and extremely necessary imaging technique. And I think that in occasions in which we have doubt, because sometimes, as I was explaining to some students today, that sometimes the patient has a combination of hypertrophic cardiomyopathy and other diseases if they are older, and if they are older than 60 years age. So you have a doubt if it's caused by the genetic disease or for instance, if it has hypertension or other problems. So here, the MRI is absolutely important. Also, in patients that have the manifestation in the apex, the apical disease is exclusively diagnosed by MRI. And also in the situations in which lateral wall hypertrophy is diagnosed, which is much more probably diagnosed by MRI than by an echo study. So, it's a very, very important point that you made, and we rely very much on MRI for the confirmation of diagnosis.

Martin Maron:

Yeah. So, if you have a suspicion of HCM, the MRI could help confirm diagnosis, particularly in certain areas of the LV chamber where focal areas of increased wall thickness may be missed, or not appreciated by a lower resolution imaging technique like echo, including, as you said, lateral wall, apex, sometimes even the posterior septum. Those are three important areas where MRI can detect disease, and sometimes be missed with echo. Do you use it also then, in terms of risk stratification, obviously, which is a really important, of course, issue in this disease, the number one cause of sudden death in young patients. Risk stratification is always part of the evaluation that we have of patients, particularly initially. Tell us about your experience with the role of the detection of fibrosis or late enhancement with MRI. Do you find it helpful? If you do, how do you find it helpful in terms of making management decisions?

Marco Torres:

Okay. It's also a very important point that you made, and it's absolutely mandatory to have stratification, risk stratification, in terms of late gadolinium enhancement, because this is the most feasible possibility, in terms of imaging techniques, to identify the candidates for sudden cardiac risk of death, and also increased risk. And sometimes they go, after this confirmation, they even go for a device to prevent the ventricular fibrillation. We are absolutely right using MRI to stratify high risk patients.

Martin Maron:

Right.

Marco Torres:

I agree totally with you.

Martin Maron:

Right. And then maybe you could touch on too, I think one of the really important areas where MRI has, in a way, kind of elevated our understanding of risk stratification beyond scar is that, and you alluded to this before, but I just kind of want to emphasize it for the listeners, is the issue of two different kinds of abnormal morphology at the apex. You can have hypertrophy, apical HCM, apical hypertrophy, or you can have an aneurysm at the apex. Thinning actually, scarred rim of aneurysm. And that aneurysm, I think we've come to appreciate, is best identified usually with MRI. And when it is identified, would you agree that... has your experience been too, that those are high risk patients because of the increased risk of ventricular arrhythmias originating from those aneurysms?

Marco Torres:

Definitely. I agree. And they are really at increased risk of sudden death and arrhythmias.

Martin Maron:

Right, right. And so, you sometimes, just based on the identification of the aneurysm, will consider a patient for primary prevention given that risk for ventricular arrhythmias is so high with that group. Right?

Marco Torres:

Very high.

Martin Maron:

Yeah. Okay, good, good. That's an important point. That's kind of juxtaposed, or in contrast to, the apical hypertrophy patients which are generally considered to be at average or lower risk, actually, for sudden death because of the limited hypertrophy confined to the apex. Would you agree with that?

Marco Torres:

I agree totally.

Martin Maron:

Great. I think the point there is MRI can be helpful for identification of hypertrophy when it's unclear or not well seen on echo for sure. Or, if there's a suspicion of HCM, MRI can be very helpful again in clarifying diagnosis, and also adding to management by identifying high risk features like scar or apical aneurysm. Let's shift for a minute, back to echo for a second. One of the most important features to reliably identify in patients, particularly when you make the diagnosis initially, is whether patients have outflow obstructions, or obstructive HCM, or non-obstructive HCM. Tell the listeners a little bit about your experience in Brazil over the years - how you did that most reliably.

Marco Torres:

Yeah. I think that this is a turning point in the patient to have, that has had a diagnosis of hypertrophic cardiomyopathy, because the identification of LV outflow obstruction imposes an extra risk of an outcome, a bad outcome, mainly in terms of developing heart failure and remodeling of the left ventricle. If it is a young patient, we have to push to try to reach the confirmation of LV outflow, not only with bedside maneuvers. We've been working along with Dr. Olivotto, Dr. Picano, and Dr. Patricia Pellikka in Mayo Clinic at Minnesota in a research project, in which we recently had a paper accepted with more than 1,000 patients. And all of them, they went for exercise echocardiography, and I do a lot of exercise echocardiography, always when these patients have no limitations to do an exercise. Or how, for instance, if they have an absolute contraindication. I would definitely try to find out, to confirm the hypothesis of LV outflow tract obstruction, mainly because for this, now, certainly we'll have something to offer additionally to the patients.

Marco Torres:

I think that this is something very important to my colleagues in my country and in South America, also, that we have a drug that was found to have definitive improvement in LVO obstruction. That is mavacamten. That's going to be available in Brazil as soon as you have approval by FDA. So I think that this is a very important point to find, to look for, LV outflow obstruction. We need to do this, not only patients, adolescents, but also in the older population that frequently is missed out, without this point being diagnosed. That's my opinion.

Martin Maron:

Okay, good. Just to kind of summarize that, the points there that are really important are that two thirds of patients with HCM have obstruction either at rest, or with some form of provocation. Sounds like your choice for determining obstruction if a patient with HCM comes to you for an evaluation, and doesn't have obstruction under resting conditions, is to use exercise.

Marco Torres:

Exercise.

Martin Maron:

Yep. And I would agree with that. That's been our experience too. We've used exercise, treadmill as our preferred method, to provoke gradients. It's obviously when patients are... It's mimicking, obviously when patients are normally developing symptoms with daily activities, treadmill is, so we like that as well. It's the most physiologic. That said, there are, of course, other methods that are out there and have historically been considered, like Valsalva maneuver, dobutamine, amyl nitrate. Do you ever use those, or do you solely use exercise to provoke gradients?

Marco Torres:

In the past, we used this. Of course, when we have a suspicion in the clinic, if I'm doing a 2D echo, a 3D echo, I'm doing this, and I found the diagnosis of hypertrophic cardiomyopathy, it's very easy to do a Valsalva maneuver.

Martin Maron:

Yeah.

Marco Torres:

Mostly, they would not be very responsive in terms of LV obstruction. So, we schedule them immediately for an exercise. And then, I feel totally that we do also treadmill. Here, we don't use bicycle exercise testing, like in European countries. We do use the treadmill, because that is the way that we do the ergonometric study. And this is fantastic to find the obstruction.

Martin Maron:

Right. Okay, good. You prefer exercise. If you do Valsalva, which is easy to do, the Valsalva maneuver, the data is actually about half the patients that have no gradient with a Valsalva maneuver will have a gradient with exercise. That kind of underscores the importance of exercise, here, to really determine if a patient with HCM obstructs blood flow or not. And of course, this is all really important because there are, as you were discussing, treatments that are available today. There may be some new treatments. I think you mentioned mavacamten, but that's not yet FDA approved, for the treatment of symptomatic obstructive HCM, that those therapies may not be applicable to non-obstructive patients. And of course, there is definitive therapy in the form of surgical myectomy or alcohol ablation in terms of invasive procedures. So, we've got drugs and procedures that patients with obstruction, who are symptomatic, can have access to to help improve substantially their quality of life, that are not available in some instances to the nonobstructive groups.

Martin Maron:

That's why it's so important here to make that characterization of obstruction or not. Once you've done that, you've made it. You've said a patient has obstruction and they're symptomatic. Tell us a little bit about your experience in Brazil with patients that have become refractory to beta blocker, calcium channel blocker, then become candidates because they don't want Norpace or disopyramide, or they try it and that doesn't work, for invasive options. In other words, tell us how the current contemporary approach is to surgery or alcohol ablation in Brazil right now.

Marco Torres:

Okay, good, good question. Because this is very important point in my view, in my personal view also.

Martin Maron:

Okay.

Marco Torres:

Here in Brazil, we rarely have a cardiac surgeon, surgery group, very willing to do myectomy. So we go for septal alcoholization. That's what we do mostly. And we follow this, we choose, and we check the results, doing at the same time a transesophageal study. And we see exactly the areas in which the hemodynamics is going to infuse the alcohol, because when they occlude the septal artery, we find very frequently a change in the wall motion, localized segmental wall motion. So, we follow these always with a 2D echo. I think that we are very proud to say that, although mostly it would be, I'd say the final result, the outcome is with surgery would be very good. But it's not very easy to find a surgical team that would be willing to do, to specialize in such a way. So we prefer to go for septal alcoholization.

Martin Maron:

Okay. We could probably talk forever about access to surgery and alcohol ablation, but I think what you're saying is, surgery is, in your view, when done with a good surgeon with a lot of experience, is a great operation and can really effectively improve the symptoms by getting rid of obstruction. You've got to find the right surgeon, of course, to get the outcomes that you want for your patient. And if you can't, then alcohol ablation, which is more widely available both in the U.S., and I'm sure Latin America as well, compared to surgery, is also highly effective. Would you agree with that in terms of symptom improvement?

Marco Torres:

I would agree completely. Sometimes the results are very, very impressive.

Martin Maron:

Good. Okay. So you got highly effective invasive treatments that are available today. And of course, access is an issue, but I think even in places outside of the U.S., and you're obviously speaking from Brazil, there are opportunities for patients all over the world to still get good treatments like alcohol ablation if surgery is not available. Let me switch for a second, because we're running out of time. Maybe one more question here, and then we'll wrap up. I was curious about this. It's part of the contemporary... of course it's part of the contemporary evaluation of a genetic heart disease like HCM, is the assessment of family members. And one of the important aspects of that is genetic testing, because genetic testing, obviously, perhaps its strongest or most important role today is the opportunity to potentially evaluate family members for their risk or not of developing HCM. If you're able to find a pathogenic mutation in your patient with genetic testing. Tell us a little bit about your experience with that recently. How do you use it?

Marco Torres:

Almost all the patients have genotyping. Almost all. Why? Because if it is not useful, at least it would not be unnecessary to have. Mainly in familial situations. I think it's of utmost importance to genotype the families. Mainly if they have a history of sudden cardiac death. Sometimes also it's important to prevent a situation in which a young woman is going to have to try a baby. And she's concerned about this because a familial member had a diagnosis of hypertrophic cardiomyopathy. So, in my view, this is a very important field that is growing up very much, including familial genetic counseling, because this is something to think about very seriously.

Martin Maron:

Good. Okay. Essentially, if you kind of summarize that, it sounds like, as you've said very well, genetic testing, really important part of the contemporary evaluation of HCM patients today. About 30%, 30 to 40% of patients with HCM, if you test them genetically, you'll find a pathogenic mutation. And then if you do, you can test their blood relatives, children, siblings, to see if they have that mutation. If they don't, then they're not at risk of developing HCM, and you can kind of exclude them for further screening with echo that way. And then, if they do have the mutation, you're going to continue to follow them closely for the possibility that they will develop HCM. Although, not all patients that carry a pathogenic mutation develop HCM. Some remain carriers their whole life as well.

Martin Maron:

And there are, of course, issues in the U.S. with genetic testing in terms of testing children that involve the implications for insurance, life and disability. Those insurers can use that information, sometimes, to make differences in policy for those patients. That's one thing to consider at least in the U.S. I'm not sure that's the case outside of the U.S. But the other point, too, is that genetic testing can help identify diseases in a proband that may look like HCM, what we call mimickers. Things, other diseases like Anderson-Fabry, potentially amyloid, other glycogen storage diseases too. So it's an important aspect of differential diagnosis as well. Would you agree?

Marco Torres:

I agree completely. Phenocopies of hypertrophic cardiomyopathy would benefit tremendously with negative mutation tests, would be much safer for the clinician, the cardiologist, to handle such patients.

Martin Maron:

That's right.

Marco Torres:

In my view, it's growing up very fast, genetics is a very close pattern of our outpatients. The clinic is specialized in hypertrophic cardiomyopathy, and I think that it's a very important field to grow up.

Martin Maron:

Well look, we're at the end of our time here, and I wanted to just say first, thank you. It was great to hear your perspective on hypertrophic cardiomyopathy from your longstanding career in this field, and also your perspective from Latin America, from Brazil, which has been really invaluable and really important. And I'm sure the audience got a lot out of what you had to tell us about HCM in that capacity. So I want to thank you very much. We really appreciate your time being with us today and sharing your expertise with us. Thank you.

Marco Torres:

Thank you very much, Dr. Maron. It was my pleasure. I hope to see you around in the near future.

Martin Maron:

Great. Thank you. Thank you, Dr.

Marco Torres:

Thank you very much.

Martin Maron:

Appreciate that. Well, that's all we have the time for today, and I'd like to thank Dr. Torres again for joining me. I enjoyed our discussion immensely. Now by way of summary, I'd like to offer a few SMART goals to our audience that summarize a little bit about what we talked about today. One, the importance of complimentary imaging. Echocardiography and MRI in terms of providing patients the best opportunity for reliable diagnosis and management, with MRI really valuable in helping make a definitive diagnosis in situations where that may be ambiguous with echocardiography, and adding to risk stratification through identification of high risk features like extensive scar and apical aneurysm.

Martin Maron:

Two is the important point of identifying outflow obstruction using physiologic tests, like exercise echo, to do that in patients that come to you that do not have obstruction under resting conditions. The importance of that is, that by identifying patients with obstruction puts them in a hemodynamic group that then opens up treatment options that are not available to non-obstructive patients. That includes drugs, like Norpace, potentially newer agents like myosin inhibitor with mavacamten, that are going to be available for obstructive patients, but not the non-obstructive. And of course, the invasive options if patients are refractory to drugs and can become candidates for something more.

Martin Maron:

And then genetic testing, the importance of that and identifying whether family members may be at risk of developing HCM or not, is a really important and powerful tool for genetic testing, no matter where you are in the world. Access to that is increasing and should be available without being prohibitive by cost. And also, the opportunity with genetic testing to exclude phenocopies, other diseases that look like HCM that have different natural histories and treatment strategies. So genetic testing can be very helpful in that capacity as well. So, those were our SMART goals. I'd like you, as I mentioned, this is the first of three new CMEO Snacks on HCM. Please visit the Cardiology Education Hub at www.CMEOutfitters.com to participate in part two and part three of this series. And don't forget to complete the evaluation to claim credit for today's activities. Thank you very much. Again, appreciate you tuning in and your attention. Thank you.

