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TRANSCRIPT - GR 09 01 23"HOCM Screening for the Internist " Michael Ayers, MD, from the University of Virginia

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During final year fellowship, he was awarded a fellow of medical education. Afterwards he joined Faculty here in Uva's Cardiology Department. Dr. Ayers' Somehow he seems to want numeracy awards at every stage of his career, including any medical student, resident and fellow. during his time as an attendee, has already been awarded that Edwin would teaching work. Mahalan and wars were teaching excellent clinical curriculum and acd, prompt or hardy young teachers.He's very active in research as well, and is the principal investigator on many projects, focus on the improvement and care for patients and hyperturbic cardiography.

- And then, as research, she, when I met with all the residents discuss research projects I am touched by how often residents indicate that they hope to work with Dr. Ayers citing his mentorship as part of cardiology without further view.
- Thank you very much for that. My favorite topic like a psychotrophic cardiomyopathy. So I'm gonna take a little time at the object because I wanna frame exactly what my whole time. So let's walk off. There's a little slogan. But after this the first objective is actually gonna be a little bit of a recall diagnostic criteria and common presentations and clinical courses. Then we'll have a little bit of a 201 objective where we're talking about what clues should trigger in particular, an internal medicine position to start a workup into apps for patients. After that you're gonna see a little bit of a gear shift, and we're gonna discuss some of the things we do at the center of excellence, right? Broad range of things. But we're gonna focus mostly on our use of genetic testing how we think about and manage out flow track disruption. I'm gonna use that term several times. Just make sure we're all on the same page. That's when there's a blockage of blood flow from the left ventricle for the aorta, and as a result. the aorta where physiologically not.
- And then finally, we'll use exercise the way, discuss, shared decision-making, and how to think about that and some of the more rare diseases. Finally, and this is probably the 301 learning objectives. So one which I'm hopeful will be able to serve as a model for others. When we talk about the lab to bedside and disease modifying approaches that aren't now big in mind, those learning checks. The outline is really going to parallel everything, I said.
- We're gonna start with a recall of diagnosis, gene and type, you know, type, the shape of the set on the shape of patients present, what happens to them after they present, and what the work of this segue into that same learning, objective or a differential diagnosis. When the screen went to refer. we'll then go into management principal, give you an idea behind things we do in the summer.
- And lastly, we'll move to interactness. So thought from the early point in medical education, that, in fact, is part of the case. So let's go ahead and begin with one very nice. All about 18 months ago it was referred to me with a new, actually very carefully documented. I heard this now this would be former division, one collegiate player who was forward. Not a goal like this is somebody that's moving around the ice, who had had competition for about a decade and a half multiple ultra monitors, which had only shown rare premature ventricular contractions or Pdcs.

- Kind of alarmingly. He also described. 15 years of chess burn! He thought, the cold air of the ring, and he started noticing it when he was running in his post hockey career. Sometimes it happens from emotions, and, as it happened, at rest, sometimes it happened, for seemingly no reason at all primary, no better when they started and want to keep the item improved, but it did not fully go. Look!
- Family history is similar to how I'm sure many family that's been predominant. But we don't really always know our family history. But what this gentleman said was, you know, my mom's brothers. No one's got some networks. This is the idea. It's down in a new market. Now if Dr. Peter Dean and I are screening a Uva athlete and this cross our desk, this there's a few reason why young adults frequently have hyperganess, and so they frequently have high perjury. And you can see the Drs complex for touching here, however, what you also see the team way inversion. Get my mouse here touted versions that are extending all the way through v. 6 young athletes, and have 2 woven versions to be 2 athletes who identify as black, particularly ones from Caribbean or African descent, and have them all the way to be 4, but v. 5, e. 6 and inferior leads with these sort of St. Depressions should bring alarm. So here we add science, black and griggler, by perfect and t-weighted versions. Now the primary within the referral, and also the alert and echo. So before I install this patient we had an active cardiogram. Now here's a directive party, Graham. I'm gonna war you. This is a perister long axis of the prose, right by the stern not showing up.
- Oh, fancy alright! And you don't see a lot of these the picture on the right, from the apex, right in the mid particular space of 6 rings down, and what that shows is again very thick heart muscle, and for those of you who like echo what you'll notice is the mindful valve which is right here is actually being drawn in towards the second right.
- This is Colorado, which shows that accelerating flow is also useful. When examining laminar versus turbulent flow. You turn the thing on. It's going smooth. You turn on fast. It gets white That's accelerating fluid and exceeds the critical velocity. We like physics. And what we're seeing there is exceeding critical velocity, and there's turbulent flow through the outflow tracks arrows 90 degrees September arrow sign. If you're Microsoft the physician who read this cold of strong hypoten cardiomyopathy on the reed and the patient also. So when you think about hydrochloric cardiomyopathy, I really want you to think about primarily 2 things. My screen is all. But I'm gonna keep going. I want you to think about heart failure. both obstructive and non obstructive. Now instructed. This kind of when there's a blockage back on blockage of blood flow from the Vanderbilt to the aorta, like we discussed earlier and non obstructive, is essentially F. Path, are familiar with preserved injection. Practice on steroids that is the script I want you thinking about as we go through more on that app.
- The diagnostic criteria, however, is thickness. More than 1.5 cm. Now, normal is around one. This number 15 is 6 standard deviations above population averages. That's how we picked it. When we wrote the latest guidelines. There's nothing special about that number. There's no sudden decrease in the capital Meyer curve. We just had to draw the line in the scan somewhere.
- What's really fascinating about Hcm. In the late nineties this became an absolute paradigm for genetic cardiac diseases, because before the nineties we had a hodgepodge of left ventricular increased thickness, diseases. They all looked a little different. They all behaved a little different. We weren't sure. Is it? One big umbrella diagnosis are no different diseases. Well, Paddy, acting off the work of the Schwartz lab cricket. Simon and her husband discovered the and NYPC. 3 mutation which is a biosynth binding protein C.

- And was present in a huge numbering of the heterogeneous increased thickness. Parts they all look, but they all have this protein, and what happened is that all these different phenotypes and shapes were put under one umbrella.
- We thought, this is going to be everybody but that forward 25 years, and what you see, is, despite incredible work done by geneticists everywhere. Only about a third of patients with ATM have one of those 2 identifiable genetic mutations that I just mentioned. Everyone else is genotype.
- That means that tonight not exactly when you look at a gene like negative group. What you find is half of them are clearly behaving in an autosomal, dominant pattern. Dad, brother cousins, cousins that of them looks thread. We're probably missing mutations.
- Mighty slidesight might be Andronic non coding for those of you who like genetics. We're missing a piece of this puzzle even 25 years later.
- Thank you. Really discuss hypertrophic cardiomyopathy without talking about Septo, because 90% of hypertrophic cardiomyopathy patients are going to have thickness of the wall between the left and right. The one that we learn about most in medical school is this picture number 2 which is a big hour last configuration going into the left ventricle before. And if you look, most of these patients compare and contrast that with what? My, the smarter doctor's ontology called the little Lady Stephen. We have just a tiny little area I heard to be up here at the Basil second, only 80% are Mdg. Gene, type positive.
- 90% of the time it involves septum. But there seems to be huge discordance in the shape of the septum and the genetics.
- We're now gonna talk a little bit about a study that helped elucidate some of this. It's the Hmrc. Card cardi Myopia Registry, where we looked at MRI. Almost 2,800 patients at 44 sites. A young lobster cardiac imager is the pi on this study, maybe name for itself and microcode, according to arguably, the most famous MRI card in this study, but relatively broad groups of patients.
- But first this hour last set different orientation of the picture. There's the vendor, there's the hour last setup again. We're scarring more likely to be genetically positive. Younger age
- comparing and wrap that with the other one, the isolated stable type less far late Galilee and decent, elderly, more obstruction, older age and onset.
- In response to this. What you've seen is a flurry of publications asking the question.
- business to diseases one. the monogenetic disorder.
- I believe, when they figure out the pause. These are young patients. They go last far. They have a lot of arrhythmias as a result of this, far less likely to have obstruction. But a lot of work. The second one appears to be actually a polygenic predisposition to hypertalia. Fancy way of saying a bunch of genes are contributing and making this part sick, sometimes variable. Sometimes it's not patients presentation more likely to have Lv. OT. Instruction. And I'm bringing this up because I want to introduce to you guys that I really do think about these as 2 different populations, and it has 3 for our next set of guidelines. Because if these are 2 different disorders.
- Do I really need to take the patient whose father was diagnosed at 82 with isolated basal sickness and starts treating them at age 20 every 2 to 5 years for the next 6 decades of their life? These are questions we need to answer.
- Similarly, if hypertension is particularly bringing on isolated baseline, should we be more aggressive and doing polygenic risk scores on this group, and aggressively reading hypertension from a not young age. So these have ramifications for future management.
- That was a little of 201, and what I said was going to be the one in one section. But what I want you to remember is thick heart usually involves septum hourglass. Isolated bases subtype good.

- Now, depending on who talk opposite you like somewhere between 200 500 patients, one and 201 500 patients together. That's based on autopsy data. When you look at registry data, how, when you're diagnosed one and 7, how do they come to? Our attention? Melts. Well. sort of is pointing. My. Only about 40% of these are coming in with symptoms, and the symptoms are vague, just paying pre syncope politicians, the team dizziness when exercising the third, I mean, basically like the first payment findings from something else. Let the testing that discovered but 10, and this is a number that's rising. We're very proud of that surprising. We're coming from delivery cascade and the relatives.
- But here's the one that should ground primary attention one in 10 patients. Their first presentation is dying now. Sometimes there's no more than sun, but one in 7. Patients are diagnosed with disease, and one out of 10 patients will have a first symptom of death.
- Now, keeping in mind that we have 2 separate types, and that the reverse earlier and isolated. This next slide. It basically shows the earlier you proc that you present the worship process. So if you look at the lighter of the red lines at the top. There's gonna be more events represented on the Y axis the earlier you present. That's the under 40
- compared to the people over 60 who might usually tell them. Clinic, this is a compliment that you're not more likely to die. The things that kill runs heart disease, not this.
- hey? Good! I want you all to see parallel, and I'm highlight. 40% of Hdm patients will develop relation.
- This is one of the 2 things on your medicine boards that you should know, no matter what the chat asks for, they get anticoagulation. The othee viral services particularly run out again. The earlier. You present the worst to do in line those 2 phenotypes we discussed earlier.
- Now for a long time we thought about this as sort of a benign, and
- people said, they're gonna get short and spread. They might get some arrhythmias. But once you get through the sudden death phase of youth, you're gonna be fine, but what we're finding, and particularly with the share registry, a large HD. He mentioned that 4 whole increased mortality bridge one in 10 will present with death. And even if they don't present with death. there's a horrible increase in mortality. Again.
- primary care. Physicians are gonna drive the improvement of care in this group.
- So you don't want to talk to your neighbor. I'm gonna take sip of my cardiac for my dive out and do here in a moment. But I wanna make sure you guys know a couple of things. Hang your own hand with your neighbor when it's here to focus, make sure you can name the diagnostic.
- Make sure you understand the relationship of the septum to the genotype, and particularly Rivers, curvature and isolated Basil.
- and ask yourself if I remember how it presents and how it progresses.
- What I said, perhaps all. What's the differential? And when do we refer?
- So we're gonna start with history and family history signals that you should be thinking about this disease.
- Somebody said, I gotta have a really bad hierarchy. Please do that. The second one will terms. You're selling cardiac death. Scd.
- If you ask stations, they'll frequently tell you Dad died of a heart attack.
- I encourage you to ask. Tell me more. and they found him in bed you know. Tell me more. I'm going. Yeah. The email said he had a heart attack. Maybe
- I mean, it was signed up for something else. So I asked that follow up a question.
- If you hear a harsh murmur, particularly a system murmuring, the season coming and going that should trigger a workout for you.

- and if you have a patient that says I'm passing out, or man, I'm really close again. This should trigger basic cardiac work. But let's move on from the history and the family history, and talk about what findings on imaging, incidental or otherwise included but suggesting E and G is important to follow up with an echo. Now, here's a disappointing figure.
- Well, 95% of HDMI. Kg, only a third are going to be really happen to Monet looks like, you know. The rest are gonna have abnormalities. But you're gonna have to suss it out.
- Hypertension, hypertension fashion model.
- Another one that we bring. What we see is deep tea, waving versions. I'm going to show you a sample of this in a minute, and my fellows will jump out of the scene of excitement. If they're so good at recognizing this, the third one is going to be septal cue waves so pathologic. Q. Ways with two-way conversion, either extending through v. 6, like our personal Ag, or even in the interior, leads the inferior way to versions, are less ideal. But we still consider that normal the other thing that should clue you in is when we write this in an echo or asymmetric septal hyperde. Sometimes we're moving real fast and we click a button, and we didn't see it. But sometimes we're telling you this is Hca.
- If you see this phrase in an echo, feel free to message me or the person a little or a lot. Tell me more. What you meant by asymmetric set. The library not infrequently referral is that 16 fees? All of which said asymmetric central Hypertv, but not hcm, and it took that long to find their dial lens. Let's look at a couple of these. Eg's as a 38 year old. No history of hypertension for you here. What did for you? Lv. H. 5. Criteria would be 26, and there's several key ways in a week, 2, 3, and AV there we are good interior. Gene laser is inside Sammy Gram. Not a good one.
- A double HC. Is the chunk and tip and stick in rather than the septum dividing the left and right part. And and I referred to you as a shortness of breath. Pharaoh was busy
- really doesn't look like it even makes sense, but it doesn't.
- They're low and hold. So I encourage my men students to hold me far away and squint.
- both look small and probably small. There's low within your regular response, and there's buying a secular flock. But there's a right on the range block, and a left was 0 block. If you don't love the Ekg's, that's just why that steps well again. Primary got an echo on on the way to me, and here is the echo and help you out again, I think, with Darrow time. Right pencil. The top circle is pointed at you left. Pincher Bowl is right.
- They're the big Zap. Them normal is one, and these are 2, 2 and a half again. Now, if you told me this in isolation, I realize that looks like HTML. But when you match the to this echo. and she moderate it bother me go to excess while I ordered a test.
- In fact, there were 2 tests. One typically gets done slightly faster than the other. The first one, apologies, Dr. Kramer. That was done with scan very quickly ordered and done. Pyro phosphate, scan, technician, pyrophosphate for diagnosing something called atr amyloid
- amyloid, has 2 flavors. It's not the subject of this talk with 2 broth pro flavors. One is light chains which leads me the next slide just cause we're sick of an evenings. HTML,
- this is a fantastic study that is led by 2 really brilliant young physicians, Elizabeth Farrah and Santa Gotty, and they looked at the last 210 referrals. About 8 months of referrals to Hcm. Clinic, and they wanted to see how often do we change a diagnosis? And these are usually cardiologists sending someone saying they have. Hcm, 2, one in 6 ended up having something else.
- By the way, kudos to alright, let's segue into the different people. So not all that is thing is hdm, what isn't.
- There are 3 broad categories that I think about. If you get lost in the morass of this slide there are 3 broad categories, I think about the first is, don't laugh at me to be a treatment challenge childhood stuff.

- These are your noon and syndrome, your left hand syndrome, mitochondrial disorders like levers disease, things that I'm not going to diagnose. But luckily they present with dysmorphic faces, failure thrive metabolic acidosis, not really targeted
- audience for those diseases. Guys. The second one is adult, but these are primarily infiltrated processes. We do see these on referral. There's a bunch of them. We get about one band disease every 2 years every 3 years. The big one, though, is analyze the one we see a lot of these, you're gonna need clinical clues plus energy.
- We're really an MRI. And so our MRI leaders are almost always able to suss this out, which is why we need on MRI so heavily star on Android for remembering remodeling, which used to be a big problem. Now, when you've got some other reason to have consent, some other left side of instruction, we're pretty good so that I can use you 3 categories, kid stuff infiltrative stuff and physiologic remodeling unit in your satellite.
- A little more on athletes hard because I get this question a lot from primaries. Hcm, overlaps a lot with sports cardiology. And so I do see a fair amount of sports, cardiology, and people frequently say athletes hard.
- Well, here's a fantastic study that the Mba did where they echoed everybody.
- And what you see there on the X axis is having more than 13 and these are the biggest teams in the world. Pretty unusual.
- 15. Nobody interestingly, and this is, could be a talking of itself self identified. Black athletes tend to have more hypertrophy. It's probably at yeah, 23 phosphorus related. It's probably juice into some systemic racism that has to do with food habits between different classes of people could be a full talking of itself. I just wanna mention that this probably is genetic. There's more to this.
- And this is just a reminder when I say, Nba athletes, that's what I need.
- So they're using a 13 septum.
- and they're not in the Mba. You should probably refer 1112. I'll give you a pass unless you're kind of a weaving warrior once once ever. You know, couple of weekends last alright midpoint review. Hopefully, you've had a little bit about that. It's our disorder. but only a third. The two-thirds of the time we had in highs. 1.5 cm is power the disease of heart failure, whether it's obstruction or EPA, and of arithmetic, patriot.
- and then triple the hypertrophy pattern predicts your genotype ergo predicts your clinical course.
- The differential is E after variable presentation, but the earlier under I mentioned the words, your product. Again, I'm together. The presentation patterns are the reverse curvature versus the IP basic session. So I promised you a gear shift after this moment. And here it is.
- We're now going to discuss some management writings.
- But let me go through this, we're really gonna use the 2020 guidelines as our main framework busy slide that I just wanted to say, kind of the mini htm fellowship and a cardiology fellowship. And this was the female physician, scientists who's just an absolute all-star, the training. So I always take a moment. Just one of the alright. The biggest winner in these guidelines, was a brand new clause that said, If you complex hcm you really need. It is coordinated care, not primary care, but coordinated care, with a center of excellence or a high one. So there's 4 of these recognized nationwide by the Hcma. Which is a patient having this group that's incredibly active for their patients. And we're wanted to
- when you prefer, just know, you're not really referring to me. What you're referring to is a team of people whether it's Dr. Lacoyer or I. Up in the top left in the corner Matt Thomas, will you more on him in a moment, doing our genetic counseling whether we're moving forward to advance therapy options with Dr. Kurne, Dr. Regassa, Dr. Bourbon or dealing

with Dr. Mcdaniels and Dr. Basin answers a lot of emails on Htm. For me or and I put Chris in the center there. Dr. Kramer in the center there. Because imaging is really a gateway to all of this. Karen. If you're listening. everyone, how do we survey all these agents?

- The slide that I'm going to bring up had small font on the right, and I couldn't make it any bigger. So I'm going to give you bullet points on the left side of the screen have to see them every one to 2 years physical, to an exam monitoring annually for every other year, every 3 to 5 years, particularly at time of diagnosis. You should consider Cardio MRI into. It's enormous prognostic potential in this disease.
- Finally, every one to 3 years you should stress this patient. Am I saying? Well, why?
- Well, we're gonna talk about this in a moment. But some patients have obstruction only that's brought out with activity. And you really want to suss those people out there. The management is, gonna be directly contradictory than not having instruction. Moreover, Cleveland did a fascinating study with all their asymptomatic Hcm patients and put them all on a treadmill. Anybody have an idea how many did age and gender math predicted exercise tolerance. 15%, 15% could do average alright.
- This is everything I need to know about Hdm, management in one slide trumpet.
- We're not gonna cover all of this. But I basically look at these things. We'll start with genetics. We'll move on to heart failure whether it's obstructive or not instructed. And then, lastly, we'll talk about sudden cardiac death
- risk, stratification or rhythm management, whether it be here or atro. Yeah, let's go through that one at a time. So when I did thatics, when I'm really talking about the same screening with the genetic counselor, we're going to focus on that few slots when I say per failure management. I'm talking about negative inotropic therapy or left ventricular alpha tract obstruction. We'll talk about that with these slides, or essentially has path treatment. If you're non obstructive.
- Things get bad. We need our surgical and international colleagues more on that gratification. Essentially, what we do is, we assess what we think your risk of dying suddenly doesn't exceed a certain point. We offer it to fibrillator some cases still strongly, some don't feel strongly. It's very much a shared conversation. Lastly, again, another another time. I'm mentioning it. Residents don't use chat for your Hdm. Patients if they have it, start a direct or strategy. They need that April cake to fill that very non-compliant there.
- These are the 2 things we're gonna focus on when it comes to genetic testing. This is a clear platform indication to genetically test. And I always very struck by getting better referred from long standing care or not, only patients who genetically test you. Wanna give 3 generations you preferably want to use a genetic counselor. Matt Thomas is one of our nation's leading experts, and you read one of Matt's.
- What do I mean by I mean most affected individual. You start there, and you want to make sure that testing includes all female copies. genetic entities that will mimic. Hcm there's a slew of them on the bottom. The point is just to show you there's a lot not to go through them individually, for those of you swinging to read they wanna take that information and screen the family.
- If they're genetically positive. When you're patient.
- you have siblings, parents, children.
- it's positive you repeat the process, sisters, positive sisters, parents have been given them, siblings, children, and so on, and so forth.
- But if I'm positive and my sister's negative.
- I don't need to chase her family anymore, her kids anymore. And I don't need to see her anymore.

- Now, the harder thing is when your genetic testing is negative. Because I told you there's 2 populations in that genetic negative. Right? There's one that's clearly behaving like an autism, dominant disease, and the other is just one person. But how do I know? Reach my patients?
- I don't. So you are genetically negative. As a patient.
- What you find is, you have to screen the family members every one to 5 years, depending on your level of concern this takes some 10 min, saying, I usually go back to that one in 10 times. If you develop this, you're gonna drop in the presentation. But again, this is an aggressive long term screen.
- So that was the genetic piece. Let's now move on to obstruction versus non-obstruction. here's to the old graph that shows that rather than Hcm. Because most of the time it is vocal. I know we've like. It's been changed slightly. Sort of emphasize this point. But that's the so. Here's an old diagram you can tell from like the Ms. Dos texture of the venue rule there. I would bother dog. They didn't make accept them big. So here was my genx solution to that. I refuse to accept that so when I haven't accepted what you see? Did the outlook when the outlook right narrows the velocity of blood through that outflow track has to feed up. You can use the continuity equation if you like. Physics, if you don't picture the Mississippi River narrow fast when it narrows, has to speed up when it speeds up. What happens is the same thing that happens to aeroplanes. Air above the wing moves faster than air below the wing, creating, lift or even think about your college shower. Wind blows micro valves in the Lv. OT. It's the micro valve as it gets pulled in the area, gets smaller. Mplb fluid moves faster and starts to silent.
- So here's a a picture of an obstructive part of the ventricle is what vehicle is here, and there's your Michael Valve right there, and it's gonna make a little curly the way we manage this is at the bombs. First of all, we keep this agent volume complete which is the same thing different than our heart. We keep them replete because we want a bigger ventricle so that the output back stays open.
- We also want to avoid things, and this is a little counterintuitive that drop after load you can think about. After loading the aorta as stenting open the Lv. OT. If you drop that after load, the Ldot collapses. Now this is difficult, because you're managing a patient. The primary sees them for most run-of-the-mill hypertension meds property. So you can see all hypertension management actually gets quite complicated. And the only time Thatramer, I use quantity very difficult control hypertension once you've done that last one have used a lot more or more specifically, septal reduction therapies, which is going to be the topic of the next slides. Put a PIN, but for the intern is in the room. You want to avoid diuresis. In fact, you want to hybrid. You want to avoid after load reduction, and if they get sick in there in the hospital and you reach peror, epinephrine, or epinephrine and you increase eye control beam. They're going to spot it Reduction. Derek.
- The guidelines see complete equipment to surgery and alcohol equation. So I made these 2 pictures absolutely identical one size.
- This is Dr. Regassa. On the right is Dr. Curt on the left, Dr. Regassa. That's our alcohol. Acceptable relations more on that. In a moment. Dr. Kurne does our cervical Miyagi's busy slide. But really, what is to say? If you're not a surgical candidate. you gotta go with the International if you're already getting party math to a surgery when you're going to circle Punch.
- Otherwise, in general younger visions we push a little towards Miami. Older vision. We tend to push a little out all way, but there are certainly exceptions that are not rated on a 70 something year old couple of weeks going there. Exceptions now. here is how alcohol

set up works. What you're seeing is a capital going through Florida, and then engage you the left name down the LAD.

- And Dr. Regassa threads it down the septal and squirts in some contrast, and he's doing that to see what lights up.
- If just the septum lights up, you're in a good spot. If the whole interior wall of the heart lights up, lights up. You're not.
- If you're in a good spot. He inflates the balloon approximately and sports alcohol down, essentially causing a heart attack a control artifact of a vegetarian porosity on the right, much conceptually easier to recognize. The certain blocks out of these are sounds much harder and very difficult surgery. There's only a few surgeon in the country who do it, but that's the approach. These are incredibly greater than 90% success rate. And, in fact, our institutions greater than about 95% success rate very low 30 day mortality side effects. However a lot of base anchors very infrequently, however, should be having to do a repeat procedure. Alright another one of those check-ins. So I got more dial to
- How is the family screening of genetic testing is negative.
- Describe a basic approach to Lv. OT. Management while you're going and more on that month.
- One recommendation is a new guidelines that shared decision making we should always use shared decision making. But they needed explicit in our guidelines. These are your decision. Making decisions like this is a relatively rare disease. We need to be honest about what we know and don't know. Where is that more evidence than in our discussions about lex and exercise on the top. Right? Let me in a rebound and scoring, and 1989, and then died on live television decade. Severe exercise prescription in this disease because it was noted. Gosh! Looks like a lot of defin.
- Then Harmon, at the end of the nineties is Group look! And said, you know what actually to the disease is more definitely, that is the thing in the population.
- In meanwhile, these days. ATM double A, now can think about this from a broader picture. Experts, people who exercise at the lowest rate of sudden death.
- But when people who exercise diet suddenly, when do they die during exercise? Exercise is almost a high-risk activity with longitudinal reward.
- How do we tie that into a disease where you're already at increased risk of sudden death?
- You started off, saying, Just don't exercise, then. Well, we studied it. We took people, and we randomized them to moderate, to the exercise. And what did we find?
- No difference in adverse events in this population, and in fact, the group who exercise developed a better exercise capacity shocker. As a result, the most recent guidelines say, we should encourage this, we should encourage modern integrations out of most people.
- There is exercise now we're still not sure. So, Nashville. This is, I don't fly.
- I used to talk about how? Vcm, we need more data soon, because the live Hcm trial is going to adjudicate June this year. And what did we find? 40% of this group. By the way, 40% of this group had defibrillators half for secondary prevention. This is high-risk patients doing vigorous exercise, with no difference in events.
- So what are we gonna do with that? Well, guidelines?
- And we'll see a lot of debate. I suspect it's still gonna be sharing territory. But I just wanna point out if you need this application. But you know, and once you just don't have alright 8 min of more hard core cardiology for those of you who are still with me.
- finish line just ahead future directions. Let's out of here. Pandemic school very much, Professor.

- We were taught you're gonna have mile fibriller disarray and hcm, and that's gonna wait. Maybe a week. Maya site. That'll be my aside. Well, then, I'm just gonna likeert you know our response.
- 80% of my site mutations result in Hindu functioning my eyesight. So why in the world with the heart, Govia, and that my site's rocking. We need a whole bunch more.
- Why would you have compensatory hypertropy in response to a hyperfunctioning mindset? Well, I made the mistake of talking my fellows through all of these various pathways before which they absolutely love when I do. But what I frequently tell the medical students is, if you see a chart like this. It means nothing we don't understand.
- However. I think that's changing deep breath. A little bit of mid school level physiology. Stay with me in Vermeer estonia. Kidding bills, calcium release
- calcium release into the cell causes more calcium to release. So calcium mediated calcium release occurs. That's how it contracts. What the calcium does is it binds to troponin which ships trophomy, which allows acronym to overlap and options?
- This is a energy requiring process. Both remove the myison head and actually even to release the Myison head from actin requires more Mtp. So both cystically and diastily, are energy requiring processes.
- Here's what you probably take learning medical school. Not all lies in the enterprise.
- existence, distrust, relaxed state in order, relax, save, excuse me, but in order to relax safe, my admin is available to act.
- The others are in a super relaxed state where they're not available. Now, this is changeable, right? So if if you have a strong had a cold allergic response to something. You'll recruit more myacin. But I didn't get time. 1850.
- Little bit of magic here but age scan results in more distress relaxed and less super relaxed. So there's more mice and available all the time. Now, if you think about how the heart's gonna view this, it's gonna say, you know, I'm constantly being asked to recruit more and more wise a huge African level. Let's recruit more of my muddies in response to that. Over time. You get sickness, disorder, and fibrosis. Now, why am I going through this almost painful level of physiology with you? I am because if you then go back to negative inotropy and you go back to my activity. And you think about what that has to do with the physiology. I just told you I'm not sure, that's all. I'm not saying. My activities are enormously successful procedures, but lobbying activ has nothing to do with the physiology of this disease.
- These are Myison Alfred muters. The one that's available right now is mad at Camden. What these do is they normalize the density of available myacin to interact with apple.
- They target what we believe to be the pathogenesis of this disease. They normalize energetics they normalize arts peace.
- We studied this 2 big times more times than that. The 2 big trials explorer and valor, and what they showed is. if you give these products to class, to all the way to class 4 hard failure. What you find is the brain's problem.
- The patient's kill that. But agents can walk part of. and while nobody wakes up in the morning bragging about their vmp, all of their main signs. Problem cool. Cool by the way, just to make sure I'm not only be a massive Cytokine soon to be available, so we'll have competition on the market, which is a good thing. But if you go backwards they're feeling that this disease modifying it's targeting the pathogenesis. But so well a small group of the explorer patients, one of the first trials we're studying with imaging before and after, and what we saw there. If these tables heard your ring. What we saw there is mass reduced. thickness reduced. atrial's eyes reduced.

- This is a suggestion, a suggestion, not proof of disease, modification. And it's mechanistically multiple.
- We're actively studying this here. We've got a a nice brand from Bms to look at cardiac flow reserve so flow and rest and flow and stress, and how that changes with cardiac Mycen inhibitors. We're about to get another grant looking at coronary flow reserve with cardiac MRI. So we are actively trying to figure out what disease modifications happening. But we think it is happening. So let's go back to this slide. All the obstructive management. If you'll notice where should be? Well, it certainly depends on who you ask a pharmacy, red. I really like it. If the drug was at the top of that chain. But what does it mean that these are $80,000 a year? How as condition should we incorporate? That shouldn't be incorporated? I don't know.
- I will tell you again, bragging on some of our fantastic positions here. Dr. And 2528 patients in this study, how many were getting drug and how much they were paying, and what we found was $10 same $10. Who are we concerned about society? Individual both? Neither. I don't know the answer, but certainly hard, but I did. Anyway. group is a very difficult measure, and Karen and Kirsten departments that actually go around the country talking about how we set up Uva system. So these 2 have done absolutely human work on writing this medicine is very impressive.
- A last, but not least. Fingerprints very exciting. So what I didn't tell you in the 2 common mutations, was it? Let me? PCB. 3. Typically. And that was the one that cricket side and discovered in the nineties, typically that the truncated mutation of the whole gene. So why don't we shove this whole gene into an add-in vector and deliberate?
- It turns out it's a little little more difficult to do than that in part, because it's a 22,000 base pair, genie, and add no vectors only so big. So you're really filling the envelope. But it's doing this study now in YA. 7. The second most common mutation typically is a miscins mutation, single-based parallel for those of you know about this for past days. Technology.
- certainly a promising area for that. You could go and send out that. And certainly good, like I use. What's the problem? So he's all right.
- Very pollen disease, 1.5 cm or more. 40% of genetics, wide range of presentations from symptoms to incidentally found to some death. and a sample. Configuration predicts the course. Your differential challenge stuff infiltrate itself.
- The clues are history, family history, and incidental findings on Asian echo.
- When in doubt. This has a very high mortality. Do not hesitate to refer.
- You need a genetic counselor to do this for left ventricular output tract construction. You're going to use negative ionotropes. You're going to be wear on the base of dilators and diuretics.
- More to come. You really need share decision making Stm. With extra thoughts. We know what we know, but we also kind of know what we don't.
- Lastly, the gene therapies very promising, but not.
- I think you guys can do this. Now, I think you can describe common presentation. I think you can talk about when to refer. I think you understand how to think about exercise, and I think you know what's in the pipeline. You think you got lost in that terrible action potential slide.
- Now that thank you very much for your time and attention.
- Thank you so much for an excellent talk. Small percentage. It looks like maybe like 30 ish energy before and after that is not logical to me, and honest, like suspicious disease of imaging. Wouldn't they want to prove that super question and it was actually brought up in the trial time.

- It's really expensive to do clinical trials. They weren't sure what the outcomes were gonna be of the MRI arm. And so they started with a subset of 32 patients from the 360. My suspicion and II kind of know this first hand in the brand we've is that imaging is going to be more and more involved because they really wanna prove disease modification. Dr. Kramer, you have any thoughts now, all the studies. All as many patients as can be are getting Cmr. Before and after. They all obviously got echo at each stage, but only a small fraction of the first study got an explorer got Season bar. We were a site for them. So a couple of our patients were in that out of that 35.
- Did they see any size? Changes on the echo echo? Also did that go? Is not as good at calculating left ventricular mass, which is what they were using as the biggest imaging endpoint, which is why Cmr. Was preferred. Echo also tends to overestimate and occasionally underestimate left ventricular thickness, whereas Cmr is extremely reliable, and people that haven't experienced making those same wonderful presentation screening prior to sports, when and how very widely debated the data we have about sports. Screening is about 15 years old and it showed essentially no benefit.
- Now, there's been something with files released or obstacle studies. But it's still using old data we think. And I'm going to put myself on the screening side of things. We think that an experienced hands interpretation of Ekg and echo is good enough now that we're pretty reliably picking up normal from abnormal and not importantly putting normal through the strife of a bunch of testing hugely debated point very difficult to run trial, because these are rare events and it's hard to do trials with rare events. Great question, though. Thank you. Dr. Banti. Italy, by the way, is one of the places that is very aggressive with screening Dr. Bati, and that's because they already see rates are so high in Italy that they're out there events much, much higher. So it's easier for them to say.
- Thank you.