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TRANSCRIPT - GR 02 16 24 "*Cardiovascular Imaging for Ischemic Heart Disease in Women*" Patricia Rodriguez Lozano, MD, from the University of Virginia

Medicine Grand Rounds

- Hello, and welcome to medicine grand rounds. It is my absolute, utter pleasure to introduce doctor. But did Seattle what would you give us on morning I saw again
- Margot Tanner. There, yeah, maybe.
- But you, we can also do the handheld. Many people choose to do that. If they're Walker and talkers. That's okay. Go ahead and talk.
- Hi, how are you? Maybe switch it. So it's on the outside of your dress. Make sure. Sorry. Is that way it will be on outside. Let's try again. Hello! Where is that side of it?
- Good morning. How are you?
- Yeah. thank you. Okay, you and try again.
- Good afternoon. That's correct.
- No, just in case all this is cooler, you know that I gonna have notes. Well, this is a little bit the bane of our existence, because almost every single grand round something goes wrong with the AV. That has never gone wrong before.
- Great Hello! Everyone! Welcome to medicine, grand rounds.
- It's my pleasure to introduce Dr. Patricia Patricia Rodriguez, Lizano.
- Dr. Rodriguez. Lazano received her medical degree at Pyotano Eradia and Lima Peru this was followed by Residency, Chief Residency, and Fellowship in cardiology at University of Texas, Medical Branch in Galveston, Texas.
- She then came to Uva for an additional fellowship in cardiovascular imaging. This was followed by a master's in Science and Clinical Research, with the School of Public Health at Uva. Dr. Rodriguez Lazano is Assistant Professor of Medicine in the Cardiology Department. She also serves as director of the Women's Health Heart Health Care Program Co. Director of the Scad Clinic and Associate Program Director of the cardiology fellowship.
- Her scholarly work is focused on cardiovascular imaging and women's cardiovascular disease, holding many active grants. Here at Uva, as well as participating in many multi centered trials. She has received many awards for her research, scholarly activity, her clinical care, and for her service and her selflessness.
- This is evident in her dedication to the Charlottesville community with regular participation in activities such as screening and education events for the women's cardiovascular health outreach and screening for the Latino community and attending regularly in the Charlottesville clinic, free clinic, and clinical Latina. We are so excited to have you to day. Please join me in welcoming Doctor Patricia Rodriguez Lizanne.
- Thank you, Cara, for that very kind introduction, and it's really my honor and and my pleasure today to talk with you about something that is very close to my heart of evaluating, scheming heart disease in women time for a paradigm shift and these are just this course of some Grant support, and I do have a patent. And then today

for learning objectives, I'm gonna try to do many, 4 things, understand the unique presentation of heart disease in women and challenges identify the gaps and biases in the current approach to evaluating scheme. Heart disease in women explore the latest research and evidence supporting the need for a paradigm shift in the evaluation of ischemic heart disease in women, and learn about the role of precision medicine in improving diagnosis and management of ischemic heart disease again in women mit Ctl, and so I gotta start the talk talking about some facts, just to say, let's say the state of the of the talk, and, as we know, cardiovascular disease is a main killer of women. This is data from 2017, like around more than 1 million deaths in the US. Over 400,000 were related to cardiovascular disease mit Ctl. And and this is all data in women. The second leading cause of their is chronic lung disease. And then we have cancer and lung cancer. But cardiovascular disease really takes more life of women when we combine any kind of cancer plus chronic disease, and in terms of prevalence we see that over 60 million women live with cardiovascular disease in the US. And comparing with breast cancer, that is, around 3.8 million women mit Ctl and the fourth cause of that actually is breast cancer. So and even we see in the press and in the media, and that breast cancer get all this attention. We really have to understand that is cardiovascular disease, the main killer point and even Mary, physicians and healthcare providers. They don't. They think that heart disease is a disease on men. And this is not true, and I don't have anything against mammogram. We all should be taking mammogram, but we shouldn't forget there is really heart disease, the main killer of women.

- This is the data on mortality. And we all have seen this graphic of a this is rates of mortality, and you can see on the eighties really, mortality in men start to decline in red for women, blue for men, and the men start getting attention, getting the settings and also preventive strategies for them. And then, unfortunately, women. Mortality was on the rise until the early 2,000, when the first preventive guidelines specifically week for women, were really mit Ctl. And and then all this on the A go red for women started. And then, you see, women started to get attention, and they started getting studies. And they started getting this cardiovascular risk stratification. And there was again for men and women mortality start to decrease. And this is so important because preventive cardiology. All obviously work.
- Unfortunately, you see, towards the other side of of the Graphic. And now we see an uprise of mortality again, both in women and men, and maybe this is related of epidemic, of increased epidemic, of cardio, metabolic diseases like diabetes and obesity. But this is absolutely in numbers of death.
- Mit Ctl. And if you see the rate of there is actually a specifically in the middle aged women when there is a rise in mortality. So it's important to think about this group of middle aged women, and how we can improve outcomes on them. And they thinking about strategies. Prevention on them just to improve these numbers.
- And what about awareness? So this is data from HA. Surveys. This are done every 3 years. The first time that HAD. Survey was back in 90 97 mit. Ctl. And look in what is a in terms of awareness, knowledge, and perception of cardiovascular disease in women, and on 1,997, only 30% of women. They identified heart disease and the main field, and the numbers were even lower in minority population, black population and Hispanic population. And then all this, a campaign mit Ctl and go red for women started, and you see how that improve, and in 2,012 the awareness

- went up to 65%, right? Unfortunately still for minority population and younger women, the number was not quite there. But there was definitely an improvement 2.
- And this is the last time the HIV survey in 2,019. Unfortunately, that number dropped to 44%. So women are less likely to recognize that heart disease is the main cause of death, and they're more likely to think that cancer and breast cancer is the main cause of death in women.
 - And this was true, especially in younger women and in women from minority. So in women are less likely to know that heart disease is a main killer, are probably less likely also to recognize that symptoms are related to heart disease. So we have to think about different ways that we should reach that population, the community to make improve that awareness of heart disease is really the main killer of women.
 - What about difference in sectors in terms of mortality? So this is all data from get from the guidelines after, am I? But unfortunately the trends look the same in more contemporary data, women are less likely to receive early medical therapy after a month less likely to get asking, less likely to get better blockers.
 - Women are also less likely to be offered and basic procedures are less likely to achieve door to balloon time door to neither time in within acceptable limits.
 - The only thing that women did better, unfortunately, is die, especially the semi-population.
 - So is there differences among sexes. So maybe the way we communicate. or maybe something like this out of jobs very different definitely between men and women.
 - And that is, we got to understand also these 2 terms of sex versus gender.
 - They mean different things. They are not interchangeable. When we're talking about sex, we're talking about biology. We're talking about anatomy, physiology, genetics, hormones. When we're talking about gender is more like a social cultural term. Here we're talking about identity, and it's not necessarily binary. It can be on the spectrum mit Ctl. And health, though, is undermined by both biology and expression of gender, so both sex and gender contribute to observe differences in women's cardiovascular health.
 - So let's talk about risk factors in women mit ctl, and so women, we do have the same risk factor for cardiovascular disease and men. We have the same traditional risk factors. But we have these non-traditional risk factors sex specific risk factors. And when we think about cardiovascular risk in women, we have to think about, not when we get into menopause of post menopauseal stage, we have to think about early on in life, things we, we have data showing that even our onset of monarchy will contribute to our future risk of cardiovascular field mit Ctl. And later on in life we have to think about history of polististical valley syndrome
 - infertility. Other pregnancy outcomes like history, of gestational diabetes, history of hypertensive disorders like pre eclampsia and then final parity. We know that breastfeeding also protects women there is some data showing that protects women against cardiovascular disease in the future, and then transition to menopause.
 - What is our own set of menopause about symptoms of menopause. And then if we receive hormonal replacement therapy. So this is a very important concept. Because if we really want to improve outcomes in women we have to engage the health care providers that take care of women through their lifestyle. We're talking about primary care physicians. and even pediatricians. Later on. Our all be our gynecologist.

- How many times for us, our gynecologists, our primary care physician right mit Ctl, and and it's essential to do this to a start early prevention strategies when we want to improve outcomes in women.
- And then what about traditional risk factors?
- We also, they're both served by men and women. But certain risk factors portrayed a greater impact among women than men. For example, women with diabetes and smoker women are on a higher risk for cardiovascular disease, comparing with their counterpart men mit Ctl, and and then, in terms of other risk factors in women. I really like this figure from the Lancer Commission on Women and cardiovascular disease to reduce global burden by 2,030. They divide risk factors in women in 3 boxes, 250.
- Yes, established traditional risk factors that we share with men and women. And then again, they talk about these sex and specific risk factors. And here's something else that we didn't talk before this systemic, inflammatory, and out immune disorders that are sometimes more often seen in women like rheumatoids and lupus.
- And then they have this box of under recognized risk factors, psychosocial socioeconomic risk factors. How many times, as physicians or cardiologists, we ask about any of these things to our female women our female patients, and then the Commission. They made this very strong statement about cardiovascular disease in women that is understudy under recognized, underdiagnosed, and under-treated. But unfortunately, women are still underrepresented in clinical trials.
- So there is a lot of evidence now that shows that it might be that women would have these differences in caveat and coronary and atom
- Women. We have smaller epicaryal coronary arteries mit Ctl, and even when you adjusted that board for body, surface area and body mass in this 11 regular mass, and this might make, for example, these are coronary arteries more difficult to evaluate. In city coronaries we have thinner myocardial walls that will make ischemia non-transmir ischemia more difficult to evaluating women. So here, for example, cardiac MRI can be a great tool because of the higher special resolution then, women, we know these biped studies have a higher coronary, blood flow, address and stress, but with the same coronary. Coronary perfusion, reserve.
- We also have a lower basal motor tone of coronary arteries. And this can be partially explained by our hormonal changes. And all these differences, especially the smaller epic career arteries, and these difference in mit Ctl, and in our coronary blood flow might increase the cheer stress. And that might explain also these non obstructive coronary artery disease that we see more common in women, and also these different phenotypes of coronary remodeling, endothelial, and non endothelia dysfunction. And here we're talking about coronary microbascular disease what about symptoms? If they are different between the presentation of between men and women on behalf is chemical heart disease.
- So this is important to talk about when we, how we recognize how we even present when we have ischemic heart disease, and if we are able to recognize symptoms. So this is a two-part long term. Really problem right? First of all, women have to recognize that their symptoms could be related with scheming heart disease, and then the health care provider that take care of us should be able to recognize that as a possible manifestation of scheming heart disease and we use these terms as a typical symptoms to code possible, no car problem and no further testing.

- But really women and men, we both present with chest pain. But women. Many times we have these prodrome syndromes, these associated symptoms, like genre of prep and even fatigue, for many months before we have this acute event mit Ctl, and and this is data from the Y trial. It was a really a big effort from funded by Nih looking and trying to understand women and chemical disease. Symptomatic women that underwent invasive coronary and geography, and it was found that more than 50% of women with an angina. They have no coronary artery disease, or minimal coronary artery disease.
- It was one year after 40% of women have persistent or worsening of symptoms. Unfortunately, these women without a structure, CID, but with persistent symptoms. They have worse outcomes.
- And so we know that women present with a different phenotype of nonast disease. But and this is data. This is a big 2 registries that shows this mit ctl, and this is an A/C national cardiovascular data registry. More than 3 more than 3,000 women that underwent invasive and geography because of of symptomatic. Concerning for the skinny heart disease. And you see, women were less likely to have obstructed CIA, and then this is data from as a city data, big registry. Again, the confirmed registry, symptomatic and asymptomatic women and men. And again, for every category of symptoms. Women, they were less likely to have obstructed the CID. But that doesn't mean that their symptoms are not real.
- All that their outcomes are benign mit Ctl, and and this is an interesting data from the custom consortium paper. And this is a big data set of more than 4,000 men, more than 20,000 women. They're always symptomatic. They follow them up for 12 years, 140.
- And you see. around the Middle Age group around 45 years old.
- When women start, they have a decline of these endogens estrogen. they start calcifying. So how important is to ask our female patients about that onset of menopause. The regular onset of, or the average sponsor of, menopause in women, is around 52 year old that some women that have, for example, diabetes, or HIV or obesity. They can have an onset of menopause before. So it's important to ask our patients about this data because it will put them in a different risk category.
- This is data against from confirmed this multinational registry of symptomatic and symptomatic female and men to when you see. we used to think like non destructive. CID. Is benign here you have women and men will not obstruct the C. Id. With a higher risk for maize when they follow them up over 5 years.
- So we need to think about this phenotype of non obstructive CID.
- Mit Ctl. And here is again a representation from the wise trial. And this is a figure taken from one of the patients of the wise trial, a 50 something year old, female hypertension, diabetes, smoker 2 mit. Ctl. And he underwent angiogram. And then, you see, here is a representation of a closed up of her coronary artery, the left anterior descending artery. And you see, like that, that is, when you get really difficult. Ready looks pretty normal. It's a huge coronary artery, you will say, like not really minimal or no disease.
- But this is all luminography. When you see this is intravascular ultrasound, that normal coronary really has some calcification and other clerosis.
- But if we don't do invasive assessment like that with Ibos or a city scan, we will call that normal Coronavirus and that was true in wise over these only women with no

destructive disease. And here we're talking about, or less than 50% estimates. Almost 80% have some kind of utter prolific disease when they did ivose.

- So this is another piece of data from the Carson consortium study and, like you see in men and women, if you have custom. Score of 0 is great predictor.
- You're you know you are good. But what happened when you start classifying?
- Unfortunately worse in women? Yes, we classify less when we have cursing any plaque is bad for us. almost more than 30% of mortality wars and men mit Ctl, and so we're talking about also like there is really a a good set of data talking about that even on Acs there is a different phenotype of a chemical heart disease in women. So we know most of the corporations on on Acs. They gonna be coming from non disruptive disease.
- But but we have find out in, like the most common cost of acs is related to plus trombosive and consequent plaud. Rupture is different in women. Women. Women most of the time. They present with black erosion. And mostly this happens in young younger women. So how important is here the answer again, of menopause in women mit ctl, and so to understand this different phenotype of skinny heart disease. In women we have some pieces of information coming from the city data. This is data coming from the promis trial, this study. Look at symptomatic patients, and they look into these high-risk features.
- When we're talking about high risk features. We're talking about this vulnerable platform. We're talking about positive, remodeling, low attenuation flag, napkin ring that can ring la assign.
- You have any of these vulnerable plug features your outcome is worth.
- But guess what it's worth in women. It was more important as a prolific catering women than men. and especially in younger women.
- And then he, this is a figure from Lauren. But the started paper. And here you see again, if you see the angiogram doesn't look that bad right? And then CID again. 36. And here is the city of that angiogram, 160.
- And look how nasty that plague looked! Right all the high risk features, positive, remodeling, spotty classification, low attenuation flag. Again, that flag is ready to rupture. But if we don't do a city, we will not know about it.
- And let's talk about women and ischemia. So we know both perfusion and function predicted prognosis in women and men and profusion appear to add more power than function variables to predict adverse events in women. This data shows that if you have ischemia and a lower, ef your prognosis is worse. But guess what? It's worse in women than men. So it's so important. Also this value of iskemia burden, 15 larger ischemia burden, worse prognosis. So that is a high-risk population.
- But we have with you these terms of all positive stress tests.
- And so many times, we think. Well, this probably was. If you have a positive stress test, and then you have an anatomical testing, and you have non obstructive. C. Id. So probably a false positive mit ctl, and then you are fine. Nothing is going to happen right. But really that is many times is not the case. Yes, sometimes it could be that it was really a false positive, but sometimes it could be related also for and that can be related to breath attenuation, artifact because of women anatomy, but many times it just obstructed C. Id. Is not able to explain symptoms in women. 2.
- And I gonna just change gears and talk a little bit about a case. This is a patient that is a patient of mine that I saw her in one of our clinic in the Women's clinic, and this lady she has a 59 year old, and she has some risk. Factors for heart disease. You have lupus, and she also have high polypirinina hypertension, and she presented

with one year of symptom, of chest, tightness of breath, really debilitating, related with exercise and also emotional stress.

- She does have a strong family history of coronary artery disease. Her brother and her father had MI, and, like I mentioned before, she does have this also a specific risk. Factors for heart disease like smoking, her late onset of menopause, early menopause, and depression. And so she went to her primary care doctor, and because of you know, her clinical profile. She decided to order stress tests and exercise nuclear stress tests that came very benign. I mean, she did develop chest tightness during the exercise stress test. But the test came normal.
- So her physician was reassured, although the patient was just keep having like this
- MI. And really debilitating symptoms. And I saw her a few weeks back, and she reminded me about this piece of information. After that stress test. 5 different doctors told her. You know your symptoms are not real. So you need to look for a psychologist because something is wrong, but it's not your heart.
- So eventually, because she kept complaining about it, she was referred to a cardiologist. And her cardiologist ordered anatomical testing with a CT scan. And again it was very reassuring. There was no calcification whatsoever in her coronary arteries, and there was no stenosis, no none even like non classified plaque.
- But she still was complaining of really debilitating symptom. So eventually she was referred to as
- I'm very excited to order a stress cardiac MRI.
- These are the first pass perfusion images, and you can see there is not really a perfusion defect here and then in a cardiac stress, cardiac MRI. We also can obtain coronary flows, and these are her coronary flows. Address and the normal think about around one, and here they were, a little high, 1.2 1.3.
- I hear our share flows of stress and maximal hyperemia. We give patients adenosine with the normal response is that the flow should double and hers they really didn't around 2.2. So then we calculate this ratio between flows are stress and flows are rest and if it's low, less than 2, we think that the response is not adequate, that is, there is some lack of response in her micro circulation, a normal response to hyperemia and hers were one, and for completion this is her legalizing husband looking for a scar. And that was normal.
- So just to put it all together, her global coronary flow reserve was 1.8 less than 2 and I'm putting it together with her clinical presentation. We thought that it was a case of coronary, microvascular dysfunction.
- We treated her with the things that we have available. We give her aspirin, and I started some ACE inhibitor and statin, and like I said, I saw her a few weeks ago, and she was doing actually much better. And she's pretty much symptoms free.
- We'll talk about therapy in a little bit and so let's talk about these terms that you probably have heard about these. These are all terms related to non obstructed coronary artery disease, less than 50% stenosis by anatomical testing. This gonna be maybe CT, maybe invasive Angiogram, and then we have a when patient present with an acute presentation with an MI, and that is called NSTEMI. You have drop in elevation.
- You have documented myocardial injury, and obviously the symptoms. And then we have these 2 stable representations of of stable chest pain that like I know, if you have documented myocardial injury, but some kind of testing, and nowadays we have a more recognized term. A NSTEMI become many times traditional testing will

fail to document this chemia. So this is angina with normal or close to normal coronary arteries. 2.

- Let's talk about a noka. This angina with normal coronary arteries is highly prevalent affects more women than men. And for the agnostic evaluation includes, first of all, document that they have known, obstructed coronary artery disease by cte or by invasive angiogram. And then we have to. We we can do different tests to look for. For example, microvascular disease, and we can do a pet stress imaging we can do a cardio stress card, MRI, we also can do a myocardial contrast. Eco cardiography. It's called Mc. Although this needs advanced training. So clinically, we is not really, that is not really available. 2, and really, the idea here is that there are multiple mechanisms or end of types that can explain presentations in patients with any normal coronavirus. And here we're talking about coronary, microvascular dysfunction. 2 learning depending. this function, or we can have in the Telia dysfunction with buses, pass them, or we have a combined, and the type of buses pass them and microvascular dysfunction.
- And this is a study recently published in patients with a Noca that underwent invasive coronary functional testing. And we saw almost 89, almost 90% of them. They have some kind of these entotes and with 51% with microvascular angina. Did 17% with us as spastic angina, and then, a good proportion, 21% have a mixed phenotype. So how we treat them well, unfortunately, we don't really know. They are really a small, and with different mix of different endotypes, cohorts, and short term follow up. So we think, like as between studies depending what endotype we are thinking, we try different anti-ango's. So definitely, there is knowledge gaps and more clinical trials are needed in this specific condition. 2.
- So let's talk about specifically this Endo type of coronary, microvascular disease.
- How prevalent it is! So this paper tells the story. This is a
- a study that was done in symptomatic patients, and they all underwent stress death, and among the patients that have normal perfusion stress tests, 50%, they have had coronary flow research less than 2 consistent with microvascular disease.
- If they have a Cfr lesson, too. their outcomes were worse, and this was true. Even if the customer score is 0.
- So when Csr is low and is very low, is more significant in women. So you see.
- when your Cfr. In less than 2 men and women. They have awards prognosis.
- But when it's very low.
- I'm talking about 1.6 or less.
- The cursor starts separating. The outcomes is actually worse in female.
- And when you look at this subgroup of a very severe Cfr less than 1.6 mit ctl. And men most of. In the case of men the majority will have obstructed coronary, artery disease, but in the case of women they have one vessel disease or non obstructive CID. So what is the bottom line here? Non obstructive? CID can give you very low. Cfr mit Ctl, and this is a paper that we put together in our group just to make a call of action, or how important, when we think about women with a no codes, and yet with normal coronaries, 2
- Mit, Ctl, and to think about a precision medicine trying to identify the end of type, the specific end of type. And then there is a lot of research going on about possibility of other biomarkers that genomicsomics, proteomics, 2 radiomics. And here also social determinant of health. And hopefully, in the future, we will be able to identify putting all these together using machine learning and trying to identify specific populations that are in a high risk and then hopefully tailored treatments for a

specific end of putting all these things together mit Ctl, and in our group we also have we're running a clinical trial. We try need to look for novel therapies for the patients with an noca possible micro vascular disease. This is a ma second year, either, scholar. This is my Kl. 2 project, and it's a clinical trial, we think, like, maybe SLT. 2 inhibitors will improve coronary flow reserve and symptoms in these women. 2 mit Ctl, and this is based on a preclinical data, and we are enrolling women that have concerns for symptoms of a possible ischemic heart disease. And we are doing a stress cardiac and Mariah best length. Then we give them ST. 2 inhibitors, and then we repeat another cardiac, MRI mit Ctl, and so you have patients that are maybe good candidates for the clinical trial we are waiting, we are. We try, please send it to our way, and they are eligible to have also city coronary that is needed for inclusion. Criteria, 2 mit. Ctl. And in our clinical trial thanks for the lpring, grant and Colleen. Thank you for your support. We are able also to look, or what is the possible mechanism of action of Sed 2, inhibitor, and we believe is related to inflammation. So we are looking at specific systemic inflammatory markers and also looking at reduced microphones, inflammatory activation, and in this case hopefully will be able to elucidate erez agmoni one more time. Exactly. How is the drop? Will improve coronary, flow? Reserve in this population? And this is something that we are doing in collaboration with Beta Siva like 2 and his love. So we have just to put all together. We have this mit Ctl, and different phenotyping women with more non obstructive coronary artery disease, less classified plug, more microvascular disease. And we pull this paper together in 2,022 to talk about this need for a time for a parallel shift when we evaluate women, 2 erez agmoni, and we tried just to to talk about that is important to consider multi modality imaging when we evaluate women and we discuss. And I'm not gonna go in the granularity of this data. But we talk about what are the pros and the cons of the different stress modalities. A specific mit Ctl, and, for example, exercise is really great in terms of of functional capacity is a good prono, but many times women will have this St. Depression, and they are just related to without coronary after the coronary artery disease, and they can be related to hormonal changes. Stress echo is a great modality, no radiation. We use a lot in younger population, also in pregnant ladies. 2 culinary city is really important to look for that hormonal for that high risk. Platform mit ctl and spec and pi important to document schema. But unfortunately we have limitation because of our anatomy and Brexit animation artifact. Then we have pet that have a higher special resolution, lower radiation that is fed and we can also quantify. Coronary flows mit ctl and cardiac MRI. Give you a comprehensive assessment. Again, a quantification of perfusion, a or quantitative perfusion, and in patients with Mi. And normal coronaries can elucidate other causes for their event, and we were very proud that we were the top 2 mit. Ctl. And 5 red in in Jack. Imagine 2,022, and is and I think this is important to say, because I mean that there is an interest of understanding these different phenotype of women and scheming heart disease mit Ctl, and then we put this algorithm together and the app, I think the message of this algorithm is like, regardless, what is your initial assessment anatomical or scheme or functional testing?

- When you have patients with persistent symptoms, consider quantitative stress imaging for evaluation, for microvascular disease.
- Briefly, I'm going to talk about this. Am I? With normal coronaries mit ctl, and is more. The prevalence is 6% of all acs. There is an overrepresentation in women. and it's not benign. It has worse outcomes.

- And in terms of a theology is really it can be. Many things can be coronary, dissection, plug, disruption, coronary, spasm, microvascular dysfunction, coronary, thrombos, emboli, biocharitis tacosuvo cardiomyopathy mit ctl and i hear it really, and my can help us out. I mean, we have okay for every patient that have Minoka to get an MRI, if possible, in-house, if not on the chart, because we can find things like the Casubo cardiomyopathy, acute myocardial things like, we really can see a cardiac MRI very well, and this study shows very well home. The clinical impact of
- Mit, Ctl and Cardio came alive with a new diagnosis in 54% and change in management in 41 mit ctl, and I'm gonna talk briefly about also, this is a condition called a spontaneous coronary dissection or a scan. The scan that is under the Amnos, and this is a kind of a mind that is not a classic mi related, but actually is, a intimate, or in an intro luminal hemorrhage, 2 mit Ctl, and is most often 90% of the time is, gonna be women, middle-aged women. The average age is around 51 51 year old
- Mit. Ctl. And there is an association, an important association with fibromuscular dysplasia and not playing. But okay. Today coronary and geography is the primary modality diagnosis and when they are persistent diagnosis and certainty, we can use other modalities like cardiac MRI. For example, here many times we can see by cardiac MRI. Where was the info retrospectively? Look at the angiogram, and then we see what was the lease on the dissection and also city can be used many times, although there there is a low special solution, so so that we can see species if there is a proximal vessel, and difficult really to to see if they are distal vessel mit Ctl. And then I want to talk about another paradigm beside evaluation of ischemic heart disease is a paradigm of how to treat women with heart disease so potentially having heart disease. And this was something that you know, this heart center for women.
- These concepts start a few years ago to improve outcomes in women with these specific centers.
- And I want to share with you. What are we doing here at Uva mit Ctl. And so this is our vision. We want to create or we create a collaboration among the many healthcare disciplines that provide care of women through their lifespan provide a personalized and high quality care with a multi-disciplinary approach
- mit Ctl. And we also want to increase awareness of kidney heart disease in women in providers, but also in the community and expand clinical research in women mit ctl, and so this is our right now our team. And you see, there is a group of congenital heart disease, interventional images, ep vascular medicine, pulmonary hypertension, heart favor heart disease. And then we have our genetic expert. And then, importantly, our Cardio obstetric section, our expert on Cardio obstetric, Dr. Kelly Winger, and she have a team of collaboration with Daughter and Christopher Anen, Christian home, led by Dr. Paula Gary. And this is a team. We started being 2 pictures, me and Dr. Winger, and look at this now, right mit Ctl. And is not only physicians we have, because when we want to improve our consuming women, it has to be multidisciplinary. We have. Our nurses are trained on a specific heart disease in women, and then we have a pharmacy every time. In every of our clinic we have a pharmacy with us 123 mit. Ctl, and we also have our cardio metabolic network team nutritionist dieticians, low weight loss specialists. We also have our social worker that she's also a therapist, and she screened every patient that comes to our clinic for depression, anxiety.

- Ptsd, that is so important, and in patients, especially with scat, 30% of women with scat after an accurate event, will have a Ptsd, we have also partnered with behavioral psychologists Mit, Ctl and our team of our research team, and also our exercise physiology team. We partnered with extra physiology. And now we are offering this also to our patients 120 mit. Ctl, and a lot of these services are done and telemarketing kind of format, because we understand that women are busy and I'm gonna come to another visit and we try to provide all these their convenience mit ctl, and these are the cleanings that we have right now in our program we have a combined model with vascular medicines, a referral center for Scott. With Dr. Adita Sharma. We have our women cleaning. We see women. We established coronary artery disease mit ctl, and also women are risk for for coronary artery disease lipids. We see microvascular disease, also a candidacy for hormonal replacement, therapy patience with Minoka mit Ctl. And we have our Cardiopcet section. We have a combined model with maternal fit and medicine. That is lever. Dr. Wingerton and Dr. MN. 2.
- Because we know pregnancy is a window of opportunity to improve young women, long-term, cardiovascular outcomes. And this is just an example of some of the things that we started in our program. This is an epic tool. Remember all these risk factors that I told you that we don't never ask our patients. So we develop this, every patient that comes to our clinic will be asked for all these risk factors, and this is available in epic. If you want to use it, you can pull it from epic and start using this tool in your clinics.
- We also have developed, starting this year a comprehensive curriculum, multidisciplinary curriculum in women and heart disease and mit Ctl. And all these people in the picture, in the big picture they are all giving lectures about women and heart disease. We also have a clinical rotation for trainees. If you come to our rotation, you will have a whole week that you will go to through all our 3 clinics. You also have an outreach clinic you have advanced imaging with me, and then you also have the opportunity to do research with us. 100 and how important is increased awareness in the community. We're not going to wait for everybody to come to our clinic, but we need to go and talk with the community. Education will empower women so important. So we have partnered with Dr. Man Luna and Dr. Yuan Pinkerton, and we do community and screening events in the Latino community, African, American community and also multicultural events. We screen men and women. But women, we use a specific tool. 2 looking for this sex specific risk factors. And we provide a period of lipids and also a one C, and this is some of the pictures on our web events.
- And this is some of the things that are going on research in our program. And if you want to send us or refer any of your patients. You just have to type, refer to cardiology and just press that button that women heart health.
- We are also. Look, we are expanding our program. We are really happy with the support, and we are having 2 Ap's so please, just spread the word. We are looking for the product and coordinator, and also clinical Ap. P. And if any you know somebody that is very passionate about women and and hard help, please join our team.
- So my takeaway points. First of all, cardiovascular disease remains a leading cause of death in women and women and men share most of the risk factors. But there are several of unique risk factors in women that we discussed.

- Reproductive history is so important when we trying to improve outcomes in women and no, no strategy is fatal, is not benign and we believe that future algorithms must integrate functional, anatomical and physiological assessment of indeteria and non-industrial dysfunction, incorporating advancement in precision, medicine to tailor treatment with greater individualized accuracy.
- And finally, we believe that new models of care and delivery are essential to change cardiovascular outcomes for all women, especially women's at higher rates.
- And thank you.
- Thank you so much. If anyone's on Zoom, please put your questions in the chat. That was fantastic. I always think, from the perspective of our residents. We have a Cs resident on call today. They might get called down to the Ed to see a female patient that has recurrent chest pain, but maybe she had some sort of imaging that showed non obstructive coronary disease.
- I feel like our residents would would send her home or tell the Ed. We've already had evaluation. This patient doesn't have coronary disease, and and now they might be hearing this and thinking, Oh, my gosh, I'm missing some patients, can you? Can you? And like, talk to our residents about how to handle those situations?
- Yeah, I mean, that is a really important question, Kara, because many times this is a story that we here in our clinic, right? How these women, where this needs many times from the E. They have recurrent of of visit to the er and they really impose a high burden financial burden for the health system right? We have to think about it. And because I think like just having no nostalgic, I mean, like mit Ctl, and those are not real what they're here, and they might have microbascular disease versus plastic and china and I mean we are obviously happy to get all those who refer us if you want us to evaluate them, if you want to curbside, if you want to start doing some testing on them. We are also happy to do that, I mean I think our goal is like at some point we cannot take care of all women. I mean, I would love to, but I mean, we want you guys to feel comfortable doing this mit Ctl, and so we are happy to educate you. How to evaluate these patients with Anoka.
- Thank you, Patricia. That was wonderful. I mean, you covered so many different things. 19 2 questions. So the MRI, the stress MRI for the Corona flow reserve. Does that have to be requested specifically, or is it part of the routine? How do we go about that? Yes, thank you. So in the past, yes, because we didn't have the sequence in all our MRI scanners. But we do so. No, it will be immediately. I mean, it will be done for automatically for all our scanners. Wonderful. Thank you. Another topic that I'm sure you didn't have enough time to cover. But is estrogen replacement therapy, you know, gone from, you know, many years ago was considered Cardio protective now. Then, maybe cardiotoxic or increased risk. Where are we now? In this mit Ctl, and so there, as you know, there is a big controversy. And this discrepancy in data and a lot of these studies. There were all the studies. They were not well designed. A lot of these women were older women, so they were already like, have a higher risk for cardiovascular disease and and events, and that probably the reason that it shows that it was more harmful than anything else. 130 mit ctl, and so we we don't have contemporary big data. I think it's a big need. But I know many, many group have tried to get an Aids to fund this study, but 123.
- It's not a hot topic, but so I receive a lot of these consults. and what I try to do is stratify women in terms that I use many times on this women custom score, for

example, to see what is the real risk and see if they will be good candidate for Hormonal replacement therapy or not.

- Thank you, so great talk and really comprehensive overview of a really important topic. But I have a really specific question. with regard to Scad, what's known in terms of the genetics is this a mileial? Do people's families need to be genotyped? Or, I mean, what's what's known about the genetics of that disorder. So that is also an area of research. I mean, they are some groups specifically groups working on this, a part of the Iscad registry. We have a specific group that is working on genetics. There is a big group in in Paris, also working on that. I think we still don't know. I mean they they I mean, Scott is such a difficult disease, because 150 is a very rare disease.
- And you know, for genetics, you need a huge bio bank of patients. So it's really hard. There is no clinical trials. Really, there is a small clinical trial of beta blockers in Italy as a part of the app. We are part of the Ice CAD registry, and this is one of the biggest registry. They asked me to be one of the chairs for the clinical trial section. So we are working on that. But it's still on the works. Great thanks. Yeah.
- Really enjoyed that as one of the residents. Something that you mentioned is this breakdown of vasospasm versus endothelial dysfunction. I, is that something on a spectrum? Is that something where you think future research is going to lead to targeted diagnostic. And then treatment based on which degrees abnormal. Yeah, that's a great question. And I didn't cover it. Like very throttle, I mean, I just went through it. But really to be able to identify this different end of you need to do invasive coronary functional testing right? And and there is a specific mit Ctl and definitions and specific things that we, we have to do an adenosine test on these women, and then also colleen challenges test. And then that is how you can identify if they have spastic angina or microvascular disease, or maybe a combination of both mit ctl, and now they are like, I said, a small trial. That shows that maybe certain medications can work for one end of type and another one for the other. But they are very small trial. So we need more research on that to be able to say, you have this and the type. And this is your therapy. And this is your end, the type. And this video therapy, we don't. We don't know yet. Yeah, thank you. Yeah.
- You know, when you are giving your talk with certain something new to me. And so basically, if you look at it histologically, this microvascular disease, what do you actually see? Do you see athletes, lesions in the small vessels, or a lot of our some kind of inflammation going on. What's what's exactly happening? So is that very mit ctl, and not only one thing you have functional dysfunction, and you also have a structural dysfunction. So the structural dysfunction it can be even diffuse at the reproducing, and it could be also smooth muscle. This function, and you can also have like not other corresponds of endothelial vasodilators. So it's several different mechanisms that can affect the micro circulation. 2.
- So you give them the same kind of preventive therapy as you give, and people have got large vessels. We do that because we don't know any better. Basically, I mean, we don't have. I mean, we just finish enrolling for the warrior trial. This is a multinational trial 75 plus we have, we? We were part of we. We are part of that trial, CID, and we are mit Ctl. And our hypothesis is to see, or we are aiming to see if aspirin studies and antagon will improve symptoms and outcomes.
- This is the unique trial. We hope that is a landmark trial. We just finished enroll enrollment on December. We hope to have data in 2 years or so, but we don't have data. So, and this lesion is mean, I would think that this region would be seen in

patients with diabetes who get small vessel disease, or is that not the case? No, this is really this is true. So we have so we share similar or microvascular disease share similar risk factors that the traditional coronary artery disease like diabetes, obesity. So a lot of the women also that have microvascular disease might have also really mit chl, and they might have like not only one thing, but they can have 2. So, for example, in my clinical practice, I find that parents that have microvascular disease by stress cardiac MRI. They also have a heart failure, preserve ejection fraction. So it's not really easy to treat these women because they are very complex.

- Okay? And that's why you started this SGLT. 2 therapy. There will be 2.
- No, it's based on pre clinical data. We have data on mice that actually show an improvement of coronary, microbasular disease of coronary flow, reserve pre and post therapy.
- Thank you so much, Dr. Rodriguez. I'm the voice of the Zoom chat. Dr. Mike Williams is asking, do patients with angina and a finding of Inoka or Minokon Cath have further testing with acetylcholine challenge or some other testing at their time of invasive angiography. So so that is what we are advocating for doing that kind of invasive coronary functional testing a Uva. Currently, we are not doing it.
- But we are working with a microgosa that is a director of workout lab to start doing that so hopefully in the near future they will be able to do that.
- Alright. Thanks so much.