ROB MCBANE: Greetings. My name is Rob McBane. I'm one of the vascular specialists at Mayo Clinic in Rochester. And today we're going to talk about a very interesting topic, fibromuscular dysplasia. I have three very renowned experts at the table who know this disease well. On my far right, I have Dr. Thom Rooke, vascular medicine at Mayo Clinic Rochester. Dr. Sanjay Misra, who is one of our interventional colleagues and has a big experience in catheter-based therapies for this disease. And Dr. Iftikhar Kalloo, who has a strong research in vascular disease and, specifically, fibromuscular dysplasia. We're excited to see you all here today.

My first question will be to Dr. Thom Rooke. And I'd like to ask Tom, tell us about fibromuscular dysplasia. What is this disease? It's gaining a lot of press lately. Who gets it? What is it? How would you classify this unusual entity?

THOM ROOKE: Well, it is an unusual entity, and I'm probably going to let people down by not being able to give folks all the answers at this stage. It's one of the mysteries we still have in vascular medicine. As best as we can tell, fibromuscular dysplasia is probably a congenital condition. Something that you're born with, but doesn't become-- necessarily manifest until we get older in life. We used to think of it as always being a disease of young people, but, as we'll probably talk about, that's changing a little bit.

There are basically several types of fibromuscular dysplasia. The most common is medial dysplasia, which affects of course, the medial layer of the arteries, and results in abnormal arrangements of the blood cell-- of the smooth muscle that can lead us, then, to stenotic lesions, aneurysms, dilatations, a variety of problems. And it's these changes in the artery that ultimately get people into trouble.

ROB MCBANE: Very good. Thank you so much. Now, 90%, or thereabout, of patients who have fibromuscular dysplasia are women. Iftikhar Kalloo, can you tell me, please, do you have any sense of why women seem to be overrepresented in this disease entity?

IFTIKHAR KALLOO: Rob, again, we really don't know fully why there's such a strong predilection. It's been shown in multiple studies, and there has been this humoral hypothesis, that perhaps some of the manifestations clinically, or presentation of these patients, is related to hormones. And supportive in this regard is from the studies that show that these individuals have also a high incidence of having taken hormone replacement therapy.

But going against the humoral hypothesis is that pregnancy, for example, doesn't seem to necessarily exacerbate the FMD, and that parity, for example, is not associated with a higher rate of FMD. So it's an intriguing observation, and as yet, it's not clear why women are more prone. I suppose there may be an interaction of the genetic variants, susceptibility variants, with the gender that then leads to the manifestation of the disease in women, but we fully don't understand this very strong predilection in women.

ROB MCBANE: Very good. Thank you. Dr. Misra, tell us-- you've done a lot of invasive studies on patients with FMD. You read cross-sectional CT ultrasound, et cetera. Is there any evidence that fibromuscular dysplasia gets worse over time? Is this a disease that progresses, or do you think, as Dr. Rooke mentioned, that we're born with it, and what we have at birth, or what we have in adolescence, is what we have?

SANJAY MISRA: That's a great question. I think it's complicated. We've seen people that are 80 that have FMD and atherosclerosis involving the renal arteries, and then conversely, we've seen 9-year-olds and 10-year-olds with it. So I like what Thom says. I think it's probably congenital, although it's hard to know. We've looked at 2,600 CAT scans for patients that had donated kidneys and found a small incidence of renal artery FMD. And so we know people have it. We know people have it and they don't know they have it. And we also know-- we've seen it in all the ages, from 10s all the way up to 80s and 90s. So I think it's really interesting.

I can tell you, we've looked at our own database from the Olmsted registry, the epidemiology registry here, to understand how many FMDs are in Olmsted County and what the prevalence is. And over the last 20 years, the prevalence, the point prevalence, is going up, and we're looking at this to understand the natural history. What happens once you get it? Do you get managed? How do you get managed? And what are the ramifications of the management? Do you go to procedures, or do you do fine with medications, et cetera? So it's a big mystery that remains unsolved.

ROB MCBANE: Thom, as Sanjay has recently published and others have shown that perhaps as many as 4% of the general public may have this disease. On one end of the spectrum, we see patients who present with dissections renal infarction, stroke, and on the other hand, we have these patients who don't have any symptoms. I mean, what is your sense? Is this a benign disease, or is it something-- where does this fall on the scale of serious diseases, do you think?

THOM ROOKE: Well, it certainly can be serious. That's the problem here. I think that there's a general agreement that the vast majority of FMD is benign, asymptomatic, doesn't cause problems. That's probably true of almost anything that causes mild stenotic or mild dilatations in arteries. The problem is that we haven't yet learned how to predict who's going to develop problems with this and who isn't.

Because when the problems occur, they can be absolutely catastrophic. And those are the ones-- those are the patients that typically are showing up on our doorsteps, are the ones who have symptoms either related to stenotic lesions that make things ischemic, or the aneurysms that cause the problem-- it's typical of aneurysms-- or dissections. Those are the folks that we're seeing. It's a small number, but it's biasing our view of this.

ROB MCBANE: And along that line, in recent months and years, a very specific disease called segmental arterial mediolysis, a disease of dissections-- which, at least on angiographic and on CT imaging looks like FMD but behaves very malignantly with dissections and infarctions-- are these the same diseases, or do you think that these are different? Is this just one manifestation on a spectrum? Or where do you think--

THOM ROOKE: Yeah. Thank you, Rob. That's a bit of a curveball there, because it's one of the great controversies that those of us that see these patients and have to wrestle with these questions don't really know right now. I had a great mentor years ago-- actually, one of the interventional radiologists-- who used to tell me that, well, you can easily tell the difference between FMD and SAM, S-A-M, because FMD never dissects and SAM does. And that's it. If it dissected, well, then by definition, it's SAM. The answer is, we really don't know yet what these subtle differences in the dysplastic components or the localization of the disease is that leads to the clinical differences that we see in things like FMD versus SAM, but it's all part of this ongoing effort that's picking up steam nationally to try to learn more about these conditions.

ROB MCBANE: Very good. Thank you. Now I'm going to turn the mic and the question back to Dr. Kalloo. In the National Registry, a number of patients had a history of tobacco exposure.

IFTIKHAR KALLOO: Right.

ROB MCBANE: A number of patients, of course, had hypertension, and you might say that's simply related to the renal artery manifestations of FMD. A number of patients had dyslipidemia. Is this-- how does this relate to atherosclerosis? Is this just a sample bias? Do you think these risk factors have any relevance to this disease?

IFTIKHAR KALLOO: That's a very interesting question. I would say that, by definition, FMD is supposed to be a bland arteriopathy without any inflammation and without any atherosclerosis. Having said that, in fact there's interesting association between, for example, risk factors and dysplastic or aneurysmal diease. As you know, diabetics are protected against aneurysms, particularly abdonminal aneurysms.

And some say that even higher lipid levels may not necessarily predispose to aneurysms, but-- so there is this dichotomy of how risk factors behave towards FMD. The only, perhaps, observational finding on merit here is there's a higher incidence of prevalence of smoking, and that may, perhaps, in some way, contribute to either the development or progression. But by definition, FMD is not atherosclerotic, and so we will have to look at other risk factors, whether they are genetic, or humoral, or others that we don't-- mechanical, for example.

But certainly, as Sanjay pointed out, you're seeing these 80-year-olds so I think that's a very interesting area where people will have both. As we discover more of these individuals, we will have patients that have both the FMD and atherosclerosis. But I would say that, by definition, FMD would be free of atherosclerotic disease.

ROB MCBANE: Now I want to move very briefly to treatment. And I want to first talk about medical treatment, and my questions then will be to you two. And then I want to move into interventional treatment.

SANJAY MISRA: Can I-- Rob, can I interrupt?

ROB MCBANE: Yeah. Please.

SANJAY MISRA: Interject. So I think it's interesting. When we looked at renal interventions done in Rochester, Scottsdale, and Jacksonville, we looked at about 1,500 renal angioplasties and stents. In that group of patients, about 10% had ASO and FMD, and I think that's forgotten. When we talk about intervention, we have some data on, how does FMD behave in the older group versus the younger group, angioplasty versus not angioplasty? So I'll reserve that for once we get there, but I think it's interesting they behave differently.

ROB MCBANE: Very good. Thank you. So Thom, if you see a patient with FMD, how are you going to manage that individual, knowing that, typically, these are young women who may or may not have had any symptoms? What is your recommendations going to be?

THOM ROOKE: Well, I think the first thing that drives your recommendation is the presence or absence of symptoms. If a patient is-- the two most common areas that we're going to find the disease is going to be in the renals and in the carotids, where it turns out it's probably close to an equal distribution. If the renal disease is symptomatic, you certainly can treat it with conservative medical therapy. Meaning, if the patient is hypertensive, you can put them on standard anti-hypertensives and use all the same rules that we use for atherosclerotic renal disease. Meaning that, if you can control a disease with medication, you're doing OK.

I always have a little bit of trouble with that approach, because so many of these people are young, and you're committing them to a lifetime of medication when, at least traditionally, we've thought of this as being something that can be managed a little easier than other vasculopathies. And I'm sure Sanjay's going to want to talk about that a little more. The issue with carotid disease or extracranial cerebral vascular disease is a little bit more problematic, because we don't have as good a medical therapy for that disease. So if the patient is symptomatic, we're often looking at some type of interventional treatment.

I guess in deference to Iftikhar, I also have to point out that I treat people with FMD as if it were a risk factor for developing atherosclerosis down the road. I don't know that that's true, but I automatically move them in my mind to a higher risk category so that I'm a little more aggressive than liberal with the aspirin and the statins and some of the other things that I might put people on with other higher grade risk factors.

ROB MCBANE: Very good. Thanks. So the standard mantra in patients who have FMD who are getting intervened upon endovascularly is to do angioplasty without stenting. Can you comment upon that--

SANJAY MISRA: Yeah.

ROB MCBANE: --Dr. Misra?

SANJAY MISRA: So I think, Rob, that's been our mantra for as long as I've known it. You know, we angioplasty. I will say, there is a group of patients, especially when you get in the sixth and seventh decade, that angioplasty failures occur much faster than they do for a 20-year-old or 30-year-old. I think angioplasty is probably safe in this group.

It's not like atherosclerotic disease, where you run the risk of more dissections and other embolization, for example. So I think for young patients-- symptomatic, hypertensive-- FMD with angioplasty works very well. When you get in the sixth, seventh, eighth decade, it fails. We wrote a paper on that, and there is a high risk of failure as you get older. That's unclear why that is.

ROB MCBANE: We just have a couple of seconds left, and I just want to-- each of you, final comment, research, future research on this disease. Dr. Kalloo?

IFTIKHAR KALLOO: Yeah. I think that there's a whole lot we don't know, as has probably come out in this discussion. I think one area that we really need to understand better is the genetic basis of the disease, and those are some activities that are ongoing here at Mayo and elsewhere.

ROB MCBANE: Very good. Dr. Misra?

SANJAY MISRA: I'd like to understand better the natural history. Once you're diagnosed, what happens? Are you at risk for aneurysms? What is that percentage? So we can better counsel our patients.

ROB MCBANE: Very good. Dr. Rooke?

THOM ROOKE: Yeah. The natural history is clearly our big weakness right now. And fortunately, there is a registry that's out there. They've begun to publish since last year some of their data on this. And I am cautiously optimistic that as we follow this registry over time, we're going to be able to understand more about the natural history and, from that, what we ought to be doing about this disease.

ROB MCBANE: Well, this is-- thank you all. There is so much to talk about. There are many avenues that we haven't had time to broach with this discussion, and I think we could go on and on for at least another hour. But I would like to thank each of our discussants, and I would like to thank you, the listening audience, for watching in on this very interesting roundtable. And I would like you to continue to follow us at the heart.org for our roundtable discussions. I'd welcome that. Thank you very much.

IFTIKHAR KALLOO: Thanks, Rob.

SANJAY MISRA: Thanks, Rob.