Cleveland Clinic

2nd International FMD Research Network and SCAD Symposium

MAY 18-19, 2017

InterContinental Hotel and Conference Center
Cleveland, Ohio

Dear Colleagues and Friends:

It is with great excitement that we welcome you to Cleveland, Ohio for the 2nd International Fibromuscular Dysplasia (FMD) Research Network and Spontaneous Coronary Artery Dissection (SCAD) Symposium. This meeting builds upon the international collaborations in the fields of FMD and SCAD that began here in Cleveland at our inaugural meeting three years ago. Clinicians and investigators will again come together from across the United States as well as Canada, and Europe for a state of the clinical science update and an opportunity for scientific strategic planning.

As you know, FMD is a morbid vascular disease that affects patients at the prime of life. In addition to impairing quality of life through symptoms such as headache and pulsatile tinnitus, FMD is a serious disease that is associated with major cardiovascular events such as stroke and myocardial infarction and other sequelae of poorly controlled hypertension. SCAD is an important cause of myocardial infarction in women. There is a strong link between SCAD and FMD, though the nuances of this relationship are complex and not fully understood.

The general sessions of the meeting will discuss the major clinical manifestations of FMD and SCAD and help to define the 2017 approach to diagnosis, medical, endovascular, and surgical therapy. The latest data from US, French/Belgian, and Canadian registries will be discussed. Emerging concepts will be presented, and researchers at the cutting edge of this field will update you on their work in progress, including some “late breaking” data. We hope that all clinicians who care for patients with FMD and SCAD will find the general sessions of the meeting useful, and we welcome your participation in the panel discussions. New this year, we emphasize the patient voice throughout the meeting as a number of speakers share their personal stories, perspectives on the progress of research, and contributions to raising awareness of these important vascular diseases.

In addition to the state of the science review, this meeting will allow for much needed in-person conversation and collaboration among our international panel of invited researchers and advocates. Four working groups will meet (hopefully not too) late into the night on Thursday and again Friday morning. Each working group will present a summary of their discussions and future plans on Friday afternoon at 4:30 pm Please try to stay for this special session (…and there will be a raffle for those in attendance too).

Many of you have come from far away, and we are most grateful for your time. We would like to thank our planning committee and the working group moderators, Dr. Santhi Ganesh, Ms. Marianne Khoury, Ms. Pamela Mace, and Ms. Kathy Murdakhaev. We thank our meeting supporters, listed below, without whom this international endeavor would not be possible. Finally, Dr. Gornik would like to acknowledge the hard work of her partners in the Cleveland Clinic FMD/SCAD program: Drs. Natalia Fendrikova-Mahlay, Deborah Hornacek, and Maya Serhal and Ms. Kathleen Petrarca, RN, as well as the unwavering support of Dr. John R. (Jerry) Bartholomew.

We believe this 2nd symposium is another momentous occasion. We anticipate multiple new international research projects will be born in the hours that follow, and we hope that this meeting will further our understanding of why FMD and SCAD develop and how to best diagnose and manage our patients to improve their vascular outcomes and quality of life. And so, the “2nd Cleveland Meeting” begins. Onward!

Heather L. Gornik, MD
Esther Soo Hyun Kim, MD
Jeffrey W. Olin, DO

ABOUT CLEVELAND CLINIC

Cleveland Clinic's Miller Family Heart & Vascular Institute is one of the largest cardiovascular specialty groups in the world, providing patients with expert medical management and a full range of therapies. The Department of Peripheral Vascular Disease (PVD) was founded in 1947 by Dr. Fay LeFevre and has a rich history of vascular clinical care, education, and research. PVD was incorporated into the Robert and Suzanne Tomsich Family Department of Cardiovascular Medicine in 2001, and Dr. John R. Bartholomew has served as Section Head of Vascular Medicine since 2004. The Cleveland Clinic FMD Program began in August, 2008 with a dedicated clinic once per month. The clinic is now run thrice weekly and follows more than 600 patients with FMD and 75 patients who have had a SCAD. The program uses vascular medicine specialists as primary vascular care providers and has built an experienced multi-disciplinary team of additional consultants, including nephrologists, neurologists, interventionalists, surgeons, radiologists, genetics professionals, and pathologists, who are engaged depending upon the individualized needs of the patient.

The program committee thanks the following individuals and organizations for their support of this meeting:

Lead Supporter:
The Schoeneman Family

Additional Support Provided By:
Fibromuscular Dysplasia Society of America (FMDSA)
Sally & Alan Bell
Dr. Steve and Robin Berlin
Gayle McElroy
Vascular Medicine Research and Education Fund (Dr. John R. Bartholomew)

MEETING CHAIRS

Heather L. Gornik, MD, MHS
Staff Physician, Cleveland Clinic Heart and Vascular Institute; Associate Professor of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University
Cleveland, Ohio

Esther SH Kim, MD, MPH
Director, Arteriopathy Clinic, Vanderbilt Heart and Vascular Institute; Associate Professor of Medicine, Vanderbilt University School of Medicine
Nashville, Tennessee

Jeffrey W. Olin, DO
Director, Vascular Medicine and the Vascular Diagnostic Laboratory; Professor of Medicine, Mount Sinai School of Medicine
New York, New York

PROGRAM PLANNING COMMITTEE

Santhi Ganesh, MD
Associate Professor of Internal Medicine and Human Genetics, University of Michigan
Ann Arbor, Michigan

Marianne Khoury, BS
Cleveland Clinic FMD Program
Serving as onsite resource coordinator for the working groups

Pamela Mace, RN
Executive Director, FMD Society of America
Rocky River, Ohio

Kathy Murdakhaev
Cleveland Clinic FMD Program

FMD/SCAD YOUNG INVESTIGATOR TRAVEL AWARD RECIPIENT

The selection committee congratulates Dr. Katarzyna Hanus, intern at the Independent Public Teaching Hospital in Warsaw, Poland. Dr. Hanus will be participating in the International FMD Registries working group. She is an early career investigator in the field of hypertension and has been an active member of the ARCADIA-POL research team since 2014. She has been a co-author on multiple oral and poster abstract presentations related to the ARCADIA-POL registry with her mentors Drs. Andrzej Januszewicz and Eva Warchol-Celinska and colleagues. She is currently working on her PhD dissertation on FMD and SCAD.

SOCIAL MEDIA POLICY

We welcome attendees to raise awareness regarding FMD and SCAD and to contribute to the social media footprint of this symposium through Twitter or other social media accounts.

For Twitter, please use **#FMDSCAD2017**

However, we are sensitive to the fact that some investigators may be presenting previously unpublished data within this forum and may prefer that these preliminary findings are not shared on social media. This would include photographs of any slides or abstract materials.

We ask speakers who do not wish for findings to be shared on social media to please state this at the start of their presentations, and we ask attendees to please respect this wish.

FRIDAY, MAY 19

General sessions will begin at 10:15 am. There will be closed working group sessions held prior to the general sessions. During this time, please take advantage of these opportunities:

Continental Breakfast (available for all attendees) beginning at 7:30 am

Cleveland Clinic Facility Tour
8:30 am–10:00 am.
Please sign up at Registration Desk. Guide will meet the group at the Registration desk at 8:30 am.

The tour will include Cleveland Clinic history, some of our prominent buildings, design philosophy, and some specific examples of structure, spaces and the innovative ways we have incorporated the patient perspective in our design process and purpose to elevate the patient experience.

United States Registry for FMD Coordinators Meeting
8:00 am–10:00 am
Meet Marianne Khoury at the Registration Desk at 8:00 am to walk over to the meeting space.

RAFFLE

Please stay through the end of our symposium for the meeting wrap-up on Friday, May 19th at 6 pm. We will be having a raffle for Cleveland Clinic apparel and Laura Britt Shoes. Participants must be in attendance to claim a prize.

FMD SOCIETY OF AMERICA

The 10th Annual FMDSA Meeting will be held on Saturday, May 20, 2017 at the Wyndham Hotel in Cleveland, Ohio. If you would like more information, please ask the staff to be introduced to Pam Mace, Executive Director, FMDSA.

FMDSA RECEPTION

Directly following the conclusion of the symposium on Friday, May 19th, attendees are invited to attend the welcome reception of the FMD Society of America (FMDSA) to be held at the Wyndham Hotel at Playhouse Square (2nd floor), 1250 Euclid Avenue, in Cleveland. The FMDSA Reception will conclude at 7:30 pm and will be followed by a group dinner (self-pay) at a nearby restaurant with FMDSA members and volunteers. Please contact the Registration Desk for details regarding transportation from the InterContinental Hotel to the Wyndham Hotel. A complimentary shuttle will depart at 6:30 pm.

2nd International Fibromuscular Dysplasia (FMD) Research Network and Spontaneous Coronary Artery Dissection (SCAD) Symposium—Working Groups

There will be four working groups, each chaired by member(s) of the planning committee. The working groups will meet in closed discussion sessions during the 2 day meeting and will give a report during the general sessions.

1) Genetics/Reassessing the FMD Phenotype

Working group charge:

1). To consider the implications of broadening definitions used for assessment of the "FMD phenotype";

2). To discuss incorporation of patients with cervical artery dissection and SCAD into ongoing genetic research collaborations.

Chairs: Santhi Ganesh, MD, University of Michigan and Jeffrey Olin, DO, Mount Sinai Medical Center

Participants:

- Nabila Bouatia-Naji, PhD, INSERM U970 and Paris Cardiovascular Research Centre, France
- Dawn Coleman, MD, University of Michigan
- Hannah Hill, University of Michigan
- Siying Huang, PhD, INSERM UMR970 Team 3—Paris Cardiovascular Research Centre, France
- Jason Kovacic, MD, Mount Sinai Medical Center
- Alberto Maud, MD, Texas Tech University Health Center
- Nupoor Narula, MD, Mount Sinai Medical Center
- Aditya Sharma, MBBS, University of Virginia
- Andrew Southerland, MD, University of Virginia
- James Stanley, MD, University of Michigan
- Marysia Tweet, MD, Mayo Clinic

2) Exercise and Activity After Spontaneous Coronary Artery Dissection (SCAD)

Working group charge:

To strategize methodology for development of an expert opinion consensus statement on post-SCAD exercise and activity for 1) medical professionals; 2) patients.

Chair: Esther SH Kim, MD, MPH, Vanderbilt University

Participants:

- David Adlam, MD, University of Leicester, UK
- Gordon Blackburn, PhD, Cleveland Clinic
- Sharonne Hayes, MD, Mayo Clinic
- Andrea Morgan, Patient Advocate
- Sahar Naderi, MD, Stanford University
- Dermot Phelan, MD, PhD, Cleveland Clinic
- Jacqueline Saw, MD, Vancouver General Hospital, Canada
- Tara Schoeneman-Brown, Patient Advocate
- Maya Serhal, MD, Cleveland Clinic
- Malissa Wood, MD, Massachusetts General Hospital

3) Maximizing Collaboration of International FMD Registries

Working group charge: To discuss identify and strategize opportunities for collaboration of the United States Registry for FMD and the European FMD Registry.

Chair: Heather Gornik, MD, MHS, Cleveland Clinic

Participants:

- Imad Bagh, MD, Cleveland Clinic
- Patsy Bruenger, BA, CCRC, University of Michigan
- Caitriona Canning, MB BCh, Cleveland Clinic
- James Froehlich, MD, University of Michigan
- Bruce Gray, MD, Greenville Health System
- Xiaokui Gu, MA, University of Michigan
- Katarzyna Hanus, MD, Institute of Cardiology, Poland
- Andrzej Januszewicz, MD, Institute of Cardiology, Poland
- Magdalena Januszewicz, MD, PhD, Institute of Cardiology, Poland
- Eva Kline-Rogers, RN, NP, MS, University of Michigan
- Alexandre Persu, MD, PhD, Cliniques Universitaires Saint-Luc (UCL), Belgium
- Alexander Prejbisz, MD, PhD, Institute of Cardiology, Poland
- Ewa Warchol-Celinska, MD, PhD, Institute of Cardiology, Poland
- Bryan Wells, MD, Emory University

4) Patient Advocacy Working Group

Working group charge: To identify the unmet needs of U.S. and international FMD and SCAD patients and to determine potential mechanisms to address these needs.

Chair: Pamela Mace, RN, FMD Society of America and Patient Advocate

Participants:

- Roberta Anderson, CNP, Patient Advocate
- Sherry Bumpas, RN, PhD, Eastern Michigan University
- Wanda Ellis, Patient Advocate
- Natalia Fendrikova-Mahlay, MD, Cleveland Clinic
- Emma Greenwood, Patient Advocate
- Deborah Hornacek, MD, Cleveland Clinic
- Cathlin Jamison, International Patient Advocate
- Katherine Leon, SCAD Alliance and Patient Advocate
- Abbie Levy, Patient Advocate
- Fran Saplis, RN, Patient Advocate
- Ido Weinberg, MD, Massachusetts General Hospital

2nd International FMD Research Network and SCAD Symposium

AGENDA | THURSDAY, MAY 18, 2017

Each speaker will be allotted 12 minutes for presentation with 3 minutes reserved for questions and topic-related discussion, unless otherwise noted (15 minutes per topic).

General sessions (Dr. Heather Gornik moderates): Setting the Foundation—FMD		
9:30 am	Registration	
10:00 am	Welcome, background and scope, introduction of participants	Heather Gornik, MD, MHS
10:15 am	FMD: Historical Perspective and Angiographic-Histologic Classification System	James Stanley, MD
10:30 am	Broadening the FMD Phenotype Beyond the String of Beads: Aneurysms, Dissections, and Tortuosity in FMD	Jeffrey Olin, DO
10:45 am	Epidemiology of FMD—What's New? What Remains Unknown?	Esther Kim, MD, MPH
11:00 am	Update from the US Registry for FMD and Late Breaking Data (25 minutes)	Heather Gornik, MD, MHS Imad Bagh, MD
11:25 am	Key Findings of the French ARCADIA Registry and Update on the European FMD Initiative (25 minutes)	Alexandre Persu, MD, PhD
11:50 pm	Panel discussion	Panel
12:05 pm	Patient perspective panel followed by interactive discussions with attendees (40 minutes) Heather Gornik, MD, MHS Moderates, Pamela Mace, RN, Cathlin Jamison, Abbie Levy, Fran Saplis, RN, Wanda Ellis	
12:45–1:30	**NETWORKING LUNCH**	
General Sessions (Dr. Olin moderates): FMD Pathogenesis and Genetics		
1:45 pm	FMD Genetics: State of the Science 2017 and Update from My Lab	Santhi Ganesh, MD
2:00 pm	FMD as a Complex Genetic Disease	Nabila Bouatia-Naji, PhD
2:15 pm	Mt. Sinai Define—FMD Study Update	Jason Kovacic, MD
2:30 pm	Project in Progress: Cognitive Function and FMD	Bryan Wells, MD
2:45 pm	Panel discussion (30 minutes): Genetic/Environmental Interactions in FMD? How Will Broadening the FMD Phenotype Help Efforts to Understand Genetic Mechanisms of FMD?	Panel
3:15–3:45 pm	**REFRESHMENT BREAK**	
General Sessions (Dr. Kim Moderates): Spontaneous Coronary Artery Dissection (SCAD)		
3:45 pm	Introduction: SCAD as a Cause of MI and the Link to FMD, Preview of AHA SCAD Scientific Statement	Sharonne Hayes, MD
4:00 pm	Angiographic Diagnosis and Management of SCAD in the Cath Lab; Emerging Data on Coronary FMD Beyond SCAD	Jacqueline Saw, MD
4:15 pm	Epidemiology and Pathophysiology of SCAD: Theories, Hypotheses, and Evidence	Sahar Naderi, MD
4:30 pm	Cardiac Rehabilitation, Chest Pain and Stress Management Post SCAD	Malissa Wood, MD
4:45 pm	UK and European SCAD Research and Educational Efforts	David Adlam, MD
5:00 pm	New Data from the Cleveland Clinic SCAD/FMD Program	Maya Serhal, MD Esther Kim, MD, MPH
5:15 pm	Patient perspective panel followed by interactive discussion with attendees (30 minutes) Esther Kim, MD, MPH Moderates, Roberta Anderson, CNP, Tara Schoeneman-Brown, Katherine Leon, Andrea Morgan	
5:45 pm	General sessions adjourn for the day	
5:50 pm	Working group photographs	
6:00–9:00 pm	Working groups meet (dinner provided)	
9:00 pm	Working groups adjourn for the night	

AGENDA | FRIDAY, MAY 19, 2017

7:30-8:30 am	Continental breakfast	
7:30–10:00 am	Working groups meet (breakfast provided)	
8:00–10:00 am	US FMD Registry Study Coordinators Meeting—Meet Marianne Khoury at breakfast at IC hotel and walk to meeting space at Cleveland Clinic	Ms. Eva Kline-Rogers to Chair CCF Room J3-122
8:30–10:00 am	Cleveland Clinic facility tour for open session attendees	
General Sessions (Dr. Olin moderates): Clinical Management Updates I		
10:15 am	Natural History of Carotid FMD: Mt. Sinai Study	Jeffrey Olin, DO
10:30 am	Brain Aneurysms and FMD: Data from the US Registry	James Froehlich, MD
10:45 am	Cervical Artery Dissection: Recent Lessons Learned	Andrew Southerland, MD
11:00 am	Intracranial FMD: Data from Cleveland Clinic	Russell Cerejo, MD
11:15 am	State of the Art Management of Cervical Artery Dissections and Brain Aneurysms in Patients with and Without FMD	Gabor Toth, MD
11:30 am	Modern Approaches to Intractable Headache, Including Botox Therapy for Chronic Migraine (30 minutes)	Mark Stillman, MD
12:00 pm	Pulsatile Tinnitus—the Patient Perspective and Activities of Whooshers.com	Emma Greenwood
12:15 pm	Case presentation and discussion with panel and audience participation (30 minutes)	Natalia Fendrikova-Mahlay, MD
12:45–1:30 pm	**NETWORKING LUNCH**	
General Sessions (Dr. Kim moderates): Clinical Management and Research Updates II		
1:45 pm	Management of FMD in Europe and the US: Similarities and Differences	Alexandre Persu, MD, PhD
2:00 pm	Approach to Renal Angiography and Intervention in FMD	Bruce Gray, DO
2:15 pm	Renal FMD: Challenging Cases from the Cath Lab	Christopher Bajzer, MD
2:45 pm	Surgical Approach to Renal FMD: Pediatric Renal Artery Disease, Mid-Abdominal Syndrome and Adult Visceral Aneurysms.	Dawn Coleman, MD
3:00 pm	Group Review of International FMD Research Network Guidance for Renal Angiography (2014/2017)	Heather Gornik, MD, MHS Jeffrey Olin, DO
3:15 pm	Panel discussion	Panel
3:30–4:00 pm	**REFRESHMENT BREAK**	
General Sessions (Dr. Gornik moderates): Research Logistics and Report of Working Groups		
4:00 pm	Incorporating Research Into an FMD Clinical Program (…with little or no funding)	Aditya Sharma, MBBS
4:15 pm	Challenges of Registry Research/the MCORRP Perspective	Eva Kline-Rogers, RN
4:30 pm	Aligning Local Research Efforts to the Broader FMD Research Initiative: ARKADIA-POL Case Study	Andrzej Januszewicz, MD
4:45 pm	What Can Qualitative Research Methods Bring to the Study of FMD?	Sherry Bumpas, PhD, RN
Presentations of the working groups and discussion (10 minute summary of discussions followed by 5 minutes of discussion for each):		
5:00 pm	Genetics/Reassessing the FMD Phenotype	Santhi Ganesh, MD Jeffrey Olin, DO
5:15 pm	Exercise and Activity after SCAD	Esther Kim, MD, MPH
5:30 pm	Maximizing Collaboration of International Registries	Heather Gornik, MD, MHS
5:45 pm	Maximizing Patient Advocacy Efforts	Pamela Mace, RN
6:00 pm	Wrap up and meeting adjourns	Heather Gornik, MD, MHS Esther Kim, MD, MPH Jeffery Olin, DO

ABSTRACT

THURSDAY, MAY 18, 2017

10:15 am: FMD: Historical Perspective and Angiographic-Histologic Classification System, Modern Nomenclature
James Stanley, MD, University of Michigan

The disease category 'fibromuscular dysplasia' includes a broad spectrum of nonatherosclerotic-noninflammatory stenoses, most often affecting medium-size muscular arteries of both genders and at all ages. Nevertheless, most dysplastic stenoses in children, compared to fibrodysplastic stenoses in adulthood, are different from a morphologic-histologic, and likely an etiologic perspective, making it logical to classify arterial dysplasia in these disparate age groups separately.

Existence of fibromuscular dysplasia in adults was convincingly established by arteriographic and pathologic studies published by clinician-scientists from the University of California San Francisco, Cleveland Clinic, and Mayo Clinic. None of these early publications or anecdotal reports from others in Europe or the Americas had systematically categorized this arterial disease.

The first comprehensive classification of fibromuscular dysplasia was a collaborative effort of Harrison and McCormack (Mayo Clin Proc 1971; 46:161-167). They described six categories, including: Intimal fibroplasia (1-2%), secondary intimal fibroplasia, medial fibroplasia with mural aneurysms (60-70%), medial hyperplasia (5-15%), perimedial fibroplasia (15-25%), and periarterial fibroplasia (<1%). Others challenged two issues of their report later, including: 1) their separation of perimedial from medial fibroplasia and 2) the relatively high frequency of medial hyperplasia.

The second widely disseminated classification was from the University of Michigan (Arch Surg 1975; 110:561-566). It identified five categories, including: primary and secondary intimal fibroplasia (5%), medial fibroplasia (85%), perimedial dysplasia (10%), and medial hyperplasia (1%). Relevant differences in this classification included: 1) combining the Harrison and McCormack perimedial fibroplasia type with their medial fibroplasia with mural aneurysm type, as a continuum in many arteries, 2) redefining perimedial dysplasia as a disease predominately involving elastic tissue, not vascular smooth muscle, and 3) questioning existence of medial hyperplasia in that it appeared more likely an early manifestation of medial fibroplasia rather than an increase in the quantity of vascular smooth muscle, but rather its transformation to myofibroblasts.

Subsequent introduction of catheter-based interventions for dysplastic stenoses established the need for a reasonable arteriographic-morphologic classification of the arterial fibrodysplasias. French investigators addressed this subject by categorizing dysplastic stenoses into unifocal or multifocal disease (Circulation 2012; 126:3062-3069). Their report supported existence of two distinct phenotypes. This former work was modified by the American Heart Association (Circulation 2014;129:1048-1078) to include: focal stenoses (intimal fibroplasia, adventitial-periarterial-fibroplasia, and medial hyperplasia) and multifocal stenoses (medial fibroplasia and perimedial fibroplasia).

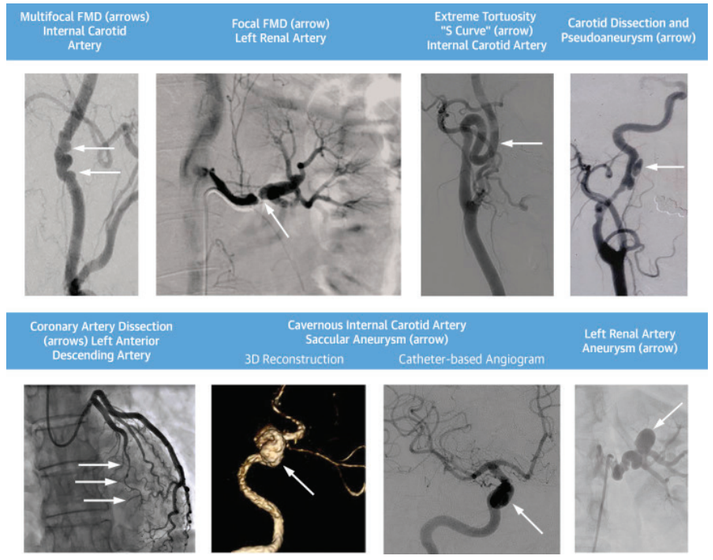
It is important to recognize that the value of any diagnostic nomenclature is primarily twofold: first, to facilitate development of clinical practice guidelines, and second, to provide for more focused and granular investigations of a disease's pathogenesis. Whether arterial fibrodysplasia's modern histologic, arteriographic and phenotypic categories are closely aligned remains to be determined.

10:30 am: Broadening the FMD Phenotype Beyond the String of Beads: Aneurysms, Dissections, and Tortuosity in FMD
Jeffrey Olin, DO, Mount Sinai Medical Center

In the past, fibromuscular dysplasia (FMD) was classified by the layer of vessel wall involvement on histopathology. However, due to the progress in treating FMD with endovascular techniques, pathologic specimens are rarely available and thus, the type of FMD is usually determined by the angiographic appearance. From 2012 to 2014, a European consensus document and an American Heart Association Scientific Statement on FMD suggested that the classification be simplified into two main types, based on the angiographic appearance. The "string of beads" appearance (previously called medial fibroplasia) is now called multifocal FMD and a focal stenosis (most commonly due to intimal fibroplasia) is now called focal FMD.

In addition to classification, it has become more apparent in recent years that FMD is more than just a string of beads. A number of different phenotypic presentations are being encountered and not all patients with FMD present with only the "string of beads" or focal stenosis. An analysis of 921 patients from the U.S. Registry for Fibromuscular Dysplasia has shown that aneurysms occur in 21.7% of FMD patients with renal arteries, carotid arteries and cerebral arteries being the most common location. However, any artery may be involved. Additionally, dissection occurred in 25.7% of patient with the carotid artery, vertebral artery, renal artery and coronary artery being the most frequent locations. Of these 921 patients, 41% had an aneurysm and/or dissection, a prevalence much higher than previously appreciated. Now that an association between spontaneous coronary artery dissection (SCAD) and FMD is clearly established, SCAD is being more frequently diagnosed, especially in centers with expertise in FMD. Another manifestation of FMD is arterial tortuosity. It has been shown that there is a greater likelihood of SCAD recurrence when the coronary arteries are tortuous as compared to when they are straight. It has also been shown that about 1/3 of FMD patients have extremely tortuous internal carotid arteries, now described as the S curve.

As our understanding of FMD increases, an expanding phenotype has appeared suggesting that FMD is much more than a string of beads but a systemic vascular disease with a number of different appearances and presentations.



10:45 am: Epidemiology of FMD – What's New? What Remains Unknown?
Esther SH Kim, MD, Vanderbilt Heart and Vascular Institute—Vanderbilt University School of Medicine

Determining the true prevalence of FMD in the general population, the risk factors for the development of FMD, and the prognosis of patients with FMD remain top priorities. Knowledge regarding the prevalence of renal FMD derives from angiographic studies of kidney donors and substudies of renal stent trials. Carotid FMD studies are even more limited to autopsy studies and cerebral angiograms performed for patients with neurologic events. Risk factors for FMD remain ill-defined, but findings from US FMD Registry will contribute to knowledge about prognosis and associated arterial events, such as dissection and aneurysm. Updates in the epidemiology of FMD will be discussed and methods of epidemiologic study of FMD proposed at the inaugural International FMD Research Network Symposium will be reviewed.

11:00 am: Update from the US Registry for FMD
Heather Gornik, MD, MHS, Cleveland Clinic on behalf of *The United States Registry for FMD Investigators*

The United States Registry for Fibromuscular Dysplasia (FMD) was formed in 2008 among 7 clinical centers. The Registry is funded by the FMD Society of America (FMDSA) and is maintained by the University of Michigan Cardiovascular Outcomes Research and Reporting Program (MCORRP). Since the 1st patient enrollment in January, 2009, a total of 1663 FMD patients have been enrolled (as of April 21, 2017), and the Registry has been expanded to 14 active clinical centers. There have been multiple poster and oral abstract presentations and six published peer reviewed manuscripts from the Registry with additional papers in process. A number of insights regarding FMD have been gleaned from the US Registry data, including:

- The most common clinical manifestations of FMD are hypertension and headache, followed by pulsatile tinnitus, dizziness, cervical bruit, and neck pain. 32.1% of patients report pulsatile tinnitus ("swooshing") in the ears as a presenting symptom of FMD.
- FMD is primarily a condition of middle age (mean at first symptom 47 years), but can present across the life span, including pediatric and elderly patients. Pediatric patients with FMD are less likely to have cerebrovascular involvement and are more likely to have renal or mesenteric involvement or middle aortic syndrome.

ABSTRACTS *(Continued)*

• Men with FMD are more likely to present with renal or visceral involvement and have a two-fold prevalence of arterial dissection or aneurysm compared to women with FMD.

• Patients with FMD who have a history of smoking (current or former) are more likely to have an aneurysm or claudication and are more likely to have undergone a vascular procedure. 11.9% of Registrants actively smoke, and 34.5% have a history of smoking.

• FMD is an aggressive vascular disease. 41.7% of patients in the US Registry have reported at least one arterial aneurysm or dissection. This statistic has led to a recommendation for all FMD patients to undergo one time brain to pelvis cross-sectional imaging (MRA or CTA) to screen for occult aneurysms or dissections.

• Among all Registrants, 72.9% take an anti-platelet agent and 71.7% take at least one anti-hypertensive medication. 21.5% of patients take 3 or more anti-hypertensive medications.

• Approximately 50% of Registrants have undergone at least one therapeutic vascular procedure, >80% of which are catheter based. The renal artery was the target vessel in 73% of vascular procedures. A procedural complication was reported in ~ 10% of cases, most commonly an arterial dissection.

A current emphasis of the US Registry is on determination of the prevalence of major vascular events among patients with FMD and the incidence of new events in follow-up. Approximately 70% of patients enrolled in the Registry for more than 1 year have had at least one clinical follow-up visit reported, and some patients have been followed for eight or more years.

On behalf of the Steering Committee, the coordinating center (MCORRP), and the sponsor (FMDSA), we look forward to exploring collaborations between the US and European FMD registries.

11:15 am: Multifocal Fibromuscular Dysplasia in Elderly Patients is Associated With a More Benign Course: Data from the United States Registry for FMD

Imad Bagh, MD, Cleveland Clinic on behalf of *Imad Bagh, Jeffrey W. Olin, Xiaokui Gu, James B. Froehlich, Bruce Gray, Esther Soo Hyun Kim, Aditya Sharma, Ido Weinberg, Bryan Wells, Eva Kline-Rogers, Heather L. Gornik*

Introduction: Fibromuscular dysplasia (FMD) is non-atherosclerotic arterial disease that predominately affects women. FMD had been considered a disease of young women, but recent data have shown that it affects all age groups.

Methods: Analysis of patients enrolled in the US Registry for FMD as of 12/15/2016. Evaluable patients ≥ 18 years at the time of enrollment and those with multifocal FMD only were included. Patients were categorized according to age at the time of diagnosis (>65 vs. <65 yrs). Major vascular event at enrollment was defined as: arterial dissection, TIA, stroke, subarachnoid hemorrhage, mesenteric ischemia, renal infarction, myocardial infarction (including SCAD), and coronary revascularization. Student's t tests, Wilcoxon rank-sum tests, Chi-square and Fisher's exact tests were used to evaluate the differences between the two age groups.

Results: 1016 patients included in the analysis. Age distribution is shown (Figure); 170 (16.7%) patients were ≥ 65 yrs at the time of diagnosis of FMD. Time between symptom onset and diagnosis was longer in patients ≥ 65 yrs (7.2 yrs vs. 3.5 yrs, p<0.001). Older FMD patients were more likely to be asymptomatic at the time of diagnosis (4.2% vs. 1.4%, p=0.02). Headache and pulsatile tinnitus were less common in patients diagnosed at ≥ 65 yrs (40.5% vs. 69.1%, p< 0.001 and 30.0% vs. 44.6%, p<0.001, respectively). The extracranial carotid arteries were more commonly involved in patients ≥ 65 yrs (87.0% vs. 79.4%, p=0.028). There was no difference in prevalence of renal artery involvement, number of vascular beds involved, or presence of any aneurysm. Patients ≥ 65 yrs were less likely to have had a major vascular event (37.1% vs. 46.1%, p=0.031), arterial dissection (16.0% vs. 32.4%, p<0.001), myocardial infarction (1.8% vs. 7.6%, p=0.003). Fewer patients ≥ 65 yrs had undergone therapeutic vascular procedures at enrollment (18.5% vs. 33.1%, p<0.001).

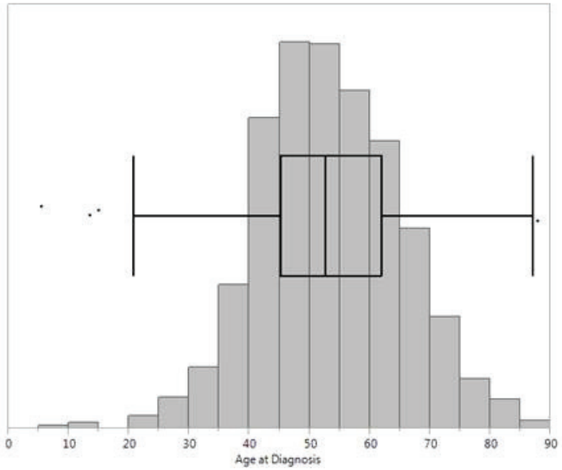


Figure. Age at diagnosis of patients enrolled in the US Registry for FMD. Mean age at dx among older patients (≥ 65 yrs at diagnosis) was 71.4 yrs.

Conclusions: Patients ≥ 65 yrs at the time of diagnosis of FMD have lower prevalence of major vascular events, including arterial dissections, than younger patients and have undergone fewer therapeutic vascular procedures. Older patients with FMD appear to have a more benign disease phenotype and fewer symptoms, which could explain the longer delay in diagnosis.

11:25 am: Key Findings of the ARCADIA Registry and Update on the European FMD Initiative (25 min)

Alexandre Persu, MD, PhD, Cliniques Universitaires Saint Luc

The aim of the French ARCADIA registry (PI: Prof. P-F. Plouin, Paris, NCT02884141) was to assess the prevalence of Fibromuscular Dysplasia (FMD) of different vascular beds and multisite FMD in a multicenter cohort of patients from France and Belgium (n=469 patients), using a standardized approach and state-of-the-art imaging. Forty-eight % of patients proved to have multisite FMD. Among patients with a cerebrovascular presentation, the prevalence of renal artery lesions was higher in patients with hypertension. Among patients with a renal presentation, the prevalence of cervical lesions was higher in patients with bilateral renal artery lesions. The ARCADIA study confirms the systemic character of FMD and will help selecting patients in whom a comprehensive vascular work up is particularly indicated.

In the wake of ARCADIA, the main aims of the European FMD initiative[1] are: (i) to standardize screening and management of FMD in Europe; (ii) to establish a network of expert centers; (iii) to promote the creation of a European patient association; (iv) to establish a European FMD registry; (v) to set up large GWAS/WES studies likely to identify genes underlying the heritable component of the disease; (vi) to offer a platform of discussion and collaboration for transnational FMD-related projects. The European FMD registry, coordinated by A. Persu (Brussels) in tight collaboration with P-F. Plouin, M. Azizi and X. Jeunemaitre (Paris) is at the crossroads of these different objectives. It will contribute to standardize clinical practice in Europe. It requires the contribution of expert centers and patient associations, and on the other hand will provide them with new evidence likely to improve detection and management of the disease.

The objectives of the presentation are: (i) to summarize the key findings of the ARCADIA registry; (ii) to provide an update on the current status of the European FMD initiative and registry.

[1]Persu A, Van der Niepen P, Touzé E, Gevaert S, Berra E, Mace P, Plouin PF, Jeunemaitre X; Working Group "Hypertension and the Kidney" of the European Society of Hypertension and the European Fibromuscular Dysplasia Initiative..Revisiting Fibromuscular Dysplasia: Rationale of the European Fibromuscular Dysplasia Initiative. Hypertension. 2016;68:832-9.

1:45 pm: FMD Genetics: State of the Science 2017 and Update from My Lab

Santhi Ganesh, MD, University of Michigan

The University of Michigan Arterial Dysplasia Study has enrolled subjects with FMD for studies using a number of complementary genetic approaches. Our most recent efforts have focused on the identification of rare variants underlying FMD in sporadic and familial cases of FMD. Our studies include case control approaches, analyses aimed at quantifying familial risk and the role of specific genetic variants. We are pleased to participate in several successful collaborations on our studies as well as corollary studies led by collaborators.

2:00 pm: What if Fibromuscular Dysplasia was a Complex Genetic Vascular Disease?

Nabila Bouatia-Naji, Msc, PhD, Paris Cardiovascular Research Centre

Fibromuscular Dysplasia (FMD) is a neglected vascular disease with severe health consequences. The genetic investigation of FMD has been challenging despite evidence for the existence of a genetic basis supported by declared and assessed intra-familial recurrence. Our recent identification of a common genetic locus that increases the risk of FMD by 40% provides first evidence for the existence of a complex genetic pattern on inheritance for FMD. Moreover, this finding connects for the first time FMD to other neurovascular and cardiovascular diseases providing new avenues to the physiopathology of arterial stenosis that characterizes FMD. Here I will provide arguments in favor of the existence of a large number of genetic determinants for FMD, describe our first genome-wide association study involving PHACTR1 and our scientific approach that aims to decipher the genetic basis of this genetically and clinically intriguing vascular disease.

ABSTRACTS *(Continued)*

2:15 pm: Mount Sinai DEFINE-FMD: Defining the Molecular and Cellular Basis of FMD Using Patient-derived Fibroblasts
Jason Kovacic, MD, Mount Sinai Medical Center

The aim of the Mount Sinai DEFINE-FMD study is to use disease-relevant samples from FMD patients and matched healthy control subjects to DEFINE the molecular and cellular basis of FMD. As suggested by the name Fibromuscular Dysplasia, it is likely that fibroblast cells play an important role in this disease. In the DEFINE-FMD study, we are collecting DNA, plasma, serum, fibroblast cells (via skin punch biopsy) and culture supernatant from rigorously phenotyped FMD patients with multifocal disease and healthy controls. Healthy controls are also carefully screened, and are matched to FMD patients by gender, race/ethnicity, age, smoking status, body mass index and number of anti-hypertensive medications. All fibroblasts are grown from skin biopsy samples under standardized conditions by a single person, and fibroblast RNA is then harvested for high-throughput transcriptomic analysis using RNA sequencing. As of March, 2017, 270 subjects have been enrolled and recruitment is ongoing.

2:30 pm: Cognitive Function and Depression in Patients with Fibromuscular Dysplasia
Bryan Wells, MD, Emory University on behalf of *Adrienne Repack, Natalie Sterrett, Roshan Modi, Barrett Bowling, Yi-An Ko, Bryan J. Wells*

Introduction: The relationship between fibromuscular dysplasia (FMD) and cognitive function or depression is not known. This study was designed to evaluate the associations of FMD with cognitive function and depression.

Methods: At a single center, participants with a diagnosis of extracranial or intracranial FMD without a history of stroke were enrolled. Demographics, past medical history, symptoms, medications, and vascular events were recorded. Cognitive function was tested using the Montreal Cognitive Assessment (MoCA, range 0-30, with > 26 representing normal cognition) and depression was tested using the Patient Health Questionnaire depression scale (PHQ-8, range 0-24, with >9 representing depression and >4 representing mild depression). For comparison, we enrolled non-matched female clinical and administrative staff from our institution. The FMD patient MoCA and PHQ-8 scores were calculated and compared to those without FMD using a nonparametric statistical approach.

Results: We are reporting results from the first 24 (12 with and without FMD, all women) participants enrolled thus far. The FMD participants had a mean age of 56.5 years (SD 10) and the non FMD participants had a mean age of 41.1 years (SD 6). In the FMD group, 3 (25%) had a carotid dissection, 2 (17%) had an intracranial aneurysm, 7 (58%) had hypertension, 7 (58%) reported headaches, and 2 (17%) reported depression. When the FMD group was compared with the non FMD group, no differences were seen in mean MoCA score (27.1 vs. 26.8, p=0.95 and the FMD group had a higher mean PHQ-8 score (6.3 vs. 2.0, p=0.029).

Conclusions: Based on preliminary observational data from our single center, FMD does not appear to affect cognitive function but may be associated with depression.

3:45 pm: SCAD, Myocardial Infarction, and its Link to FMD
Sharonne Hayes, MD, Mayo Clinic

Non-atherosclerotic spontaneous coronary artery dissection (SCAD) is now known to be a far less “rare” etiology of myocardial infarction than previously appreciated and its demographics are better understood that even two years ago. SCAD is an overwhelmingly female condition, affecting younger individuals, those with few CVD risk factors, and those in the peripartum period. The association of SCAD and FMD, first described in 2005 and subsequently confirmed in a number of small to medium-sized case series, has positioned FMD as a clearly associated and possibly causal comorbid factor in many patients with SCAD. The reported prevalence of concomitant FMD in extracoronary vascular beds among SCAD patients varies greatly, ranging from 17% to 86%, depending on the patient population, number of imaged vascular beds and the mode of imaging used for screening.

Patient-initiated research, improved diagnostic definitions and tools, and a growing awareness among healthcare providers have also propelled our understanding of SCAD. Crucial differences in pathophysiology, response to treatment, and clinical outcomes between SCAD and atherosclerotic disease have been described and inform current practice. This presentation will provide context for the link between SCAD and FMD and an update on the state of the science and research on SCAD.

4:00 pm: Angiographic Diagnosis and Management of SCAD in the Cath Lab; Emerging Data on Coronary FMD Beyond SCAD
Jacqueline Saw, MD, Vancouver General Hospital, Canada

Spontaneous coronary artery dissection (SCAD) is underdiagnosed and the true prevalence is underestimated. Unfortunately, SCAD is frequently missed on coronary angiogram since the arterial wall is not imaged with this test. Thus, a SCAD angiographic classification and algorithm for diagnosis has been described. Type 1 is the pathognomonic appearance of arterial wall stain of multiple lumen. Type 2 is the angiographic appearance of diffuse stenosis of varying severity. Type 3 describes a focal-tubular stenosis that mimic atherosclerosis, which typically requires intracoronary imaging to aid diagnosis. The management of SCAD remains largely conservative, restricting percutaneous coronary intervention or bypass surgery to patients with ongoing ischemia, left main, or hemodynamic instability. Ancillary management of SCAD includes screening for predisposing and precipitating stressors. Fibromuscular dysplasia (FMD) is strongly associated with SCAD, being present in ~70% of patients with SCAD. Diagnosis of coronary FMD has been rare and challenging, but recent angiographic appearance of coronary FMD has been described. These findings include coronary tortuosity, irregular stenosis, smooth stenosis, and segmental dilatation. This talk will focus on the diagnosis and management of SCAD.

4:15 pm: Epidemiology and Pathophysiology of SCAD: Theories, Hypotheses, and Evidence
Sahar Naderi, MD, Stanford University

The true epidemiology of SCAD is unknown as it was, until recently, a generally unrecognized and underdiagnosed condition. This was and still is driven by a low index of suspicion for a cardiac cause of presenting symptoms in young women, as well as limitations of angiography and lack of clinician familiarity with the condition. Much of the published knowledge of SCAD comes from several single center registries. Initial series indicated a prevalence ranging from 0.07-1.1%. Emerging data now suggest that SCAD may be a more frequent cause of ACS than previously thought, particularly in younger women. Here, we will discuss the prevalence of SCAD as well as some of the characteristics that appear to be unique to the condition.

While the underlying pathophysiology of SCAD is not fully understood, a number of precipitants for the event have been observed, including emotional, physical, and hormonal triggers. An association with fibromuscular dysplasia, and in less common cases, connective tissue disease has also been observed. We will also explore the hypotheses regarding the pathophysiology of the condition and summarize the available evidence to date.

4:30 pm: Cardiac Rehabilitation, Chest Pain and Stress Management Post SCAD
Malissa Wood, MD, Massachusetts General Hospital

The long-term benefits of regular physical activity are clear. There has been, however, a great deal of uncertainty regarding exercise recommendations for survivors of spontaneous coronary artery dissection (SCAD). Physical activity has been identified as a potential trigger for SCAD, thus many SCAD survivors and their physicians have been very cautious in suggesting return to physical activity. Many SCAD patients report a pre-existing history of anxiety or high levels of stress and most experience increased levels of anxiety after their SCAD presentation. Options for managing their anxiety and stress include pharmacologic management, particularly in the acute setting, cognitive behavioral or talk therapy and mind body interventions. Many cardiologists remain ill-equipped to recognize anxiety in their patients and lack the training to appropriately manage psychological factors associated with SCAD. Cardiac rehabilitation not only provides exercise training post-SCAD but also can help manage the psychological complications associated with SCAD and can help identify patients who may benefit from more intensive interventions. The overall goal of cardiac rehabilitation for SCAD patients is to carefully and gradually re-introduce physical activity. This type of approach must be personalized to provide an exercise and behavioral health program which will allow the SCAD survivor to resume activities which they previously were able to comfortably perform. Baseline stress ECG and or cardiopulmonary stress testing allows for the development of a more precise exercise prescription and plan. This session will also include discussion about the pharmacologic options available to manage the ongoing chest pain which frequently occurs in the weeks and months following the initial SCAD presentation.

4:45 pm: UK and European SCAD Research and Educational Efforts
David Adlam, MD, University of Leicester

Europe has contributed a number of important national registry studies on Spontaneous Coronary

ABSTRACTS *(Continued)*

Artery Dissection building on US and Canadian series. International collaboration is clearly key to future clinical and pathophysiological research as well the education of health care professionals in the identification of what is still an under-recognised condition and the development and refinement of management guidelines. The ESC-ACCA European SCAD Study Group was launched in 2016 supported by our patients groups including BeatSCAD and Eurordis. The aims of the Study Group are:

- To establish a collaborative partnership to advance research into SCAD
- To maintain a European registry of SCAD patients to advance understanding of epidemiology and variations in patient management and outcomes
- To coordinate and support clinical and pre-clinical research into SCAD
- To formulate and disseminate a European consensus on the diagnosis and management of SCAD
- To improve accurate diagnosis by raising awareness of SCAD
- To support patients with this condition

Early progress includes the drafting of a European Position Paper on SCAD and adoption by the European Observational Research Program (EORP). An update on progress will be presented.

5:00 pm: The Cleveland Clinic Experience—Spontaneous Coronary Artery Dissection

Maya Serhal, MD, Cleveland Clinic on behalf of *Maya Serhal, Ashok Mittal, Marianne Khoury, Ellen Brinza, Natalia Fendrikova-Mahlay, Deborah Hornacek, Heather L. Gornik, Esther S.H. Kim*

Since August 2015, the Cleveland Clinic SCAD Registry has been prospectively enrolling patients with a history of SCAD from the outpatient cardiovascular clinics. The purpose of the registry is to characterize SCAD by describing patient presentation, medical and family history, diagnostic imaging findings, prevalence of FMD and other underlying non-coronary arterial pathology, and signs and symptoms during post-SCAD follow up. In this talk, we will present the initial findings of 64 patients with SCAD seen at Cleveland Clinic with focus on the family history of significant cardiovascular events including aneurysm, dissection, early stroke and early myocardial infarction in first and second degree relatives. Common symptoms post-SCAD and medical management of SCAD patients in the outpatient setting will also be discussed. We will compare the features of the Cleveland Clinic SCAD cohort to those reported from other leading centers.

FRIDAY, MAY 19, 2017

10:15 am: Natural History of Cervical Artery Fibromuscular Dysplasia and Associated Neurovascular Events

Jeffrey Olin, DO, Mount Sinai Medical Center

Background and Purpose: Fibromuscular dysplasia (FMD) is a non-atherosclerotic arteriopathy most often affecting the carotid and renal arteries. In the United States Registry for FMD, 41.7% of patients experienced an aneurysm and/or dissection by the time of FMD diagnosis. Subsequent occurrence of vascular events, or new development of FMD in arteries previously imaged, is unknown.

Methods: The medical records of prospectively collected data and cervical artery imaging [carotid artery duplex ultrasound (CDU), magnetic resonance angiogram (MRA) and/or computed tomographic angiogram (CTA)]) were reviewed. Patients with confirmed FMD and > 1 cervical artery imaging study were included. Subsequent dissection, aneurysm, TIA, stroke, or new FMD findings were recorded.

Results: Among 146 FMD patients with complete information, 52 (35.6%) had an aneurysm and 52 (35.6%) had a dissection. Mean clinical follow-up was 35.3 ± 25.3 months (range 5 – 153); patients underwent 4 ± 2.7 CDU (range 1 – 17); 86.3% had at least one neck MRA or CTA. After FMD diagnosis, 3 patients experienced a new carotid artery dissection. Two of these three patients had a previous dissection. One patient experienced a stroke due to concomitant atherosclerosis. No patient developed a new aneurysm. In patients without cervical FMD (35 carotid, 88 vertebral), none developed new cervical artery findings on follow-up imaging. In patients with known cervical artery FMD, there was no progression in any patient.

Conclusions: New cervical artery FMD or aneurysm did not occur in any patient. The development of neurovascular events after FMD diagnosis is rare. The overall rate of aneurysm and dissection in this population is greater than previously reported.

10:30 am: Brain Aneurysms and FMD: Data from the US Registry

James Froehlich, MD, University of Michigan

Dr. Froehlich will present data regarding the prevalence of intracranial aneurysm among patients enrolled in the United States Registry for FMD from a manuscript in press.

10:45 am: Cervical Artery Dissection: Recent Lessons Learned

Andrew Southerland, MD, University of Virginia

Cervical artery dissection (CeAD), affecting the extracranial carotid and vertebral arteries, remains a leading cause of stroke in young and middle-aged adults. While the underlying etiology of CeAD remains cryptic, recent research has furthered our understanding of the natural history and pathogenesis. Published analyses in the past year addressed important areas such as age-related differences in presentation, seasonal variation of occurrence, the timing of incident stroke risk following dissection, and the prognosis and management of dissecting aneurysms.

Multiple large cohorts, including the CADISP-Plus consortium and US FMD Registry, suggest a co-prevalence of CeAD and fibromuscular dysplasia (FMD) ranging from 5-25%. The link between CeAD and FMD has been further strengthened by the recent discovery of a mutation (rs9349379) in the PHACTR1 gene on chromosome 6 associated with both CeAD and FMD in independent cohorts. This gene mutation is particularly appealing given prior associations with migraine and coronary artery atherosclerosis, with the latter exhibiting an inverse direction of risk compared to CeAD and FMD. Moreover, a recent genetic analysis from the CADISP group found an unequal distribution of copy number variations in patients with CeAD compared to controls, particularly in areas affecting cardiovascular system development.

Ongoing efforts look to build on these discoveries, refine the hypothesis that CeAD is a condition of both genetic and environmental risk, and inform practice as to the optimal management and prevention of stroke in this vulnerable population.

11:00 am: Defining Clinical Presentation, Imaging Findings, and Management of Intracranial Fibromuscular Dysplasia: a Single Center Experience

Russell Cerejo, MD, Cleveland Clinic on behalf of *Russell Cerejo, Ellen K Brinza, Megan M Donohue, Natalia Fendrikova-Mahlay, Muhammad S Hussain, Gabor Toth, Ken Uchino, Mark Bain, Peter Rasmussen, Esther S Kim, Heather L Gornik*

Introduction: Intracranial (IC) artery involvement in fibromuscular dysplasia (FMD) may manifest as stenosis, dissection, or cerebral aneurysm. We sought to identify clinical, imaging, and treatment characteristics of FMD patients with IC manifestations.

Methods: Analysis of prospectively collected data from a single center of the US FMD patient registry with additional medical record and imaging review. Patients were consented for enrollment if FMD was confirmed by imaging in at least one vascular territory.

Results: From 2/2/2009 to 7/10/2015, 474 FMD patients were enrolled in the registry. Of the 420 patients with IC arterial imaging, 53 (12.6%) had IC FMD, with catheter angiography available in 29 (55.8%) patients. Median age of initial FMD symptoms was 48 years (IQR 39 – 55.5) and 52 patients were female. Concomitant extracranial (EC) carotid FMD was present in 90.6%, vertebral FMD in 45.3%, and renal FMD in 50.9%. Among 53 patients with IC FMD, 42 had IC aneurysm (10% of entire cohort with IC imaging), 7 had IC dissection, 8 had IC stenosis. Fifteen patients with IC FMD were symptomatic (9 TIA/ischemic stroke, 2 hemorrhagic strokes, 4 isolated cranial neuropathy). Among patients with IC FMD, 23 required intervention. Surgical or endovascular intervention was undertaken in 20 patients with aneurysm, 1 for dissection and 2 extracranial –intracranial bypass for stenosis. At the time of last follow-up, nearly all the patients were treated with an antiplatelet agent.

Conclusions: In a single center cohort, 12.6% patients with FMD had IC involvement. Arterial aneurysm was the most common manifestation followed by stenosis and dissection. Aneurysm was present in 10% of patients who underwent IC imaging, highlighting the importance of comprehensive vascular assessment of patients with FMD.

11:15 am: State of the Art Management of Cervical Artery Dissections and Brain Aneurysms in Patient with and without FMD

Gabor Toth, MD, Cleveland Clinic

Fibromuscular dysplasia (FMD) can be associated with cervical artery dissection, stroke and brain aneurysms, which creates a great deal of concern for both patients and caregivers. Management options may vary depending on severity, symptomatology, location, and disease

ABSTRACTS *(Continued)*

progression. Management is often similar to that of patients without FMD. Stenting may be considered for carotid or vertebral artery dissection, but is usually a last resort for patients with continued cerebrovascular ischemic symptoms despite adequate medical therapy. Careful attention should be made to avoid creating iatrogenic dissection during groin access, guide catheter placement or worsening of the dissection when crossing the lesion with microwires and catheters. Balloon angioplasty is available for lesions with severe associated stenosis when stenting is not feasible or favored at the same time. If good flow through the stent is not attained due to residual stenosis, additional angioplasty may be required. Post-dissection pseudoaneurysms have shown no definite increased risk of long-term ischemic events, and therefore rarely require endovascular treatment. The management of intracranial aneurysms is similar in FMD and non-FMD patients, although a higher potential rupture risk in FMD patients is assumed. Observation may be reasonable in some unruptured cases. Many aneurysms are amenable to endovascular embolization with coils, stents or newer flow diverters. Surgical clipping is also often feasible, and the decision for best treatment modality will depend on location, size, patient age, and anatomical factors.

11:30 am: Modern Approaches to Intractable Headache, Including Botox Therapy for Chronic Migraine
Mark Stillman, MD, Cleveland Clinic

Patients with FMD are often visited by headaches. There are a variety of reasons for this. One reason is that cerebrovascular involvement by the disease is common and symptoms will obviously occur in the vascular bed of the diseased artery. Another more obvious reason is that both FMD and migraine headaches are predominantly diseases of young adult women. This point is complicated by the fact that a greater representation of FMD exits among migraineurs just as there is a greater representation of migraines among FMD sufferers. For the clinician this creates diagnostic dilemmas, and a working knowledge of headache types and their clinical mimics is warranted. This lecture will review the clinical spectrum of migraines with and without auras, trigeminal autonomic cephalalgias, such as cluster headaches and the paroxysmal hemicranias, and most importantly, thunderclap headache disorders, all of which can be seen in a patient with symptomatic fibromuscular dysplasia. Current treatment options for intractable headache will also be discussed, including Botox therapy for chronic migraine.

12:00 pm: Pulsatile Tinnitus—The Patient Perspective and Activities of Whooshers.com
Ms. Emma Greenwood

This presentation, a patient's perspective of pulsatile tinnitus, will discuss what pulsatile tinnitus is, how it differs from "tinnitus," and efforts to raise awareness and support for those impacted by pulsatile tinnitus, including patients and doctors. I'll play several audio sounds of actual pulsatile tinnitus recordings that patients have sent in to Whooshers.com. I'll mention the four new (as of Oct 1, 2016) ICD codes for pulsatile tinnitus, for which Whooshers.com led an international campaign and petition to establish. These have already helped patients secure approval from insurance companies for extensive diagnostic testing that pulsatile tinnitus often requires:
H93.A1 Pulsatile tinnitus, right ear
H93.A2 Pulsatile tinnitus, left ear
H93.A3 Pulsatile tinnitus, bilateral
H93.A9 Pulsatile tinnitus, unspecified ear

Common myths about pulsatile tinnitus will be briefly discussed. The difference between helping a patient "cope" and helping a patient isolate and treat the underlying cause of their pulsatile tinnitus will be mentioned, and the parallel importance of each effort will be stressed. Pulsatile tinnitus is sometimes a psychologically difficult (in some cases devastating) symptom for a patient to experience. Not all patients convey this well, which may be preventing doctors from helping them adequately. The spectrum of severity of PT will be mentioned, and I'll propose some questions doctors may ask the patient to help him/her convey the experience (trouble sleeping? changes in social activities, etc.). Finally I'll display patient testimonials (anonymously) from members of the Whooshers.com community to whom I asked, "If you could tell a room full of doctors anything, what would you say?

1:45 pm: Management of FMD in Europe and the US: Similarities and Differences
Alexandre Persu MD, PhD, Cliniques Universitaires Saint Luc

In 2014, both the European Society of Hypertension[1] and the American Heart Association[2] issued consensus documents regarding the diagnosis and management of Fibromuscular Dysplasia (FMD). Both documents share important similarities, including for instance the arteriographic classification of FMD lesions proposed by Savard et al. (Circulation. 2012; 126:3062-9), and subsequently endorsed by European and US expert panels (with minor modifications). However, the European and US perspectives also differ in several respects, including the main presenting symptoms of FMD (headache/pulsatile tinnitus/dizziness), the first-choice imaging modality for the diagnostic and follow-up of cervical FMD, the indications of acetylsalicylic acid therapy in FMD patients, the concepts of aortic and coronary FMD, and the follow-up of treated or untreated FMD patients. The objectives of the presentation are to compare both documents, to review the evidence/expert opinions supporting different approaches and, whenever possible, to pave the way towards a consensus. The discussion will incorporate relevant new findings generated since publication of the recommendations. The presentation will be interactive and leave room for participation of the audience.

[1]Persu A, Giavarini A, Touzé E, Januszewicz A, Sapoval M, Azizi M, Barral X, Jeunemaitre X, Morganti A, Plouin PF, de Leeuw P; ESH Working Group Hypertension and the Kidney. European consensus on the diagnosis and management of fibromuscular dysplasia. J Hypertens. 2014; 32: 1367-78.

[2]Olin JW, Gornik HL, Bacharach JM, Biller J, Fine LJ, Gray BH, Gray WA, Gupta R, Hamburg NM, Katzen BT, Lookstein RA, Lumsden AB, Newburger JW, Rundek T, Sperati CJ, Stanley JC; American Heart Association Council on Peripheral Vascular Disease.Fibromuscular dysplasia: state of the science and critical unanswered questions: a scientific statement from the American Heart Association. Circulation. 2014; 129:1048-78.

2:00 pm: Approach to Renal Angiography and Intervention in FMD
Bruce Gray, DO, Greenville Health System

Patients with suspected renovascular hypertension often undergo a workup that includes renal artery duplex ultrasound and either computed tomography (CTA) or magnetic resonance angiography (MRA). These "screening" tests have limitations in the determination of the presence and significance of renal artery FMD. Consequently, catheter-based arteriography is necessary for confirmative or "diagnostic" evaluation of renal artery disease in symptomatic patients.

Traditionally, a non-selective (i.e.-pigtail) catheter is placed in the aorta above L1 for the initial contrast injection. This evaluates the number of renal arteries, takeoff angles of these arteries, and relative contribution of each to the kidney parenchyma. Selective renal artery images can then be obtained with catheters that engage the renal ostium. These images provide the greatest detail of the renal artery architecture, branch artery involvement, kidney perfusion and presence of aneurysms.

When renal artery disease is seen, the hemodynamic significance needs to be assessed. The best method is to advance a small (0.014") transducer wire through the renal artery to simultaneously measure the pressure from the aorta to the renal parenchyma. A ratio of these pressures of <0.9 is felt to be significant.

When significant renal FMD needs treatment, balloon angioplasty is preferred. The initial balloon should be sized to the distal normal renal artery based on calibrated angiography, intravascular ultrasound or OCT. The balloon size should be incrementally increased by 0.5-1.0 mm until the translesional gradient is resolved. Stents are reserved for recalcitrant or recurrent lesions.

2:45 pm: Surgical Approach to Renal Artery Dysplasia: Pediatric Renal Artery Disease, Mid-Aortic Syndrome and Renal Artery Aneurysms
Dawn Coleman, MD, University of Michigan

Renovascular hypertension is the third most common cause of pediatric hypertension (HTN), and if left untreated risks devastating cardiopulmonary complication, stroke, renal failure and mortality. The University of Michigan surgical experience includes >150 children with developmental abdominal aortic and renal artery stenosis suggests managed surgically. The contemporary surgical treatment of pediatric renovascular HTN requires an individualized approach providing sustainable benefit to nearly 90% of patients with negligible morbidity and no mortality. Extremes of youth increase the likelihood of reoperation. Patients undergoing remedial surgery and those with abdominal aortic coarctation are less likely to be cured of HTN.

Renal artery aneurysms are extremely rare with historically morbid outcomes associated with rupture. Previous guidelines, supporting repair at 2cm, have recently been questioned in light of evolving data that supports a slow to null growth rate of these aneurysms. The etiology of these aneurysms remains unclear in most cases, and certainly no single genetic risk factor has been identified to date. Importantly, fibromuscular dysplasia has long

ABSTRACTS *(Continued)*

been associated with renal artery aneurysm in up to 68% of cases, and there is a well-defined female predilection for renal aneurysm formation. Those with renal artery aneurysms often have concurrent aneurysms or other arterial dysplasia. We hypothesize that renal artery aneurysm in young women may be a variant phenotype of FMD and a better understanding of the natural history of renal aneurysm that considers age, gender and additional risk factors is prudent to tailor individualized, patient-centered care including (1) indications for aneurysm treatment, (2) additional screening, and (3) frequency of surveillance.

3:00 pm: Group Review of International FMD Research Network Guidance for Renal Angiography and Angioplasty (2014/2017)
Jeffrey Olin, DO, Mount Sinai Medical Center
Heather Gornik, MD, MHS, Cleveland Clinic

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4:00 pm: Incorporating Research into an FMD Clinical Program (…with little or no funding)
Aditya Sharma, MBBS, University of Virginia

The University of Virginia Clinical FMD Multidisciplinary program consists of multiple different specialties including, but not limited to vascular medicine, interventional radiology, vascular neurology, neuro-interventional radiology, vascular surgery, genetics, interventional cardiology and neurosurgery. Although the clinical program consists over 200 patients and keeps growing, it has always been challenging to pursue clinical studies due to lack of funding and time. The FMD registry is an excellent clinical and imaging database which has tremendously progressed clinical knowledge of this condition; however it is an extensive and time-consuming process. Additionally retrospective data collection may not always provide all the data points required for the registry. Using electronic medical record systems, we created smart phrases in order to auto-populate clinical notes which would incorporate thorough clinical data sufficient also to provide all the data points necessary for FMD registry. The next step of incorporating this data into the registry electronically can be time consuming. We discuss the utilization of potential resources that can be time and financially favorable such as involvement of scribes, research associates, medical trainees research programs which also benefit them in better understanding such rare conditions, utilization of registries in advancing medical science and publish.

4:15 pm: Challenges of Registry Research/The MCORRP Perspective
Eva Kline-Rogers, MS, NP, University of Michigan

Rare diseases are a clinically heterogeneous group of disorders that are difficult to study due to their relative infrequency. These diseases are often inherited, can be diagnosed in childhood, with little known about prevalence and long term effects. No single institution has sufficient numbers of patients to study, making is nearly impossible to do generalizable or translational research. Clinical registries have emerged as a way to advance knowledge to improve the health and wellbeing of patients with rare diseases, or other disorders difficult to study, on a large scale.

The U.S. Registry for Fibromuscular Dysplasia (FMD) was started in 2009 with the goal of increasing our understanding of the natural history of FMD, evaluate our current diagnostic and treatment strategies and to observe long-term outcomes in a real world setting, all for the purpose of improving the care of patients with FMD. In a recent editorial, the authors acknowledged the registry, noting that "The U.S. FMD registry is an excellent example of collaboration between patients and physicians", providing opportunity to acquire new information to enhance our understanding of this disease[1].

Dr. Kim Eagle founded the Michigan Cardiovascular Outcomes Research and Reporting Program (MCORRP) twenty years ago. The first registry was the International Registry of Aortic Dissection (IRAD), another "understudied" disease. Today, IRAD staff continue to add contributing sites (n > 50), have published over 80 manuscripts in peer-reviewed journals, and have expanded the interventional section of data collection to allow the collection of more granular data regarding surgery and endovascular interventions.

In addition to aortic dissection and fibromuscular dysplasia, MCORRP is coordinating an international registry of cardiac sarcoidosis, with goals similar to the aforementioned registries.

Data obtained from these real world, voluntary registries is not without challenges. Strong leadership is key to the success of the registries. The leader(s) are known experts in their respective areas with clinical trial experience and unwavering passion for continued success of the registry. The leaders are responsible for forming a Steering Committee with these members providing scientific and logistical oversight of the registry. The Steering Committee is responsible for site recruitment, design of the data collection form and database, interpretation of results, and publications.

One of the more challenging aspects of conducting voluntary registries is insuring data validity. There is often a high turn-over rate with individuals doing the data collection, often due to lack of funding. The staff at the MCORRP Coordinating Center continue to deal with these challenges in a number of ways, including, but not limited to, the following: 1) create a detailed data dictionary, 2) program validation checks into the on-line database to promote data correction in real-time, 3) conduct follow-up queries with individual site staff for data clarification, 4) provide feedback to coordinators, 5) create a Frequently Asked Questions document available to all coordinators, and 6) create an Abstractor Certification Exam that each new coordinator must complete prior to gaining access to the database.

This presentation will present the overall structure of MCORRP, review some of the current registries, and discuss lessons learned from conducting a variety of state, national, and international registries.

References

[1]Beckman, JA and Creager MA, People Have the Power, JACC 2016, 68(2): 186-8.

Elefteriades JA, Ziganshin BA, Gratitude to the International Registry of Acute Aortic Dissection From the Aortic Community, JACC 2015, 66(4), 359-62.

Forrest CB, Bartek RJ, Rubinstein Y, Groft, SC. The case for a global rare-diseases registry. Lancet 2011, 377; 1057-1059.

4:30 pm: Aligning Local Research Efforts to the Broader FMD Research Initiative: ARKADIA-POL Case Study
Andrzej Januszewicz, MD, Institute of Cardiology, Warsaw

The ARCADIA-POL study was instituted in January, 2015 on the basis of Polish-French collaboration in the Institute of Cardiology, Warsaw, Poland to better understand the epidemiology, clinical characteristics, management and outcomes of patients with FMD. This report includes the first 210 patients who entered the multicenter registry involving 32 centers in Poland with coordination of Department of Hypertension. Each of these centers followed referral pattern and identified patients with newly diagnosed or established renal FMD, FMD in any vascular bed or with spontaneous artery dissection [particularly in carotid, vertebral or coronary arteries]. All patients underwent detailed clinical evaluation including ABPM, biochemical evaluation, biobanking, duplex Doppler of carotid and abdominal arteries and whole body angio-CT [renal FMD defined as multifocal or unifocal].

The data of ARCADIA-POL registry showed that renal FMD was the most frequent, but also cerebrovascular FMD was found in relatively large proportion of patients. Our data revealed high incidence of FMD lesions coexisting in different vascular beds as well as relatively frequent occurrence of vascular complications. Systematic evaluation of cervical and intracranial arteries in patients with renal FMD resulted in revealing relatively high prevalence of FMD lesions and vascular complications in cervical and/or intracranial arteries. Patients with FMD did not differ from patients with essential hypertension in respect to BP profile and intensity of subclinical target organ damage.

4:45 pm: What Can Qualitative Research Methods Contribute to the Study of FMD?
Sherry Bumpus, PhD, RN, Eastern Michigan University

Individuals with fibromuscular dysplasia (FMD) report a varied constellation of psychological, physical, emotional, social, and healthcare experiences before and after being diagnosed. Recent advances in both vascular medicine and data registries are facilitating a better understanding of the epidemiology of FMD and its pathophysiology. However, there are questions that have yet to be asked or studied that cannot be found in pathology or large data. Questions related to the effects of FMD on day-to-day activities, and on mental and emotional health require a different approach. When research is discovery oriented (i.e., to identify, describe, examine) qualitative methodology is an ideal choice to gain knowledge and to generate hypotheses on phenomena about which little is known.

A recent qualitative inquiry of the experiences of 19 individuals diagnosed with FMD revealed five discrete themes that participants shared; symptom burden, worries and concerns, experience of health care, loss and change, and resilience. These themes represent new knowledge about the psychosocial dimensions of FMD. As well, the richness of the individual stories and the similarities between experiences underscore the complexity of living with FMD and highlight opportunities for enhancing patient care.

PROTOCOL

From the International FMD Research Network: Expert Consensus Recommended Protocol for Renal Angiography and Angioplasty in Patients with FMD

1. Flush aortogram (or cross sectional imaging, previously) to look for all renal arteries and clearly profile the ostia of all renal arteries prior to selective catheterizations

2. Selective renal arteriography of all the renal arteries with a field of view that allows visualization of the entire renal vasculature to define branch vessel involvement, aneurysms, renal size and parenchymal perfusion. Multiple projections may be needed to better define areas of arterial overlap or tortuosity.

3. A simultaneous translesional pressure gradient (between the distal renal artery and the aorta) should be measured, ideally with a pressure wire.

4. If a pressure wire is not available or use of one is not feasible, an endhole microcatheter may be acceptable. A pressure gradient threshold of 10% of the mean (aortic) pressure should be used to decide whether to perform balloon angioplasty (i.e., Pd/Pa <0.90)1*

5. The initial balloon diameter used should be based upon the diameter of the distal normal renal artery using a calibrated catheter and quantitative vascular angiography software, intravascular ultrasound or optical coherence tomography.

6. The balloon diameter size should be incrementally increased by 0.5-1.0 mm until the translesional gradient is resolved or until there is a less than 10% mean translesional gradient. Angioplasty should be aborted if the patient experiences moderate to severe pain during balloon inflation.
7. Renal artery stenting is generally not indicated in the setting of FMD and is limited for off-label use to treat complications related to angioplasty, in some cases of primary renal artery dissections, or for the treatment of a renal artery aneurysm related to FMD.

*These parameters are extrapolated from study of patients with atherosclerotic renal artery stenosis and have not been validated in patients with FMD. Reference: 1De Bruyne B, et al. J Am Coll Cardiol 2006; 48:1851

2017 committee: Jeffrey W Olin, Heather L. Gornik, Bruce H Gray, Robert Lookstein, Alan Matsumoto, Sanjay Misra

2014 International FMD Research Network Symposium Participants (add list)

2017 International FMD Research Network/SCAD Symposium Participants (add list)

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