Coronary Artery Manifestations of Fibromuscular Dysplasia: Infrequent and Easily Missed

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The United States Registry for Fibromuscular Dysplasia
Results in the First 447 Patients

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Background—Fibromuscular dysplasia (FMD), a noninflammatory disease of medium-size arteries, may lead to stenosis, occlusion, dissection, and/or aneurysm. There has been little progress in understanding the epidemiology, pathogenesis, and outcomes since its first description in 1938.

Methods and Results—Clinical features, presenting symptoms, and vascular events are reviewed for the first 447 patients enrolled in a national FMD registry from 9 US sites. Vascular beds were imaged selectively based on clinical presentation and local practice. The majority of patients were female (91%) with a mean age at diagnosis of 51.9 (SD 13.4 years; range, 5–83 years). Hypertension, headache, and pulsatile tinnitus were the most common presenting symptoms of the disease. Self-reported family history of stroke (53.5%), aneurysm (23.5%), and sudden death (19.8%) were common, but FMD in first- or second-degree relatives was reported only in 7.3%. FMD was identified in the renal artery in 294 patients, extracranial carotid arteries in 251 patients, and vertebral arteries in 82 patients. A past or presenting history of vascular events were common: 19.2% of patients had a transient ischemic attack or stroke, 19.7% had experienced arterial dissection(s), and 17% of patients had an aneurysm(s). The most frequent indications for therapy were hypertension, aneurysm, and dissection.

Conclusions—in this registry, FMD occurred primarily in middle-aged women, although it presents across the lifespan. Cerebrovascular FMD occurred as frequently as renal FMD. Although a significant proportion of FMD patients may present with a serious vascular event, many present with nonspecific symptoms and a subsequent delay in diagnosis. (Circulation. 2012;125:3182-3190.)
Dissection and Aneurysm in FMD

- 1008 patients in last analysis of data
  - 966 patients had complete aneurysm information
  - 921 patients with complete dissection information

- In order to make the diagnosis of FMD in an artery with an aneurysm or dissection, there must be evidence of FMD elsewhere.
  - In other words, the healing of a dissection can give the artery the appearance of multifocal FMD.
Prevalence and Vascular Distribution of Arterial Dissections in 921 FMD patients

<table>
<thead>
<tr>
<th>Any dissection</th>
<th>237 (25.7%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid artery</td>
<td>159 (67.1%)</td>
</tr>
<tr>
<td>Vertebral artery</td>
<td>48 (20.3%)</td>
</tr>
<tr>
<td>Renal artery</td>
<td>26 (11.0%)</td>
</tr>
<tr>
<td><strong>Coronary artery</strong></td>
<td><strong>25 (10.5%)</strong></td>
</tr>
<tr>
<td>Mesenteric artery</td>
<td>14 (5.9%)</td>
</tr>
<tr>
<td>Aorta</td>
<td>8 (3.4%)</td>
</tr>
<tr>
<td>Iliac artery</td>
<td>5 (2.1%)</td>
</tr>
</tbody>
</table>
Coronary Artery Manifestations of Fibromuscular Dysplasia

Katherine C. Michelis, MD, Jeffrey W. Olin, DO, Daniella Kadian-Dodov, MD, Valentina d’Escamard, PhD, Jason C. Kovacic, MD, PhD

ABSTRACT

Fibromuscular dysplasia (FMD) involving the coronary arteries is an uncommon but important condition that can present as acute coronary syndrome, left ventricular dysfunction, or potentially sudden cardiac death. Although the classic angiographic “string of beads” that may be observed in renal artery FMD does not occur in coronary arteries, potential manifestations include spontaneous coronary artery dissection, distal tapering or long, smooth narrowing that may represent dissection, intramural hematoma, spasm, or tortuosity. Importantly, FMD must be identified in at least one other noncoronary arterial territory to attribute any coronary findings to FMD. Although there is limited evidence to guide treatment, many lesions heal spontaneously; thus, a conservative approach is generally preferred. The etiology is poorly understood, but there are ongoing efforts to better characterize FMD and define its genetic and molecular basis. This report reviews the clinical course of FMD involving the coronary arteries and provides guidance for diagnosis and treatment strategies. (J Am Coll Cardiol 2014;64:1033-46) © 2014 by the American College of Cardiology Foundation.)
CENTRAL ILLUSTRATION  Angiographic Features of Fibromuscular Dysplasia Involving the Coronary Arteries

(A) Dissection, (B) smooth narrowing, (C) intramural hematoma, and (D) tortuosity. Spasm may also occur but is angiographically similar in appearance to smooth narrowing and is differentiated by intracoronary vasodilator administration.

J Am Coll Cardiol 2014;64:1033-46
Presentation of Patients with Coronary Fibromuscular Dysplasia

• Most patients have a dissection (SCAD) which may produce symptoms of:
  – Chest Pain
  – Shortness of Breath
  – Sweating
  – Neck, Jaw or Arm Pain

• Which may result in:
  – Unstable angina
  – Myocardial Infarction
  – Heart Failure
  – Sudden Death

• The “String of Beads” does not generally occur in coronary artery FMD
34 Year Old Female with STEMI One Week After C-Section
Mid LAD Dissection

Coronary Artery Dissection
Intramural Hematoma

Saw J et al. Cath Cardiovasc Intervent 2015; on line before print
Features to Suggest the Presence of SCAD

- MI in women less than age 60
- Absence of cardiovascular risk factors
- No evidence of typical atherosclerosis in coronary arteries
- Peripartum state
- Connective tissue disorders: Marfan, EDS IV, Loeys-Dietz
- Fibromuscular dysplasia in other arteries
- Precipitating stress event
  - Intensive exercise
  - Severe emotional stress
  - Childbirth
  - Sex
  - Intense valsala- severe vomiting/retching, coughing etc.
  - Drugs: cocaine, amphetamines
Age at SCAD Presentation (n=168)

Prevalence of Fibromuscular Dysplasia Patients with Spontaneous Coronary Artery Dissection

<table>
<thead>
<tr>
<th>Prevalence of FMD</th>
<th>N=168</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMD diagnosed</td>
<td>121 (72%)</td>
</tr>
<tr>
<td>FMD not diagnosed</td>
<td>47 (28%)</td>
</tr>
<tr>
<td>Incomplete Screening</td>
<td>23 (13.7%)</td>
</tr>
<tr>
<td>Screened cerebral, renal, iliac</td>
<td>24 (14.3%)</td>
</tr>
<tr>
<td>What could have been missed?</td>
<td>TAA</td>
</tr>
<tr>
<td></td>
<td>The gold standard diagnosis is catheter based angiography</td>
</tr>
</tbody>
</table>

Coronary Artery Tortuosity in Spontaneous Coronary Artery Dissection  
Angiographic Characteristics and Clinical Implications  

Mackram F. Eleid, MD; Raviteja R. Guddeti, MBBS; Marysia S. Tweet, MD; Amir Lerman, MD; Mandeep Singh, MD, MPH; Patricia J. Best, MD; Terri J. Vratis, MD; Megha Prasad, MD; Charanjit S. Rihal, MD, MBA; Sharonne N. Hayes, MD; Rajiv Gulati, MD, PhD

Background—Spontaneous coronary artery dissection (SCAD) is an increasingly recognized nonatherosclerotic cause of acute coronary syndrome. The angiographic characteristics of SCAD are largely undetermined. The goal of this study was to determine the prevalence of coronary tortuosity in SCAD and whether it may be implicated in the disease.

Methods and Results—Patients with confirmed SCAD (n=246; 45.3±8.9 years; 96% women) and 313 control patients without SCAD or coronary artery disease who underwent coronary angiography were included in this case–control study. Angiograms were reviewed for coronary tortuosity and assigned a tortuosity score. Tortuosity was common in patients presenting with their first SCAD event (78% versus 17% in controls; $P<0.0001$; tortuosity score, 4.41±1.73 versus 2.33±1.49 in controls; $P<0.0001$) despite a low prevalence of hypertension (34%). Recurrent SCAD (n=40) occurred within segments of tortuosity in 80% of cases. Severe tortuosity (≥2 consecutive curvatures ≥180°) was associated with a higher risk of recurrent SCAD (hazard ratio, 3.29; 95% confidence interval, 0.99–8.29; $P=0.05$). Tortuosity score >5 was associated with a trend toward higher risk of recurrent SCAD ($P=0.16$). Prespecified angiographic markers of tortuosity including corkscrew appearance and multivessel symmetrical tortuosity were associated with extracoronary vasculopathy including fibromuscular dysplasia ($P<0.05$ for both).

Conclusions—Coronary artery tortuosity is highly prevalent in the SCAD population and is associated with recurrent SCAD. Recurrent SCAD most often occurs within segments of tortuosity. Angiographic features of SCAD are associated with extracoronary vasculopathy, including fibromuscular dysplasia. These findings suggest that coronary tortuosity may serve as a marker or potential mechanism for SCAD. (Circ Cardiovasc Interv. 2014;7:656-662.)
Extracoronary Vascular Abnormalities in Patients with SCAD

- 112 patients underwent screening of other vascular beds with CTA, MRA or catheter based angiography
  - 79 (70%) had extracoronary vasculopathy (EV)
    - 63 (80%) had FMD
    - 6 (8%) had extracoronary dissection
    - 5 (4%) had aneurysmal disease
    - 4 (5%) had marked carotid tortuosity
  - FMD was associated with higher tortuosity score (4.76 vs 3.82, p = 0.008)

Angiographic characteristics in spontaneous coronary artery dissection.


Prevalence of coronary artery tortuosity.

Angiographic Features of Patients with Recurrent SCAD (n=40)

Survival Free of Recurrent SCAD

**P=0.16**

<table>
<thead>
<tr>
<th>Years</th>
<th>No. at risk</th>
<th>Tortuosity score &gt;5</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>81</td>
<td>165</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>51</td>
<td>105</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>37</td>
<td>66</td>
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<td>52</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>20</td>
<td>35</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>16</td>
<td>29</td>
</tr>
</tbody>
</table>

- Recurrent dissection within tortuous segment: 32 (80%)
- Recurrent dissection near vessel hinge point: 24 (60%)
- Recurrent dissection near bifurcation: 32 (80%)

SCAD indicates spontaneous coronary artery dissection.
SCAD

- High prevalence of coronary artery tortuosity
- Coronary artery tortuosity is associated with a higher risk of recurrent SCAD
- SCAD is associated with FMD and other vascular manifestations such as aneurysm, dissection and tortuosity
Arterial Tortuosity

The S curve: A novel morphological finding in the internal carotid artery in patients with fibromuscular dysplasia

Sanjum S Sethi, Joe F Lau, James Godbold, Susan Gustavson and Jeffrey W Olin

Abstract
Fibromuscular dysplasia (FMD) is a non-atherosclerotic vascular disease commonly affecting the renal and internal carotid arteries (ICAs). A previously unrecognized finding is a redundancy of the mid-distal ICA in FMD patients causing an ‘S’-shaped curve. Carotid artery duplex ultrasounds were reviewed in 116 FMD patients to determine S-curve prevalence. FMD patients with an S curve were matched to four control patients divided equally into two groups: (1) age and sex-matched and (2) age ≥70 and sex-matched. S curves were present in 37 (32%) FMD patients. Of these, nine (24%) had angiographic evidence of FMD in their ICA only, 13 (35%) had renal artery FMD only, and 15 (41%) had both ICA and renal FMD. Two patients in the age and sex-matched group had S curves (odds ratio 16.86, 95% CI 3.92–72.48; p<0.0001) while 12 (16.2%) patients in the age ≥70 and sex-matched group had S curves (odds ratio 2.42, 95% CI 1.16–5.03; p=0.016). In conclusion, the S curve is a novel morphological pattern of the mid-distal ICA. While the S curve may not be specific, its presence in individuals <70 years old should alert the clinician to the possibility that FMD is present.
Spontaneous Coronary Artery Dissection
Revascularization Versus Conservative Therapy

Marysia S. Tweet, MD; Mackram F. Eleid, MD; Patricia J.M. Best, MD; Ryan J. Lennon, MS; Amir Lerman, MD; Charanjit S. Rihal, MD, MBA; David R. Holmes Jr, MD; Sharonne N. Hayes, MD; Rajiv Gulati, MD, PhD

Background—Spontaneous coronary artery dissection (SCAD) is a nonatherosclerotic acute coronary syndrome for which optimal management remains undefined.

Methods and Results—We performed a retrospective study of 189 patients presenting with a first SCAD episode. We evaluated outcomes according to initial management: (1) revascularization versus conservative therapy and (2) percutaneous coronary intervention (PCI) versus conservative therapy stratified by vessel flow at presentation. Demographics were similar in revascularization versus conservative (mean age, 44±9 years; women 92% both groups), but vessel occlusion was more frequent in revascularization (44/95 versus 18/94). There was 1 in-hospital death (revascularization) and 1 late death (conservative). Procedural failure rate was 53% in those managed with PCI. In the subgroup of patients presenting with preserved vessel flow, rates of PCI failure were similarly high (50%), and 6 (13%) required emergency coronary artery bypass grafting. In the conservative group, 85 of 94 (90%) had an uneventful in-hospital course, but 9 (10%) experienced early SCAD progression requiring revascularization. Kaplan–Meier estimated 5-year rates of target vessel revascularization and recurrent SCAD were no different in revascularization versus conservative therapy (30% versus 19%; P=0.06 and 23% versus 31%; P=0.7).

Conclusions—PCI for SCAD is associated with high rates of technical failure even in those presenting with preserved vessel flow and does not protect against target vessel revascularization or recurrent SCAD. A strategy of conservative management with prolonged observation may be preferable. (Circ Cardiovasc Interv. 2014;7:777-786.)
Example of revascularization defined as unsuccessful by conventional definition (severe residual stenosis) but successful by spontaneous coronary artery dissection (SCAD)—specific definition (improved vessel flow).

Comparison of long-term outcomes after spontaneous coronary artery dissection (SCAD) according to initial treatment strategy and presenting vessel flow.

Recurrent MI
Revascularization vs Conservative Management

Free of recurrent MI (%)

P=0.17

No. at risk 189  118  89  70  54  43

Years

## TIMI Flow

<table>
<thead>
<tr>
<th>TIMI Flow</th>
<th>Saw et al. (n=168)</th>
<th>Tweet et al. (n=189)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>29%*</td>
<td>32%</td>
</tr>
<tr>
<td>2-3</td>
<td>71%*</td>
<td>68%</td>
</tr>
</tbody>
</table>

*204 dissected segments

Chart showing the outcomes of conservatively managed patients.

Chart showing the outcomes of patients who underwent percutaneous coronary intervention (PCI).

Conclusions

• The primary manifestation of coronary artery FMD is Spontaneous Coronary Artery Dissection (SCAD)
  – Arterial Tortuosity may also be seen.
  – String of beads, or focal disease does not occur!
• Thus, stress tests, cardiac catheterization cannot determine if the arteries have FMD unless the patient presents with SCAD.
• Therefore, it is not recommended to routine screen for coronary artery FMD.
Thank You