The European Consensus on Fibromuscular Dysplasia

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Diagnosis and management of fibromuscular dysplasia: an expert consensus

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European consensus on the diagnosis and management of fibromuscular dysplasia


On behalf of the ESH working group ‘Hypertension and the Kidney’

Definition of Fibromuscular Dysplasia

An idiopathic, segmental, nonatherosclerotic and non-inflammatory disease of the musculature of arterial walls, leading to stenosis of small and medium-sized arteries.

The diagnosis of FMD requires exclusion of renal artery spasm, arterial diseases of monogenic origin, and inflammatory arterial diseases.

The diagnosis of **multifocal FMD** can be established when a “string-of-beads” appearance is observed in a medium-sized artery, in the absence of aortic involvement or exposure to vasoconstrictor agents.

The diagnosis of **unifocal FMD** can be established in young patients (usually less than 40 years), in the absence of atherosclerotic plaque, multiple vascular risk factors, inflammatory syndrome or vascular thickening, and familial or syndromic disease.
Angiographic classification of renal artery FMD

String of beads  Focal (< 1cm)  Tubular (≥ 1 cm)
Multifocal  Unifocal

Lower female prevalence, more severe and early presentation, higher hypertension cure rate after revascularisation

Plouin PF. et al. *Orphanet J Rare Dis.* 2007; 2: 1-8
Angiographic classification of FMD of the supra-aortic trunks

String of beads Multifocal  Focal Unifocal  Tubular Atypical

Touzé. E. et al. *Int J Stroke* 2010; 5:296-305
Screening for renal FMD (patients with HTN)

- Age < 30 yo, especially in women
- Grade 3, accelerated or malignant HTN
- Resistant HTN
- Small kidney without history of uropathy
- Abdominal bruit without atherosclerosis
- FMD in at least another vascular territory

FMD: not so rare!

**Prevalence of FMD in potential kidney donors**

<table>
<thead>
<tr>
<th>First author</th>
<th>Source</th>
<th>Potential donors</th>
<th>FMD cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cragg, 1989</td>
<td>Universities of Iowa, Minnesota, California San Francisco and Los Angeles, Mayo Clinic 1964-86</td>
<td>1862</td>
<td>71</td>
</tr>
<tr>
<td>Neymark, 2000</td>
<td>University of California San Francisco, 1988-1998</td>
<td>716</td>
<td>47</td>
</tr>
<tr>
<td>Andreoni, 2002</td>
<td>University of North Carolina, 1995-2001</td>
<td>159</td>
<td>7</td>
</tr>
<tr>
<td>Kolettis, 2004</td>
<td>University of Alabama, 1995-2001</td>
<td>1176</td>
<td>66</td>
</tr>
</tbody>
</table>

Total 3913 191 (4.9%)
FMD: not only a disease of young women

Table 1. Demographics and Comorbidities of Patients With FMD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
</tr>
<tr>
<td>Age, mean±SD</td>
<td>55.7±13.1 y (range, 18–86)</td>
</tr>
<tr>
<td>Age at first FMD-related symptom, mean±SD</td>
<td>47.2±14.6</td>
</tr>
<tr>
<td>Age at diagnosis of FMD, mean±SD</td>
<td>51.9±13.4 y (range, 5–83)</td>
</tr>
<tr>
<td>Female</td>
<td>406/447 (91)</td>
</tr>
</tbody>
</table>

FMD in a 65 yo man with Coronary Heart Disease
Clinical suspicion of FMD

Renal duplex ultrasound

- Negative
  - Low clinical probability: Stop investigations
  - High clinical probability: CT-angiography

- Positive
  - confirm
  - CT-angiography
  - MR-angiography

High suspicion of FMD and/or expected low performance of renal duplex ultrasound

- confirm
  - Positive: Digital substraction angiography

High clinical probability:

- confirm
  - PTA is considered

Low clinical probability:

- Stop investigations

Screening for cervico-cephalic FMD

- Retinal or cerebral ischemic events
- Intracranial aneurysms
- Subarachnoid hemorrhage
- Cervical or intracranial dissection
- Pulsatile tinnitus

Distribution of FMD lesions

In case of hypertension

In case of suggestive symptoms or if likely to alter management

Screen for cerebral aneurysms if likely to modify management

If suggestive symptoms
Screening for carotid FMD: echography is not enough

CT- and MR-angiography are likely to perform better than Doppler in detecting lesions involving the medium and distal thirds of carotid and vertebral arteries.
Spontaneous coronary artery dissection (SCAD) and FMD of extra-coronary vascular beds

Table 4. Involvement With Noncoronary FMD Among These Patients With SCAD (N = 50)

<table>
<thead>
<tr>
<th>Involvement</th>
<th>Percentage (Count)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMD in ≥1 noncoronary territories</td>
<td>86.0% (43)</td>
</tr>
<tr>
<td>FMD in ≥2 noncoronary territories</td>
<td>42.0% (21)</td>
</tr>
<tr>
<td>FMD not observed</td>
<td>14.0% (7)</td>
</tr>
<tr>
<td>Incomplete screening</td>
<td>10.0% (5)</td>
</tr>
<tr>
<td>Screened cerebral, renal, iliac</td>
<td>4.0% (2)</td>
</tr>
<tr>
<td>FMD vascular involvement (n = 43)</td>
<td></td>
</tr>
<tr>
<td>Renal arteries</td>
<td>58.1% (25)</td>
</tr>
<tr>
<td>Iliac arteries</td>
<td>48.8% (21)</td>
</tr>
<tr>
<td>Cerebrovasculature</td>
<td>46.5% (19)</td>
</tr>
<tr>
<td>Cerebral aneurysm</td>
<td>16.3% (7)</td>
</tr>
</tbody>
</table>

Spontaneous coronary artery dissection

Look for renal, iliac and cervical FMD
Different FMD angiographic subtypes in two sisters

Multifocal: string of beads
Unifocal: tubular

Courtesy of X. Jeunemaitre
# FMD, a familial disease?

## Table 2: Characteristics of patients with apparently sporadic or familial fibromuscular dysplasia (FMD)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Sporadic FMD (n = 89)</th>
<th>Familial FMD (n = 11)</th>
<th>Significance (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>9 (10.1)</td>
<td>0 (0)</td>
<td>0.27</td>
</tr>
<tr>
<td>Parental history of hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal</td>
<td>42 (47.2)</td>
<td>6 (54.5)</td>
<td>0.48</td>
</tr>
<tr>
<td>Paternal</td>
<td>16 (18)</td>
<td>1 (9)</td>
<td>0.45</td>
</tr>
<tr>
<td>Age at diagnosis of hypertension (years)</td>
<td>36.3 ± 12.3</td>
<td>38.4 ± 11.5</td>
<td>0.58</td>
</tr>
<tr>
<td>Age at diagnosis of FMD (years)</td>
<td>44.1 ± 13.6</td>
<td>43.5 ± 10.9</td>
<td>0.89</td>
</tr>
<tr>
<td>Multifocal/unifocal FMD</td>
<td>67/15</td>
<td>11/0</td>
<td>0.12</td>
</tr>
<tr>
<td>Solitary kidney</td>
<td>5 (5.7)</td>
<td>0 (0)</td>
<td>0.42</td>
</tr>
<tr>
<td>Bilateral FMD</td>
<td>43 (48.3)</td>
<td>9 (81)</td>
<td>0.03</td>
</tr>
<tr>
<td>FMD extension score &gt; 3</td>
<td>18 (20)</td>
<td>6 (54)</td>
<td>0.056</td>
</tr>
<tr>
<td>Maximum stenosis &gt; 75%</td>
<td>45 (51)</td>
<td>4 (36)</td>
<td>0.14</td>
</tr>
<tr>
<td>Ischemic small kidney</td>
<td>18 (20)</td>
<td>0 (0)</td>
<td>0.09</td>
</tr>
<tr>
<td>Extrarenal FMD</td>
<td>7 (9.8)</td>
<td>2 (28.5)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SD and numbers (percentages).

<table>
<thead>
<tr>
<th>Family History</th>
<th>n (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>289/366 (79.0)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>171/302 (56.6)</td>
</tr>
<tr>
<td>Stroke</td>
<td>175/327 (53.5)</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>76/323 (23.5)</td>
</tr>
<tr>
<td>Sudden death</td>
<td>60/303 (19.8)</td>
</tr>
<tr>
<td>FMD</td>
<td>26/354 (7.3)</td>
</tr>
<tr>
<td>Dissection</td>
<td>6/303 (2.0)</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>2/299 (0.7)</td>
</tr>
<tr>
<td>Ehlers-Danlos syndrome</td>
<td>1/302 (0.3)</td>
</tr>
</tbody>
</table>

Screening for hereditary FMD

It is recommended to question a patient with FMD about precocious HTN, history of dissection, aneurysm or cerebral haemorrhage among his/her first-degree relatives.

In case of a positive answer to at least one of these questions, the patient may inform the respective relative(s) about the possibility of hereditary FMD.
The prevalence of current smoking is greater in patients with FMD than in matched controls. Current smoking is associated with more severe and more rapidly progressing disease in patients with multifocal FMD. This study highlights the critical importance of encouraging patients with FMD to quit smoking.

**Smoking cessation should be strongly encouraged in patients with FMD**

Renal FMD is not always a curable disease

Meta-analysis: HTN cure rate following PTA

Meta-analysis: HTN according to publication year


More and more incidental findings?
FMD-related renal artery stenosis
Indications of revascularisation

- HTN of recent onset
- Medical treatment failure
- Renal function degradation
  (especially after administration of a RAS inhibitor)
- Renal size reduction
FMD-related renal artery stenosis
PTA vs. surgery

- Renal PTA is the first-line revascularisation technique.
- Stenting is usually not recommended (risk of kinking or stent fracture)
- Surgery should be considered in the following cases:
  - Stenosis associated with complex aneurysms
  - Restenosis despite two attempts of PTA
  - Complex lesions of arterial bifurcation or branches
Cervico-cephalic FMD
Indications of revascularisation

It is recommended to revascularize only symptomatic carotid FMD lesions. The indication should take into account the symptoms, the lesions, the experience of each centre, and the patient’s preferences. The decision must be taken within a multidisciplinary team with a large experience of the disease.
Follow-up

No revascularisation

• Blood pressure: every 3 months
• Creatinine and kidney length: yearly

Revascularisation

• Blood pressure and creatinine: at 1 month
• Renal imaging: 6 months
• Subsequent follow-up: see higher
Take-home messages on FMD

• FMD is less rare than previously thought
• FMD is not only a disease of young women
• FMD is a systemic vascular disease
• FMD patients may have a genetic predisposition
• PTA does not always cure renal FMD
• Stenting is not recommended
• FMD is also a disease for cardiologists (SCAD)
• FMD deserves to be revisited