The European FMD initiative

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The European FMD initiative and registry

Origin and rationale
European consensus on the diagnosis and management of fibromuscular dysplasia

Alexandre Persu\textsuperscript{a,b}, Alessandra Giavarini\textsuperscript{c,d}, Emmanuel Touzé\textsuperscript{e}, Andrzej Januszewicz\textsuperscript{f}, Marc Sapoval\textsuperscript{g,h}, Michel Azizi\textsuperscript{c,h}, Xavier Barral\textsuperscript{i}, Xavier Jeunemaître\textsuperscript{h,j}, Alberto Morganti\textsuperscript{d}, Pierre-François Plouin\textsuperscript{c,h}, Peter de Leeuw\textsuperscript{k}, on behalf of the ESH Working Group ‘Hypertension and the Kidney’

Journal of Hypertension 2014, 32:000–000
FMD needs to be revisited

- FMD lesions may be found in up to 5% of apparently healthy adults.
- In current cohorts, the mean age at diagnosis is > 50 years, but FMD may also occur in children and elderly men.
- FMD is a systemic disease with frequent involvement of multiple vascular beds, including but not limited to renal and carotid arteries.
- FMD can be associated with spontaneous coronary artery dissection.
- FMD has an hereditary component and the first susceptibility genes are currently being identified.
FMD: research priorities

• Identification of the environmental and genetic factors involved in the pathogenesis of FMD.

• Assessment of the risk of disease progression, extension to other vascular beds and occurrence of complications; definition of an evidence-based screening and follow-up algorithm; improvement in the detection and quantification of FMD-related renal artery stenosis.

• A common prerequisite of most of these investigations is to collect FMD cases systematically and prospectively in a standardized way in national and international registries.
The European FMD initiative and registry

Aims and structure
European FMD initiative
(Coord. A. Persu, X. Jeunemaitre, M. Azizi, P-F. Plouin)

- Standardize clinical practice/ update the consensus
- Establish a network of expert centers
- Establish a European patient association
- Establish a European FMD registry
- Coordinate research on FMD in Europe
- Genetic dissection of FMD (GWAS/WES)
The European FMD registry

Adapted from the French FMD registry (coord. P.-F. Plouin), created in 2010 to merge existing local FMD databases and to share data semantics with the US registry.

Includes over 50 items covering demographic and clinical characteristics of FMD, family history, type, localization, associated complications and interventions.

A flexible, user-friendly online version has been developed (L. Toubiana), allowing to add an indefinite number of new events.

Specific modules can be developed according to local interests.

Toubiana et al., Stud Health Technol Inform. 2015; 210:887-891
Outline of the European FMD registry

**General characteristics**
Year of birth; gender; ethnicity; number of pregnancies; oral contraception

**Characteristics of FMD**
Year of diagnosis; type of FMD (multi- vs. unifocal); associated atheroma lesions; clinical presentation (hypertension; neurological signs/symptoms; other); family history

**Clinical and biological assessment**
Smoking; antihypertensive medication; body mass index; blood pressure; renal function

**Vascular imaging**
Localization of FMD lesions (renal, cervico-cephalic, mesenteric, lower limb, coronary); imaging modality (Ultrasound, CTA, MRI, angiography); side (left/right); type of lesion (stenosis, occlusion, aneurysm, dissection)

**Interventions**
Localization; side; procedure (angioplasty, angioplasty + stent, aneurysm repair, surgical revascularization)

Persu et al., FMD revisited, Hypertension 2016
Laurent TOUBIANA, PhD. Physique, Epidémiologiste

Directeur de l'IRSAN,
"Institut de recherche pour la valorisation des données de santé"
Responsable du SCEPID :
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INSERM UMRS 1142 LIMICS, Paris, F-75006;
UPMC : Université Pierre et Marie Curie - Paris 6
Informed consents

Fill the data
http://etude-dfm-belgique.forxit.eu

a. Collect 3 tubes
   - 2 EDTA tubes 5ml
   - 1 PAX tube

b. Label the tubes for Ex.: BEL-UCL-FMD1

c. Store them at 4°C for one week maximum
   - Stored at -80°C
   - Or
   - Send to us at room temperature

Since October 2017
FMD Atlas/ Image data bank
The European FMD initiative and registry

Implementation and networking
First National Meeting on Fibromuscular Dysplasia

Saturday 12th December 2015
9h00-16h00
Auditoire Maisin

Endorsed by the European Society of Hypertension

Brief Review

Revisiting Fibromuscular Dysplasia
Rationale of the European Fibromuscular Dysplasia Initiative

Alexandre Persu, Patricia Van der Niepen, Emmanuel Touzé, Sofie Gevaert, Elena Berra, Pamela Mace, Pierre-François Plouin, Xavier Jeunemaître; on behalf of the Working Group "Hypertension and the Kidney" of the European Society of Hypertension and the European Fibromuscular Dysplasia Initiative

Hypertension. 2016;68:832-839
Fibromuscular dysplasia (FMD) needs to be revisited

FMD is not only this rare but curable cause of renal artery stenosis in young women.

Did you know that:
- FMD lesions may be found in up to 5% of apparently healthy adults.
- In current cohorts, the mean age at diagnosis is > 50 years, but FMD may also occur in children and elderly men.
- FMD is a systemic disease with frequent involvement of multiple vascular beds, including but not limited to renal and carotid arteries.
- FMD can be associated with spontaneous coronary artery dissection.
- FMD has a hereditary component and the first susceptibility genes are currently being identified.

We are developing a comprehensive research program focusing on epidemiology, clinical aspects, imaging, biomarkers and genetics of FMD.

If you follow a cohort of patients with FMD, and are willing to contribute to the European FMD registry and join a network of specialists interested by the clinical and basic aspects of the disease, please contact us (FMD-saintluc@uclouvain.be).

Thank you very much in advance.

Best regards,

Prof. Alexandre PERSU  
Chairman of the ESH Working Group  
"Hypertension and the Kidney"  
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Prof. Michel AZIZI  
Vice-President of the European Society of Hypertension  
Hypertension Unit  
Hôpital Européen Georges Pompidou  
Paris, France  
E-mail: michel.azizi@aphp.fr
Invitation to the

Second National Meeting on Fibromuscular Dysplasia

Saturday 10th December 2016
9h00-15h30
Auditoire Maisin
ACCA SCAD Study Group

Collaborations  FMD/SCAD study groups

- Consensus building (e.g. screening for non-coronary FMD in patients with SCAD)
- Cross-fertilization and compatibility of registries
- Expanding networks
- Search for common genetic determinants (GWAS)/biomarkers
- Funding opportunities
OPENING CEREMONY
AUDITORIUM ALBERT II - GROUND FLOOR
Friday, February 23rd 2018 – Morning

Session I – Registries, networks and databases: what have we learnt?

Session II – Fibromuscular Dysplasia: a multifaceted vascular disease

Thursday, February 22nd 2018 - Afternoon

Friday, February 23rd 2018 – Afternoon

Session III – Genetic dissection of FMD and other vascular diseases

Session IV – Vascular function and emerging biomarkers in FMD patients

Saturday, February 24th 2018 – Morning

Session VI – Spontaneous coronary artery dissection

Session VII – Management of FMD: from medical consensus to patient-centered approach
The Belgian and European FMD registries

Current status
Persu et al., FMD revisited, Hypertension 2016; 68:832-9 update.
Enrollment during the years

- 2015
- 2016
- 2017

- FMD
- SCAD
The European FMD registry

Contribution of countries
Contribution of different countries

EUROPEAN FMD REGISTRY

DNA  FMD  SCAD

Argentina  Belgium  Bulgaria  Finland  France  Germany  Greece  Italy  Japan  Netherlands  Norway  Poland  Spain  Sweden  Switzerland  Tunisia  United Kingdom
The European FMD registry

Preliminary results
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<th>European registry</th>
<th>US Registry</th>
<th>ARCADIA Study</th>
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<tr>
<td><strong>N°</strong></td>
<td>609</td>
<td>447</td>
<td>469</td>
</tr>
<tr>
<td><strong>Age at inclusion</strong> (years)</td>
<td>51.2 ± 15.1</td>
<td>55.7 ± 13.1</td>
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<tr>
<td><strong>Age at diagnosis</strong> (years)</td>
<td>45.8 ± 15.8</td>
<td>51.9 ± 13.4</td>
<td>53 ± 13.4</td>
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<tr>
<td><strong>Females (%)</strong></td>
<td>508 (83.3)</td>
<td>406 (91.0)</td>
<td>394 (84.0)</td>
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<td><strong>Caucasians (%)</strong></td>
<td>537 (88.0)</td>
<td>395 (95.4)</td>
<td>415 (88.5)</td>
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<td><strong>Systolic Blood Pressure</strong> (mmHg)</td>
<td>138.3 ± 23.0</td>
<td>130 ± 20</td>
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<td><strong>Diastolic Blood Pressure</strong> (mmHg)</td>
<td>83.7 ± 14.3</td>
<td>75 ± 12</td>
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<td><strong>Hypertension (%)</strong></td>
<td>449 (73.7)</td>
<td>322 (72.0)</td>
<td>363 (77.4)</td>
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<tr>
<td><strong>Age at hypertension diagnosis</strong> (years)</td>
<td>36.5 ± 14.8</td>
<td>43.1 ± 14.9</td>
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<td><strong>Number of antihypertensive drugs</strong> (IQR)</td>
<td>2 (1-3)</td>
<td>2 (1-3)</td>
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<td><strong>Current smokers (%)</strong></td>
<td>125 (20.5)</td>
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<td>90 (19.2)</td>
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<td><strong>Ever smokers (%)</strong></td>
<td>147 (37.2)</td>
<td>199 (42.4)</td>
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<td><strong>Body Mass Index</strong></td>
<td>24.6 ± 4.9</td>
<td>25.5 ± 5.2</td>
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<td><strong>Estimated Glomerular Filtration Rate – CKD-EPI (ml/min/1.73m²)</strong></td>
<td>91.2 ± 37.5</td>
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US Registry (Olin et al., Circulation. 2012); ARCADIA study (Plouin et al., Hypertension. 2017)
## EUROPEAN FMD REGISTRY

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<td>N°</td>
<td>609</td>
<td>447</td>
<td>469</td>
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<tr>
<td>Multifocal FMD (%)</td>
<td>438 (71.9)</td>
<td>447 (100)</td>
<td>429 (91.5)</td>
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<tr>
<td>Multisite FMD (%)</td>
<td>189 (31.0)</td>
<td>211 (47.2)</td>
<td>311 (66.3)</td>
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<tr>
<td>Bilateral renal arteries lesions (%)</td>
<td>217 (35.6)</td>
<td></td>
<td>193 (41.2)</td>
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<td>Bilateral cervico-cephalic lesions (%)</td>
<td>129 (21.2)</td>
<td></td>
<td>178 (38.0)</td>
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<td>Cephalic aneurysms (%)</td>
<td>65 (10.7)</td>
<td>37 (8.3)</td>
<td>28 (6.0)</td>
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<td>Cervical arteries dissections (%)</td>
<td>9 (1.5)</td>
<td>82 (18.3)</td>
<td>45 (9.6)</td>
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<tr>
<td>Family history of FMD (%)</td>
<td>17 (2.7)</td>
<td>33 (7.3)</td>
<td>11 (2.3)</td>
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*US Registry (Olin et al., Circulation. 2012); ARCADIA study (Plouin et al., Hypertension. 2017)*
Single-site and multisite FMD

1 site | 2 sites | 3 sites | 4 sites

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
EUROPEAN FMD REGISTRY

Vascular beds involved in FMD

- Renal arteries: 91.9%
- Cervico-Cephalic arteries: 58.6%
- Visceral arteries: 20.9%
- Limb arteries: 25.0%

Legend:
- Positive imaging
- Negative imaging
- No imaging
New developments for the near future

- Mention « not available »
- More on gynecological aspects
- More on smoking
- More on neurological symptoms
- More on aneurysms/dissections
Message for the investigators (I)

Regardless of initial site of vascular bed involvement, patients with FMD should undergo imaging of all vessels from brain to pelvis, at least once and usually with CTA or contrast-enhanced MRA, to identify other areas of FMD, as well as to screen for occult aneurysms and dissections.


Messages for the investigators (II)

- Please fill in timely the information in the platform
- Please do not forget to send us an image of the main lesion
- Please do not forget to fill in follow-up visits
- If not the case, please consider contributing to the DNA biobank
- Please help us identifying patient advocates in your country willing to contribute to a European patient association
- Please help us help recruiting more centers and involve new countries (esp. Central and Northern Europe)
## Acknowledgements

### EUROPEAN FMD REGISTRY

### Participating centers

<table>
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<th>BELGIUM</th>
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<tr>
<td>Cliniques Universitaires Saint-Luc (Brussels)</td>
<td>Alexandre Persu, Silvia Di Monaco, Simina Ciurica, Francesca Severino, Patrick Chenu, Pierre Hammer, Pierre Goffette, Parla Astarci, Robert Verhelst and Miikka Vikkula</td>
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<tr>
<td>Centre Hospitalier Universitaire Ambroise Paré (Mons)</td>
<td>Philippe Delmotte</td>
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<td>Universitair Ziekenhuis Brussel (Brussels)</td>
<td>Patricia Van der Niepen and Frank Van Tussenbroek</td>
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<td>Universitair Ziekenhuis Gent (Gent)</td>
<td>Tine De Backer and Sofie Gevaert</td>
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<td>Hilde Heuten, Laetitia Yperzeele and Thijs Van der Zijden</td>
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<td>Grand Hôpital De Charleroi (Charleroi)</td>
<td>Jean-Philippe Lengelé</td>
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<td>Jean-Marie Krzesinski</td>
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<td>Peter Verhamme and Thomas Vanassche</td>
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<td>Jean-Claude Wautrecht, Joëlle Nortier, Pasquale Scoppettuolo and Noëmie Ligot</td>
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<td>GZA ziekenhuizen - campus Sint-Augustinus (Wilrijk)</td>
<td>Wouter Vinck</td>
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<td>Hopital Européen Georges Pompidou and Paris-Descartes University (Paris)</td>
<td>Pierre-François Plouin, Xavier Jeunemaitre, Pierre Boutouyrie, Juliette Albuisson, Laurent Toubiana, Marie-Christine Jaulent, and Michel Azizi</td>
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<td>INSERM UMR-S 970 (Paris)</td>
<td>Nabila Bouatia-Naji</td>
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<td>University of Caen (Caen)</td>
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<td>Bordeaux University (Bordeaux)</td>
<td>Stéphanie Debette</td>
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<td>Centre Hospitalier Universitaire de Grenoble- Université Grenoble Alpes (Grenoble)</td>
<td>Christophe Seinturier, Olivier Ormezzano and Frédéric Thony</td>
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## Acknowledgements

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<td>Teodora Yaneva, Dobrin Vassilev</td>
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<td>Saaraaken Kulenthiran, Felix Mahfoud</td>
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<td>Elena Berra, Franco Rabbia</td>
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<td>Constantina Chrysochou</td>
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<td>Tunisia</td>
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<td>Hanen Chaker, Faiçal Jarraya</td>
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<td>China</td>
<td>Shanghai Institute of Hypertension</td>
<td>Jianzhong Xu, Jiguang Wang</td>
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Without their help
We could not maintain the registry

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AOU Città della Salute e della Scienza
urin
Without your contribution there would be no registry

We are grateful for all your efforts

Thank you