

Painful symptoms and spine-specific activity limitations associated with dural ectasia in individuals with Marfan syndrome: a cross-sectional comparative study (MarfanLomb)

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Disclosures

None to declare

Marfan syndrome (MFS)

Most frequent inherited disorder of the conjunctive tissue

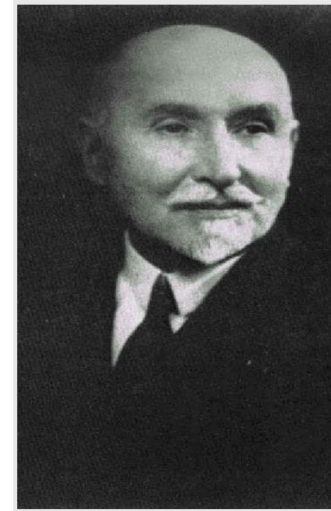
- First described in 1896
- Incidence: 2/10.000, prevalence: 1/5.000
- Sex ratio: 1

Genotypical features

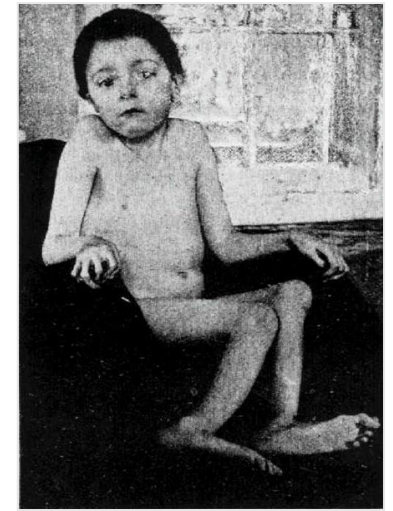
- Autosomic dominant transmission, but ~ 1/3 *de novo* mutations
- FBN1 gene > 2/3 cases, known mutations > 600, < 1/3 detected
- Impaired synthesis of fibrilin-1 extracellular matrix protein

Phenotypical features → heterogeneous +++

- Ocular involvement
- Cardiovascular involvement
- Spinal and non-spinal musculoskeletal involvement



Prof. Antoine Bernard
Jean Marfan

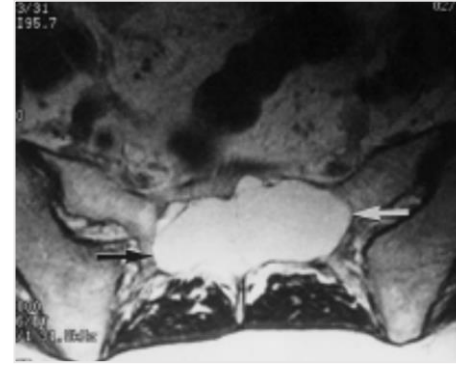


5-yo Gabrielle

Spinal phenotypes

Two spinal phenotypical features are more “specific” to MFS

- Spinal deformity
- Dural ectasia



→ Phenotypical feature 1: spinal deformity

- ~ 60 of individuals with MFS
- ~ 10% spinal surgery (at the end of puberty)
- All 3 segments: neck, upper back and lower back

Scoliosis (3D deformity)

Reversed curvatures (sagittal deformity)

→ Phenotypical feature 2: dural ectasia

- ~ 60-90 % of individuals with MFS
- **Enlarged dural sac**
- ↗ pressure of CSF at the lumbosacral level + defect of the dura mater

→ Symptoms associated with dural ectasia?

Characterization of the Symptoms Associated With Dural Ectasia in the Marfan Patient

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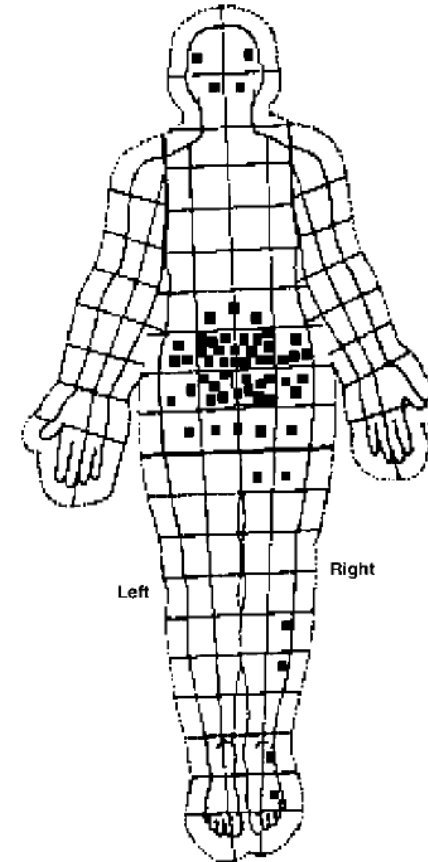


TABLE VII. Frequency of Symptoms in Marfan Patients With Dural Ectasia From Previous Literature

Back pain	Headache	Leg pain	Abdominal pain	Motor deficits	Sphincter disturbance	Gait abnormalities	Neurologic defects
33/83 40%	11/36 31%	11/50 22%	4/40 10%	4/43 9%	3/40 8%	1/39 3%	3/56 5%

A pattern of symptoms that increases with standing position

- ↘ CSF pressure at the cephalic end → **headache**
- ↗ CSF pressure at the caudal end → **back pain, leg pain**

Limitations

- Small studies (max = 22 participants)
- No comparative population (ie, MFS individuals without dural ectasia)

Objectives and design (MarfanLomb)

Hypothesis: painful and spine-specific activity limitations symptoms may be associated with dural ectasia in individuals with MFS **as compared to individuals with MFS without dural ectasia**

Design: comparative cross-sectional study in France, from January to March 2022

Objective: to describe and compare MFS individuals with and without dural ectasia for

- Patterns of spinal painful symptoms
- Patterns of activity limitations

Population

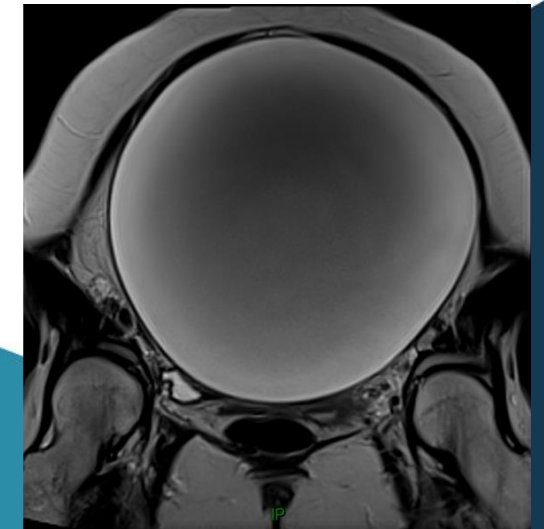
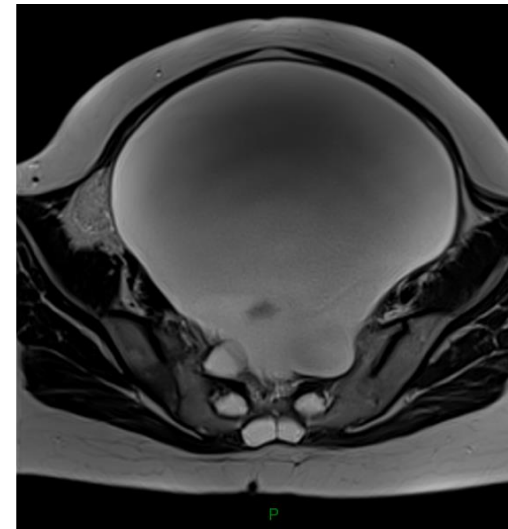
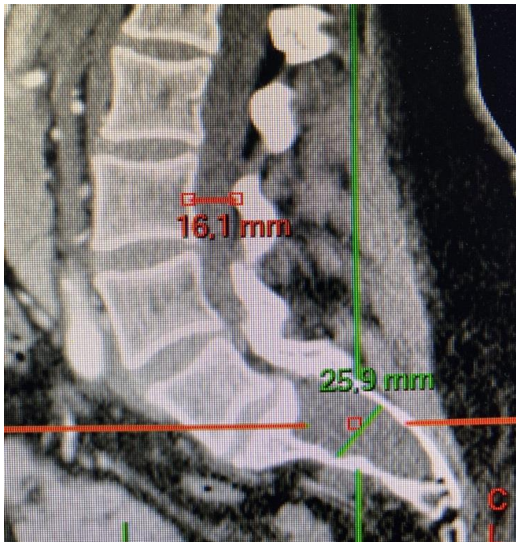
- MFS diagnosed at a single French reference center (Bichat)
- FBN1+ mutations
- Age 18 from 55 years (↘ risk of concomitant spinal degenerative changes)
- Lumbar CT-scan or MRI available

➔ **classification as having or not having a dural ectasia**

Dural ectasia imaging-based classification

1 major criterion or 2 minor criteria

Major criteria	Larger dural sac below S1 than above L4 Anterior meningocele
Minor criteria	Nerve root cyst ~ L5 > 6.5 mm Scalloping ~ S1 > 3.5 mm



Endpoints

Comparative analyses between participants with and without dural ectasia

- Quantitative variables: Student t-test or Mann-Whitney test
- Frequencies: Fisher exact test

Primary

- Frequency of back pain
- Frequency of back pain when standing, trampling or coughing
- Frequency of headache when standing

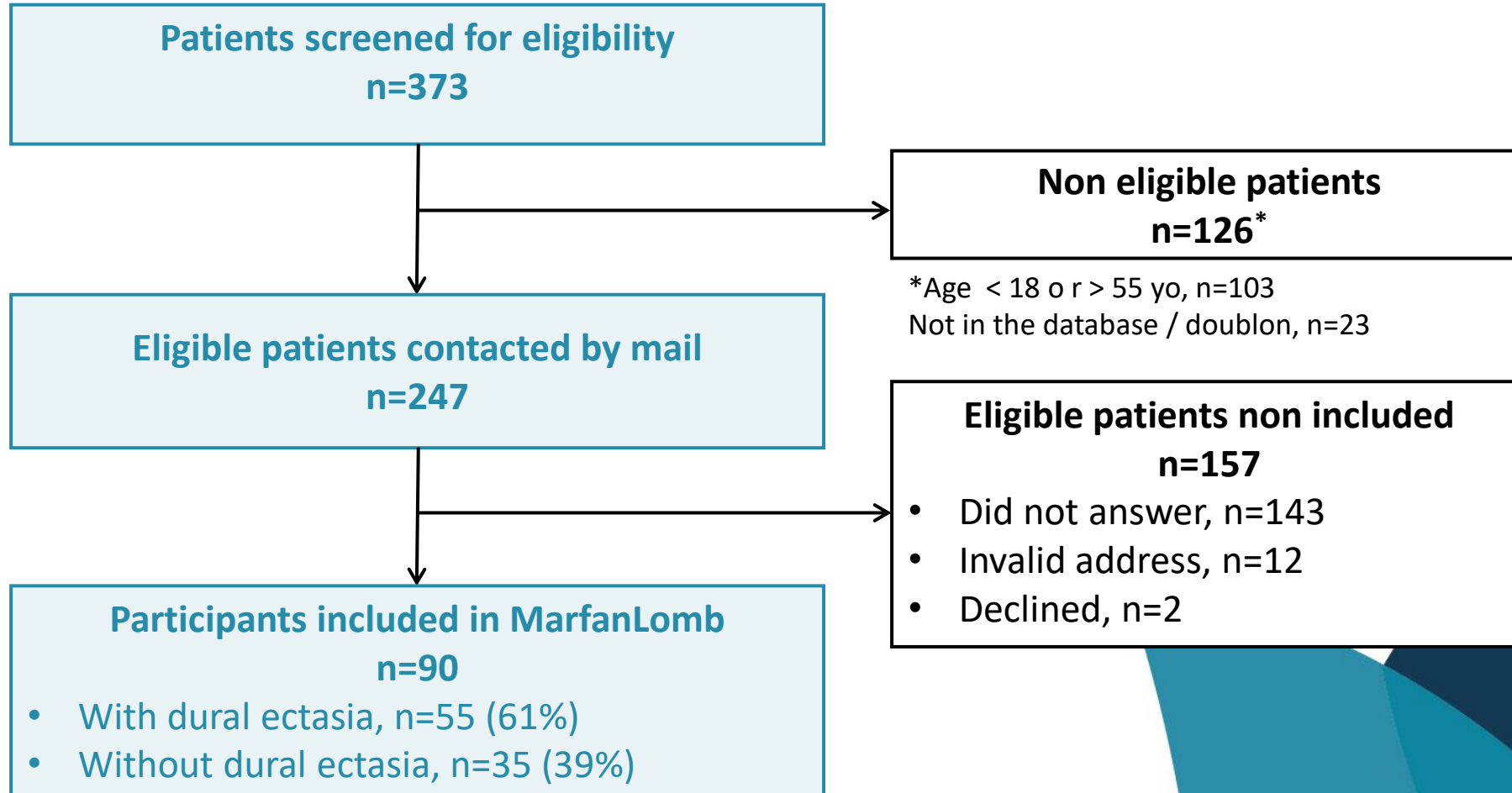
Secondary

- Spine-specific activity limitations: Oswestry Disability Index (ODI, 0 = none and 100 = maximal)



Results

Flow diagram



Participants' demographics

	With dural ectasia n=55	Without dural ectasia n=35	All n=90
Age (years), mean (SD)	39.2 (9.7)	39.5 (9.0)	39.3 (9.4)
Female, n (%)	25 (45)	20 (57)	45 (50)
BMI (kg/m ²), mean (SD)	23.6 (3.9)	24.5 (5.3)	23.9 (4.5)
Higher education, n (%)	36 (65)	25 (71)	61 (68)
Currently working, n (%)	40 (73)	24 (69)	64 (71)

Participants' medical history

	With dural ectasia n=55	Without dural ectasia n=35	All n=90
SPINAL HISTORY			
Spinal surgery	6 (11)	2 (6)	8 (9)
Scoliosis	39 (71)	25 (71)	64 (71)
NON-SPINAL HISTORY			
Aorta surgery	35 (64)	17 (49)	52 (58)
Ascending aorta involvement	52 (95)	32 (91)	84 (93)
Descending aorta involvement	12 (22)	6 (17)	18 (20)
High blood pressure	13 (24)	2 (6)	15 (17)
Acetabular protrusion	14 (25)	7 (20)	21 (23)
Pes planus	28 (51)	15 (43)	43 (48)
Pectus excavatum / carinatum	31 (56)	16 (46)	47 (52)

Outcomes

	With dural ectasia n=44	Without dural ectasia n=32	All n=76	P-value
Back pain	49 (89)	31 (89)	80 (89)	1.000
Back pain when standing	34 (62)	19 (54)	53 (58)	0.516
Back pain when trampling	19 (35)	12 (34)	31 (34)	1.000
Back pain when coughing	7 (13)	0 (0)	7 (8)	0.021
Headache when standing	27 (49)	9 (26)	36 (40)	0.030
Activity limitations (ODI, 0-100)	17.7 (14.6)	13.1 (13.9)	15.9 (14.4)	0.161

Summary and perspectives

Main finding 1 → in all individuals with MFS with and without dural ectasia

- **Back pain was very frequent ~ 90%** (only 40% in Foran study)

Foran JR et al, Am Me Genet A, 2005

Main finding 2 → in individuals with MFS with dural ectasia

- **Back pain when coughing and headache when standing were more frequent**
- Activity limitations scores were numerically higher
- Severe vascular pattern was numerically more frequent

Future → back pain when coughing and headache when standing in individuals with MFS

- May be considered as 2 very simple clinical biomarkers to detect symptomatic dural ectasia early
- May be used to identify patients who will need rehab targeting spinal and vascular impairments

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Thank you

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