Hospital Universitario Virgen de la Victoria
Servicio Andaluz de Salud
CONSEJERÍA DE SALUD

Marfan syndrome requires specialized units

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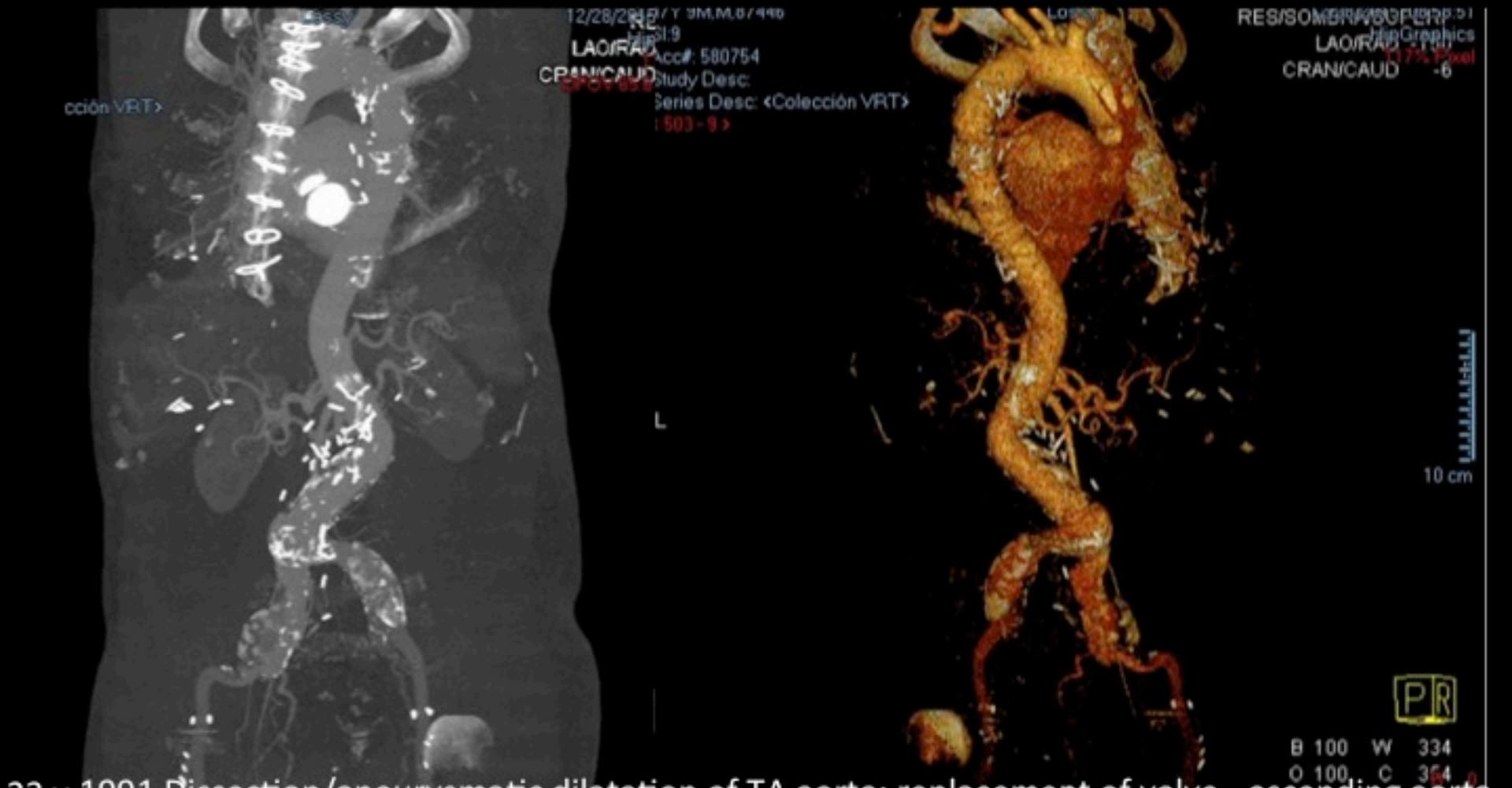
What is the clinical evolution of a survivor patient after aortic dissection with undiagnosed Marfan syndrome?



23 y 1991 Dissection/aneurysmatic dilatation of TA aorta: replacement of valve - ascending aorta
1999 descending aortic replacement
1999 infrarrenal aortic replacement
2006 re-composite replacement of aortic valve and aorta
2008 mitral valve replacement; Severe MR (prolapse)
2015 (Pr. Shaefers) Thoracoabdominal aortic replacement
47 a 2017 Waiting iliac replacement (alive today)


anit

Needs for optimal management of patients with Marfan syndrome and other hereditary, syndromic or non-syndromic aortic diseases

AFTER > 600 patients since 2010

Needs for optimal management of patients with Marfan syndrome and other hereditary, syndromic or non-syndromic aortic diseases

EXPERIENCE after 600 p

1. Clinical diagnosis (at different ages)

Characteristic	Marfan syndrome	Congenital contractural aracnodactyly*[2,57]	Type I Loeys–Dietz syndrome[14,52]	Type II Loeys–Dietz syndrome[14,52]	Ehlers–Danlos syndrome (vascular or type IV)[39]	Shprintzen–Goldberg syndrome‡[58]	Arterial tortuosity syndrome[59,60]
Phenotype	Skeletal manifestations, ectopia lentis, aortic aneurysms and dissection, dural ectasia, skin and pulmonary involvement	Dolicoestenomelia, aracnodactyly, scoliosis, multiple joint contractures, crumpled ears, no ocular manifestations, mild and nonprogressive aortic dilatation	Hypertelorism and cranio-synostosis, cleft palate and/or bifid uvula, arterial tortuosity and aneurysms	Absence of facial manifestations, except for bifid uvula, similar to type IV Ehlers–Danlos Syndrome (easy bruising, visceral fragility or rupture, etc)	Easy bruising, thin, translucent and velvety skin, joint hypermobility, spontaneous visceral rupture, obstetrical complications, characteristic facial appearance	Cranyosinostosis, severe exophtalmos, maxilary and mandibular hypoplasia, low-set ears, arachnodactyly, abdominal hernias, mental retardation	Tortuosity of aorta and large arteries, localized arterial stenoses, hernias, joint laxity, elongated face
Genes known to be mutated	*FBN1* and *TGFBR2*	*FBN2*	*TGFBR1* and *TGFBR2*	*TGFBR1* and *TGFBR2*	*COL3A1*	*FBN1*	*SLC2A10*
Prevalence	1 in 3,000–5,000	Unknown	Unknown	Unknown	1 in 25,000 (type IV accounts for 4% of cases)	Unknown	Unknown
Inheritance	AD	AD	AD	AD	AD	AD	AD
Pathophysiology	Altered synthesis of fibrillin-1 and increased TGF-β signaling	Altered synthesis of fibrillin-2	Increased TGF-β signaling	Increased TGF-β signaling	Abnormal synthesis of type III collagen	Altered synthesis of fibrillin-1	Deficiency of glucose transporter (GLUT10) and increased TGF-β signaling
Diagnosis	Ghent criteria ± genetic testing	Clinical assessment ± genetic testing	Clinical assessment ± genetic testing	Clinical assessment ± genetic testing	Clinical assessment (Villefranche criteria), biochemical diagnosis or genetic testing	Clinical assessment ± genetic testing	Clinical assessment ± genetic testing
Prognosis	Median survival if treated = 70 years	Not well established; normal lifespan unless cardiovascular problems arise	Median survival = 37 years; mean age at death = 26 years	Median survival = 37 years; mean age at death = 26 years	Median survival with no treatment = 48 years; high risk of surgical complications	Not well established	Not well established
Treatment	β-B/ARBs; surgery[5] if diameter ≥50 mm or rapid progression of dilation	Physical therapy, cardiovascular monitoring on yearly basis	β-B/ARBs; surgery[5] if diameter ≥40 mm	β-B/ARBs; surgery[5] if diameter ≥40 mm	Surgery[5] if diameter ≥40 mm	Cardiovascular monitoring and prophylactic surgery if dilated; [illegible] treatment.	Vascular surgery if needed

Cañadas, V. et al. Nat. Rev. Cardiol. 7, 256–265 (2010)

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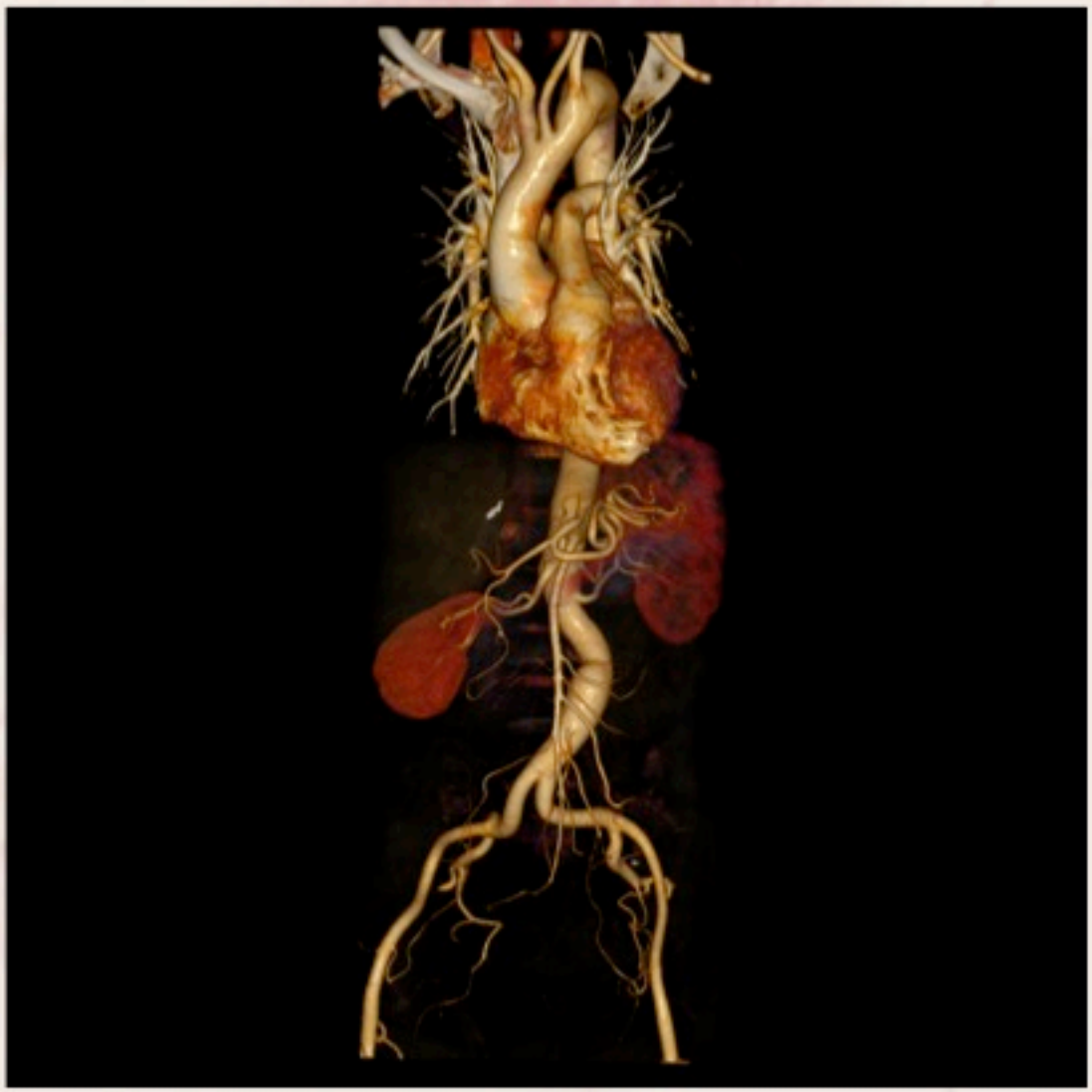
EXPERIENCE after 600 p

1. Clinical diagnosis (at different ages)
2. **Efficient use of imaging techniques**

Efficient use of imaging techniques

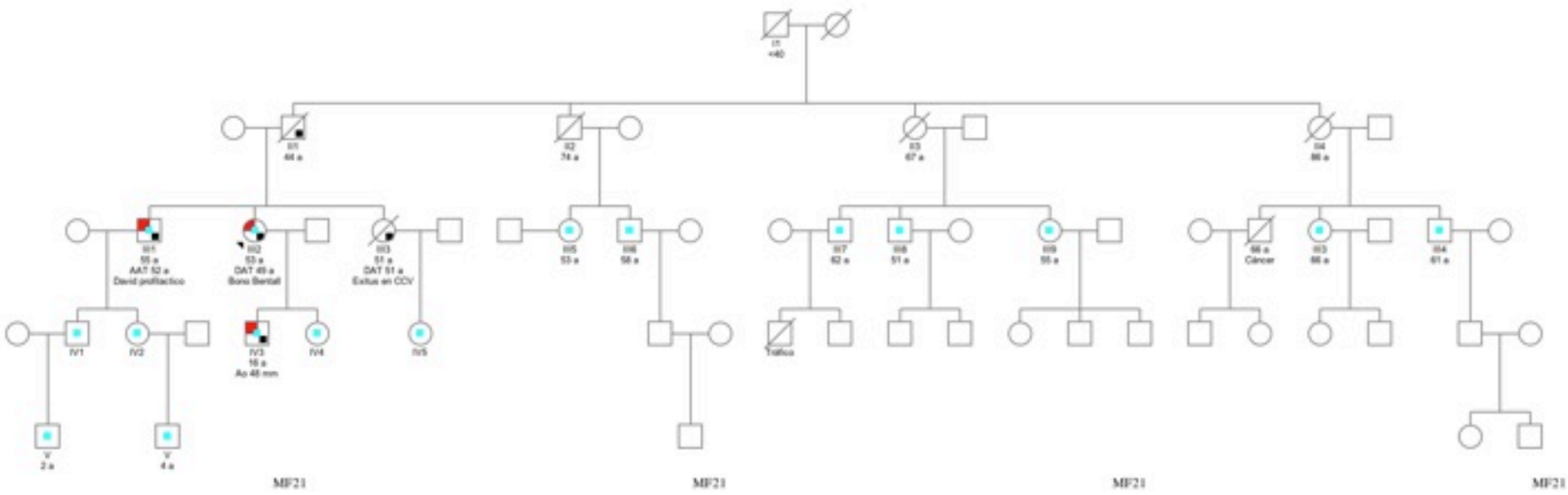


Needs for optimal management of patients with Marfan syndrome and other hereditary, syndromic or non-syndromic aortic diseases

EXPERIENCE after 600 p

1. Clinical diagnosis (at different ages)
2. Efficient use of imaging techniques
3. **Advanced knowledge in genetics**

AATFNS


I1
+40
II1
64 a
II2
74 a
II3
67 a
II4
86 a
III1
55 a
AAT 52 a
David profiláctico
III2
53 a
DAT 49 a
Bono Bentall
III3
51 a
DAT 51 a
Exitus en CCV
III5
53 a
III6
58 a
III7
62 a
III8
51 a
III9
55 a
III2
Cáncer
III3
66 a
III4
61 a
IV1
IV2
IV3
16 a
Ao 46 mm
IV4
IV5
Trébol
V
2 a
V
4 a
MF21
MF21
MF21
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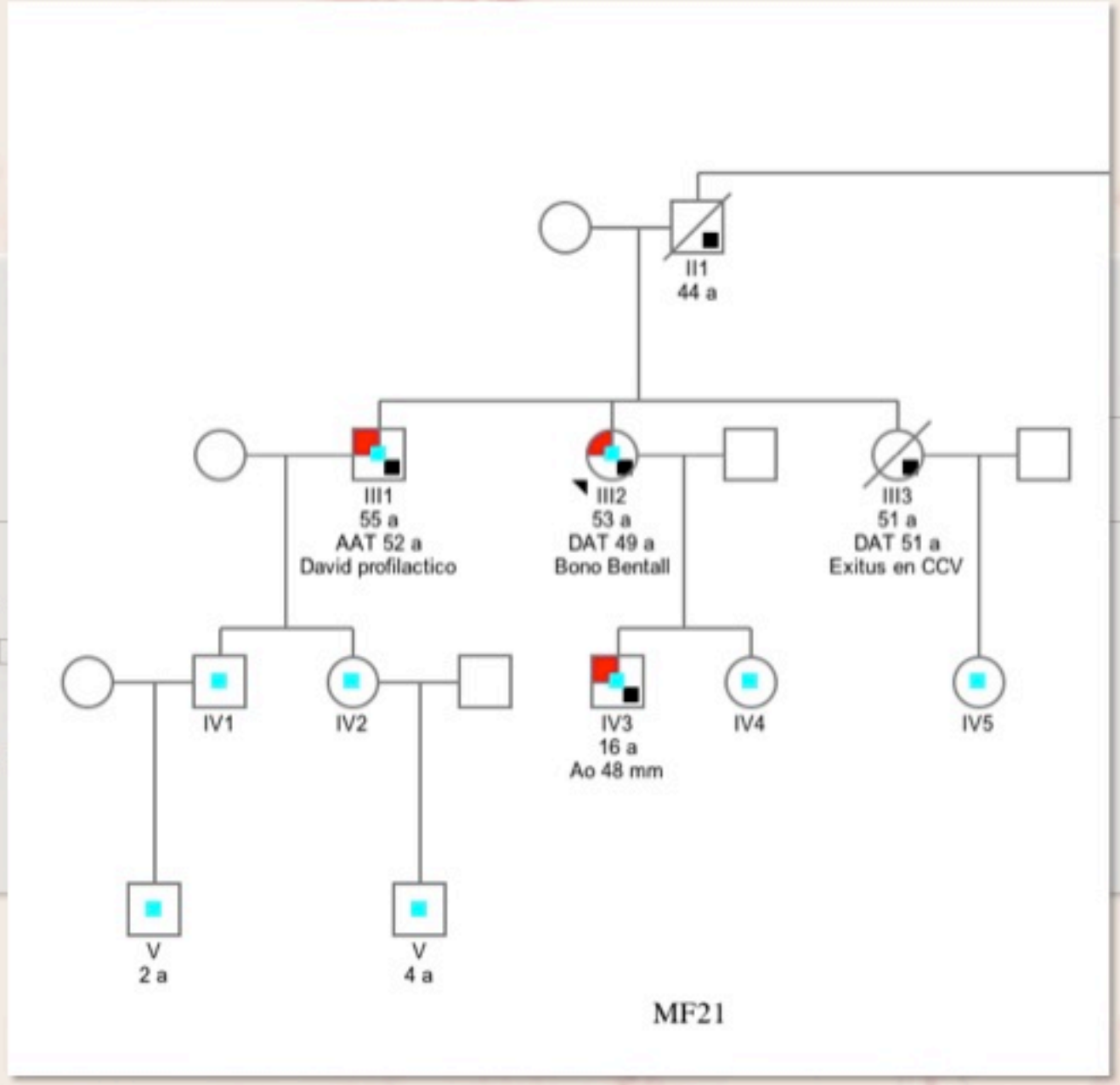
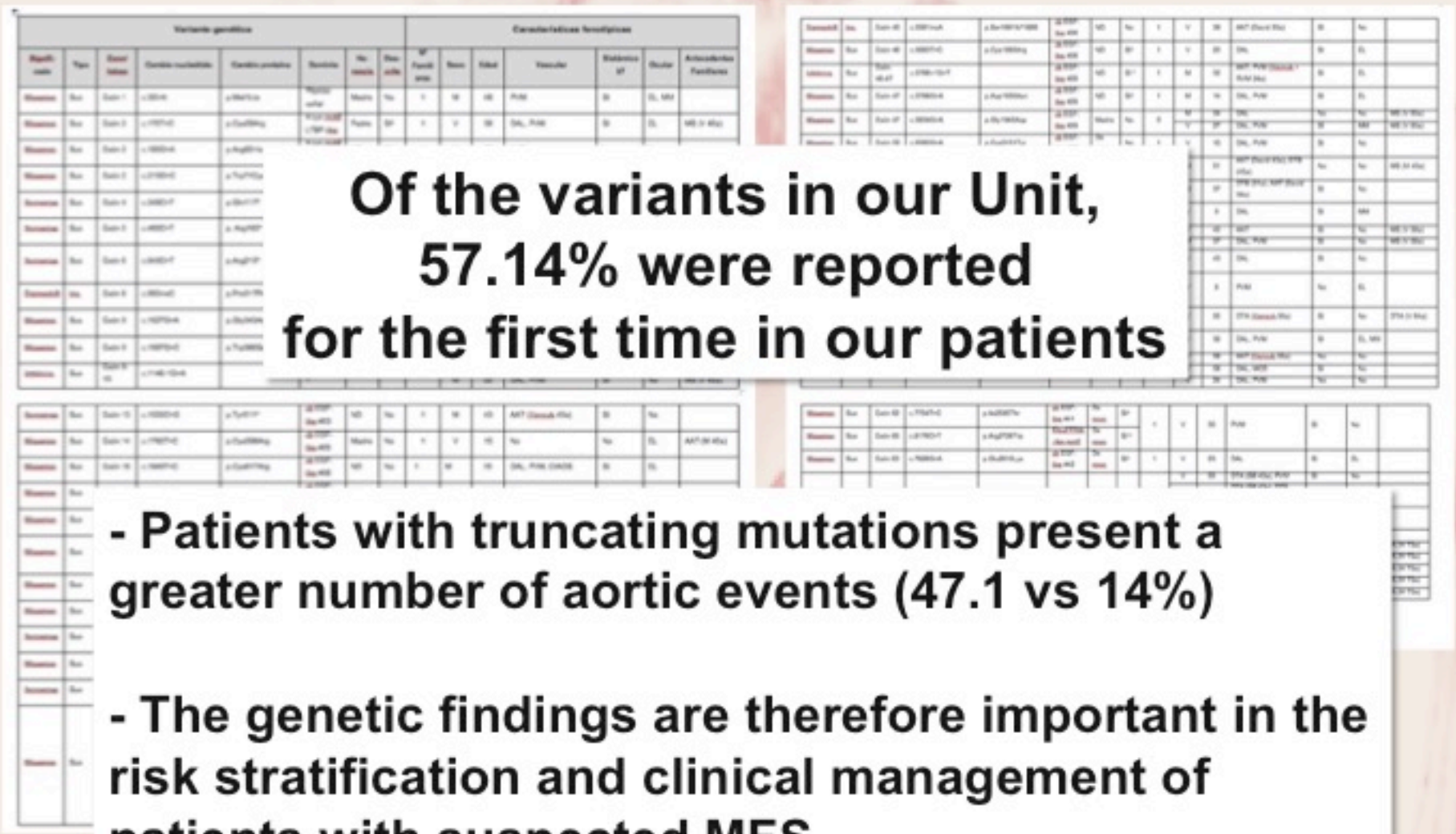

II1
44 a
III1
55 a
AAT 52 a
David profilactico
III2
53 a
DAT 49 a
Bono Bentall
III3
51 a
DAT 51 a
Exitus en CCV
IV1
IV2
IV3
16 a
Ao 48 mm
IV4
IV5
V
2 a
V
4 a
MF21

Variante genética								Características fenotípicas						
Significado	Tipo	Exón/ Intrón	Cambio nucleótido	Cambio proteína	Dominio	De novo	Disección	Nº Familiares	Sexo	Edad	Vascular	Sistémico	Ocular	Antecedentes Familiares
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

AAT = Aneurisma de aorta torácica; **BB** = Bono-Bentall; **CIAOS** = Comunicación interauricular tipo ostium secundum; **DAL** = Dilatación aórtica ligera; **DCE** = Disección coronaria espontánea; **Del** = Deleción; **DTA** = Disección tipo A; **DTB** = Disección tipo B.



Of the variants in our Unit, 57.14% were reported for the first time in our patients

- Patients with truncating mutations present a greater number of aortic events (47.1 vs 14%)

- The genetic findings are therefore important in the risk stratification and clinical management of patients with suspected MFS

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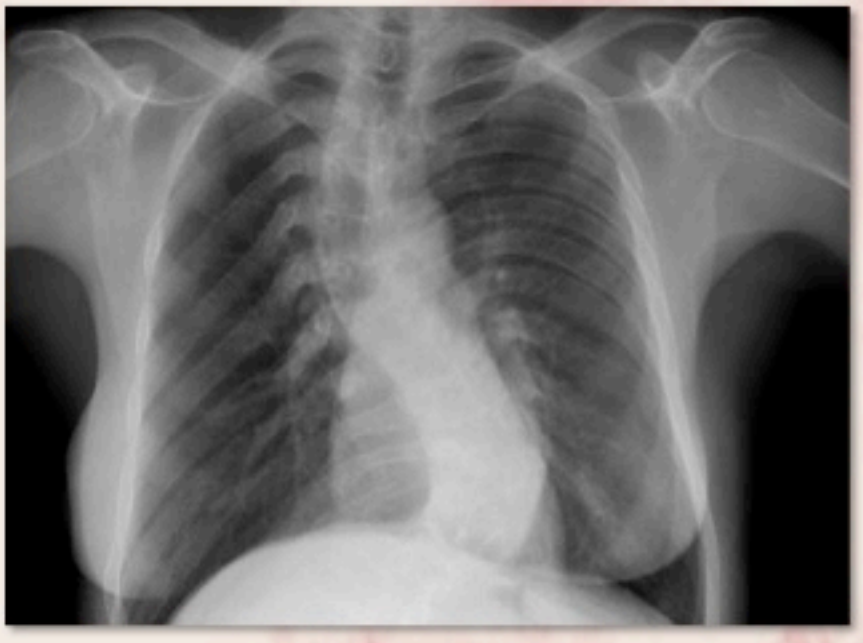
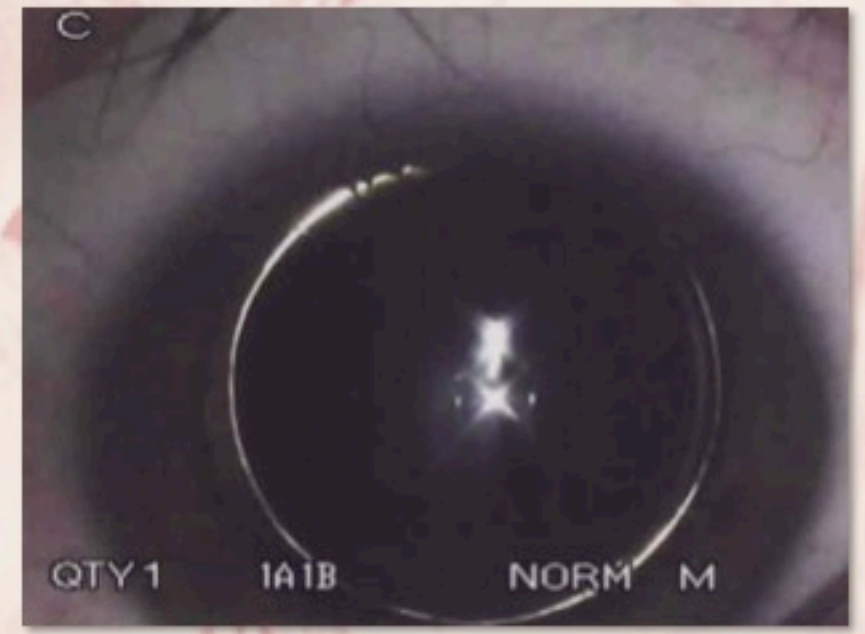
EXPERIENCE after 600 p

1. Clinical diagnosis (at different ages)
2. Efficient use of imaging techniques
3. Advanced knowledge in genetics
4. **Medical management including those of associated pathologies**

Medical treatment, and….





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EXPERIENCE after 600 p

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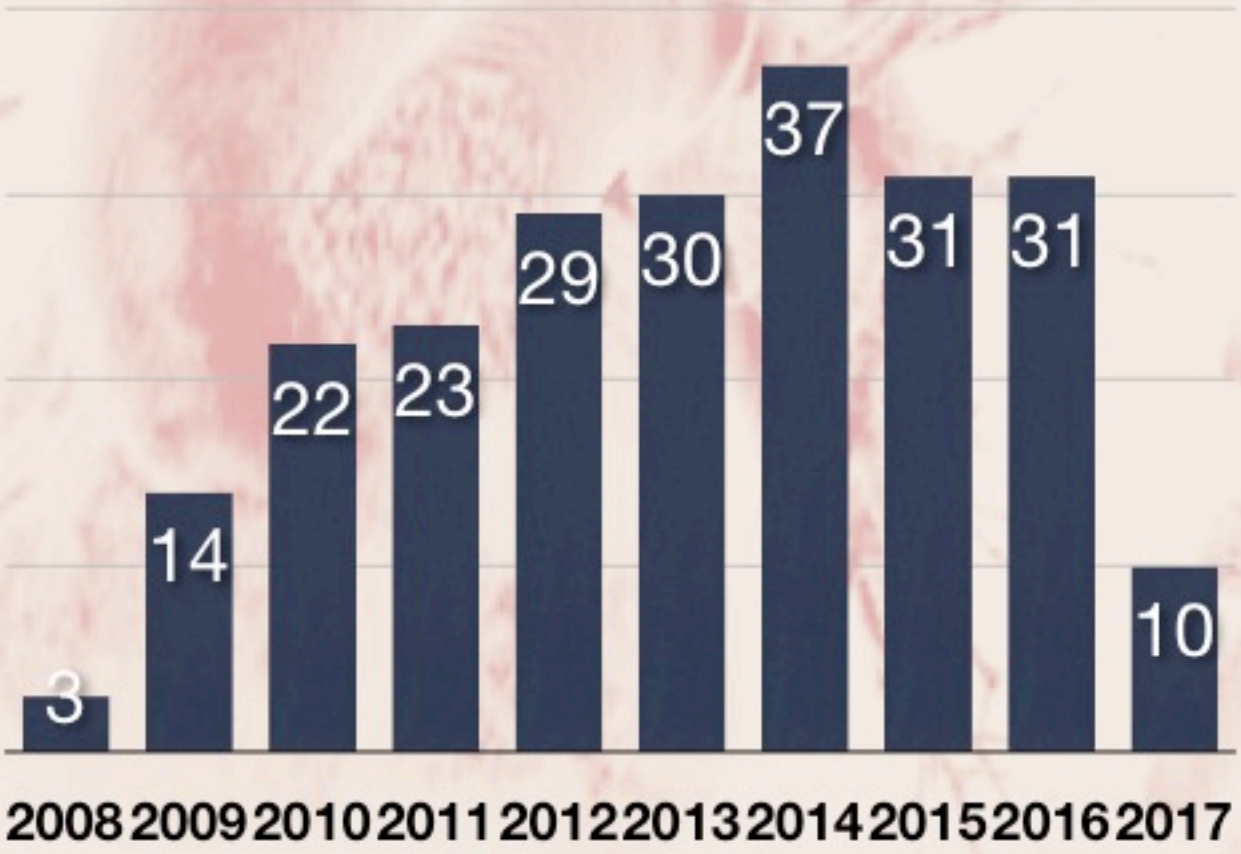
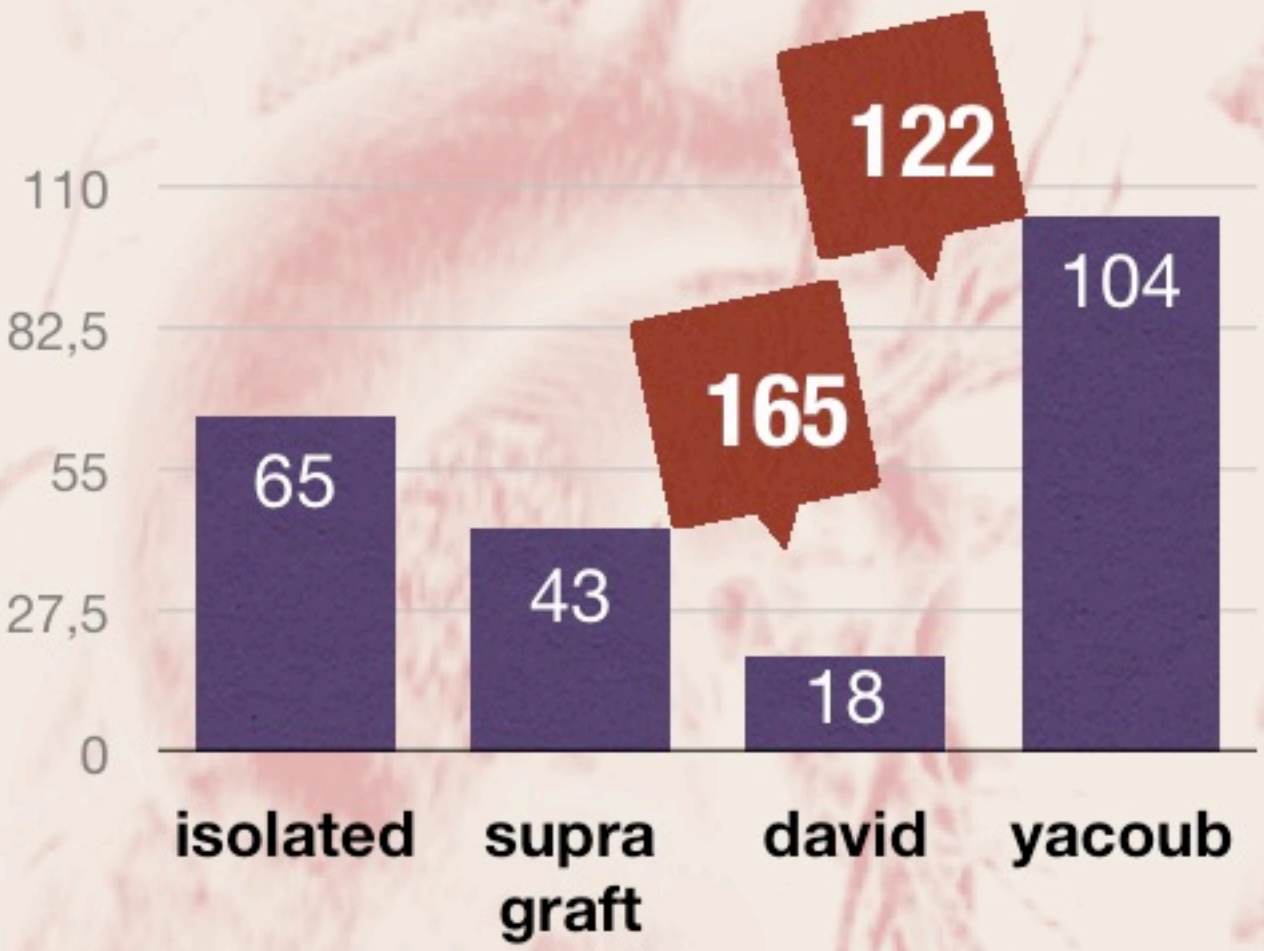
3. Advanced knowledge in genetics
4. Medical management including those of associated pathologies
5. **Prophylactic surgical management and complications in survivors of aortic dissection**

November 2008 → March 2017

230 pts





*21 patients with MFS
(DAVID/YACOUB preventive)

Marfan syndrome requires specialized units because needs for optimal management of patients

EXPERIENCE

1. **Clinical** diagnosis
2. Efficient use of **imaging** techniques
3. Advanced knowledge in **genetics**
4. **Medical** management including those of associated pathologies
5. Prophylactic **surgical** management and complications in survivors of aortic dissection

Malaga Valve 2017

A journey into contemporary heart valve therapies

29-31 March 2017

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Thanks!