Fokus na hrudní aortu

Genetické aortopatie očima kardiologa

Radka Kočková
Michal Klán, Barbora Míková

Co svědčí pro genetickou aortopatii

Dilatace/dissekce hrudní aorty

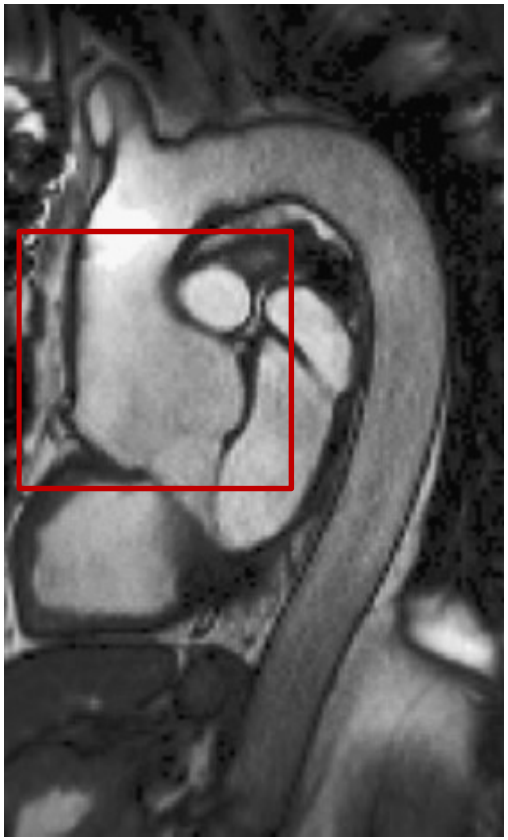
Mladý věk

Výskyt v rodině

Absence hypertenze

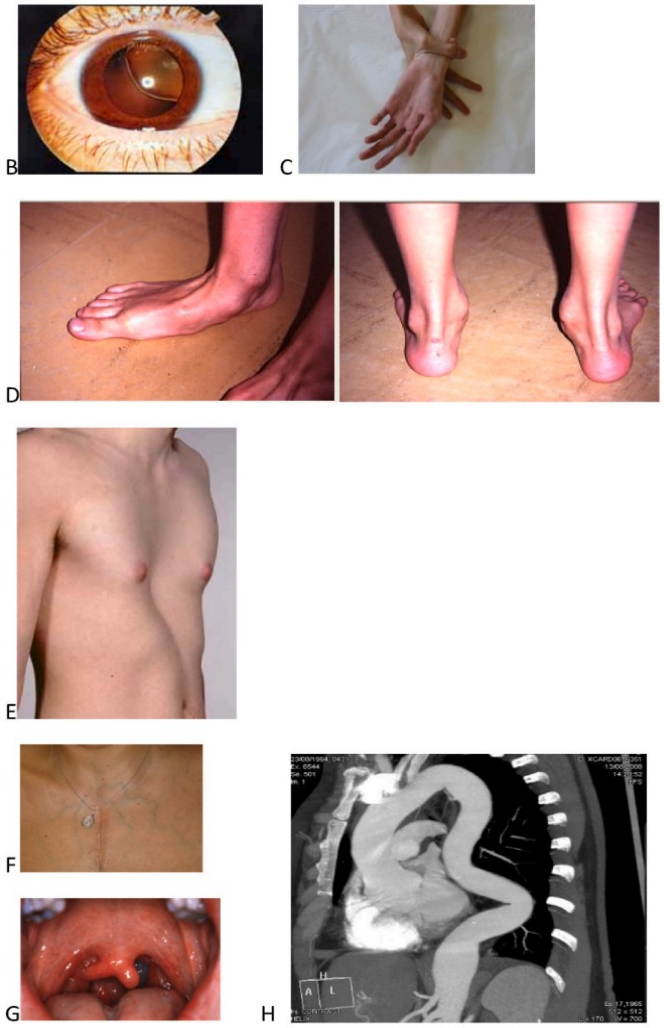
(jiných rizik. faktorů)

Syndromální forma



VASCERN. European Journal of Medical Genetics 2022

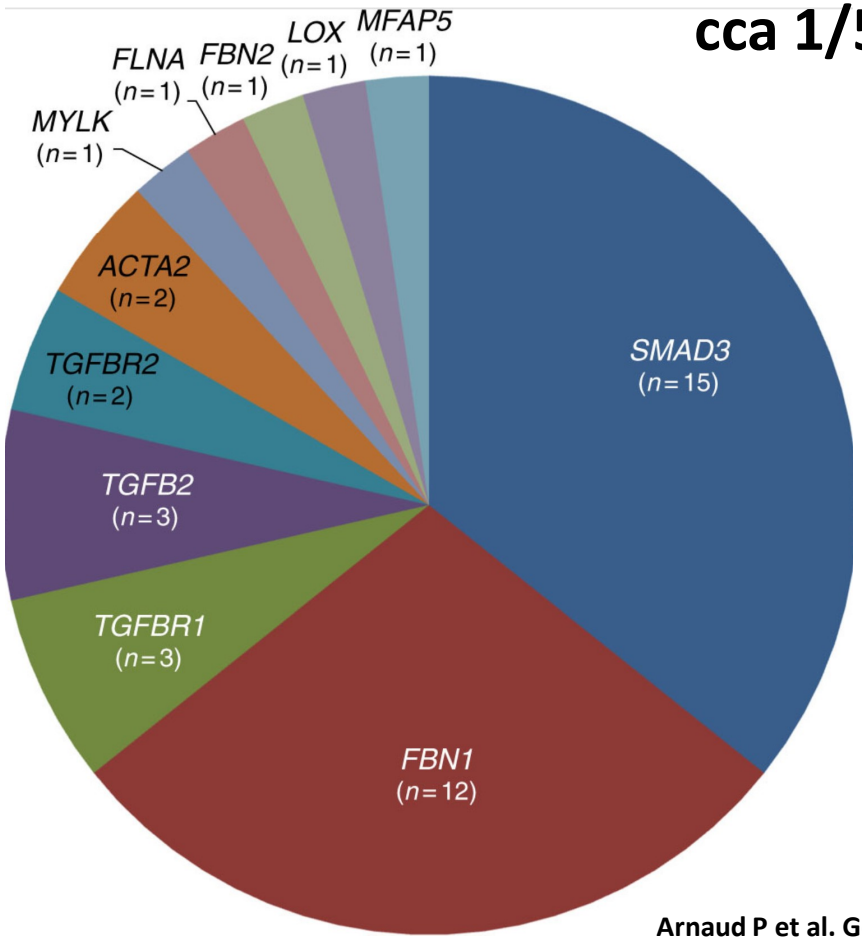
Syndromální projevy



VASCERN. European Journal of Medical Genetics 2022

Aneurysma/disekce aorty ve věku <45 let, bez syndromu či BAV a HTN

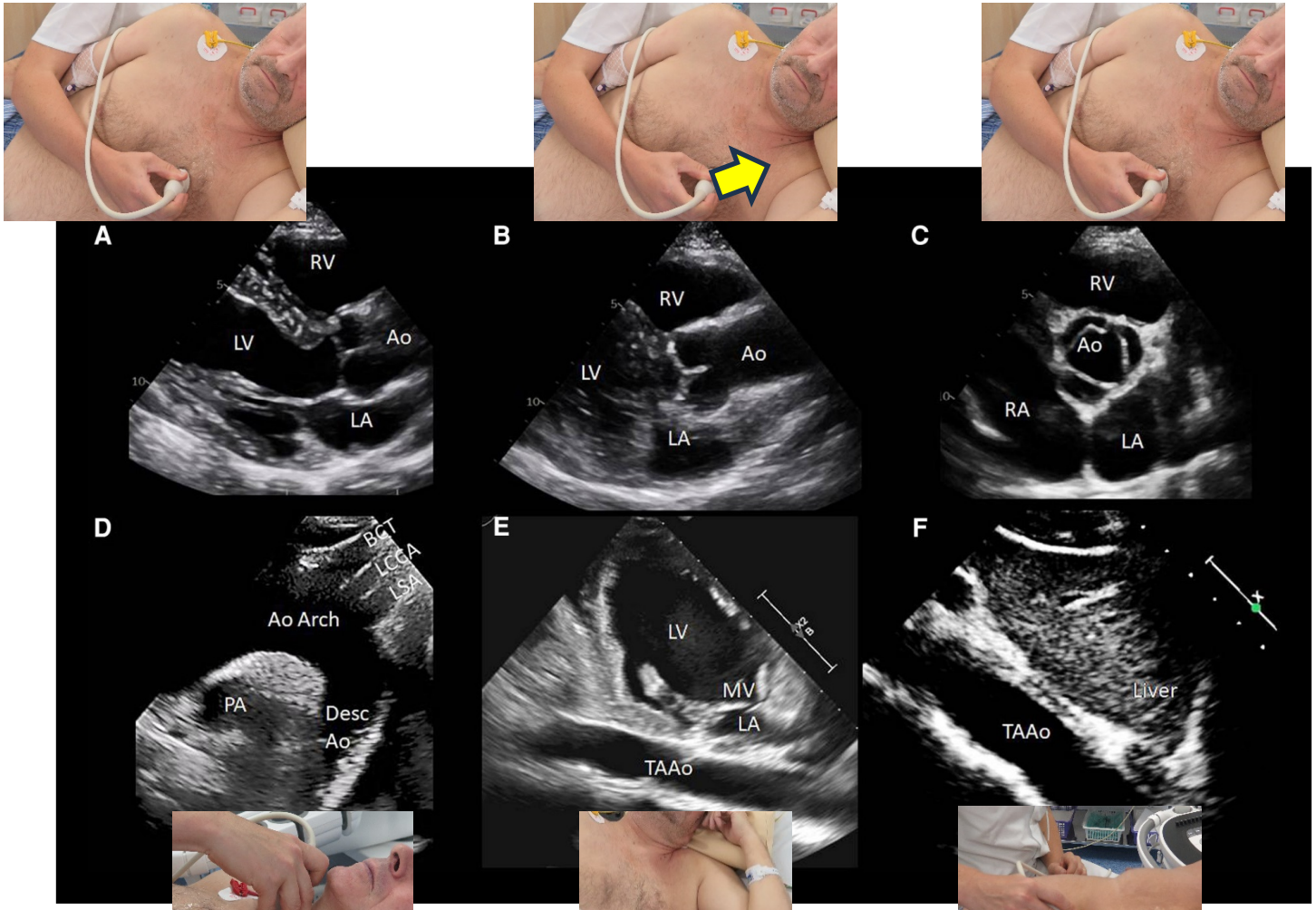
226 pacientů



cca 1/5 pacientů (n=42)

Arnaud P et al. Genetics in Medicine 2019

Echokardiografie - TTE



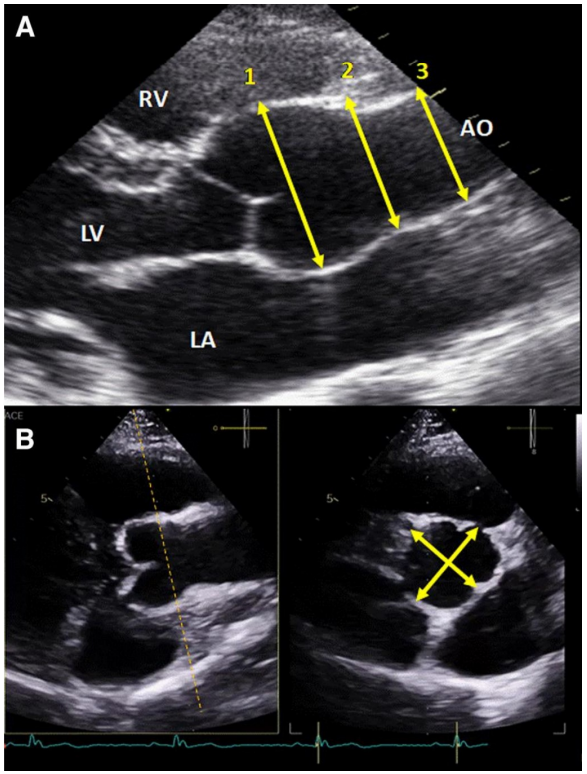
Evangelista A et al. g. Eur Heart J Cardiovasc Imaging 2023

Echokardiografie - TTE

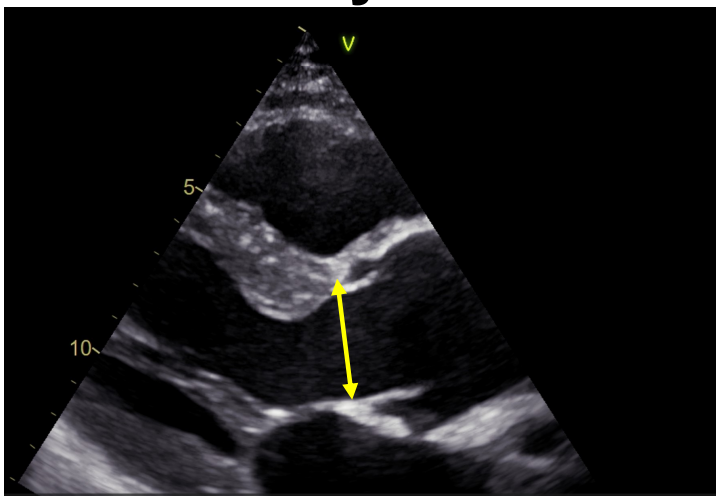
PLAX, PSAX

Leading edge to leading edge

End-diastole



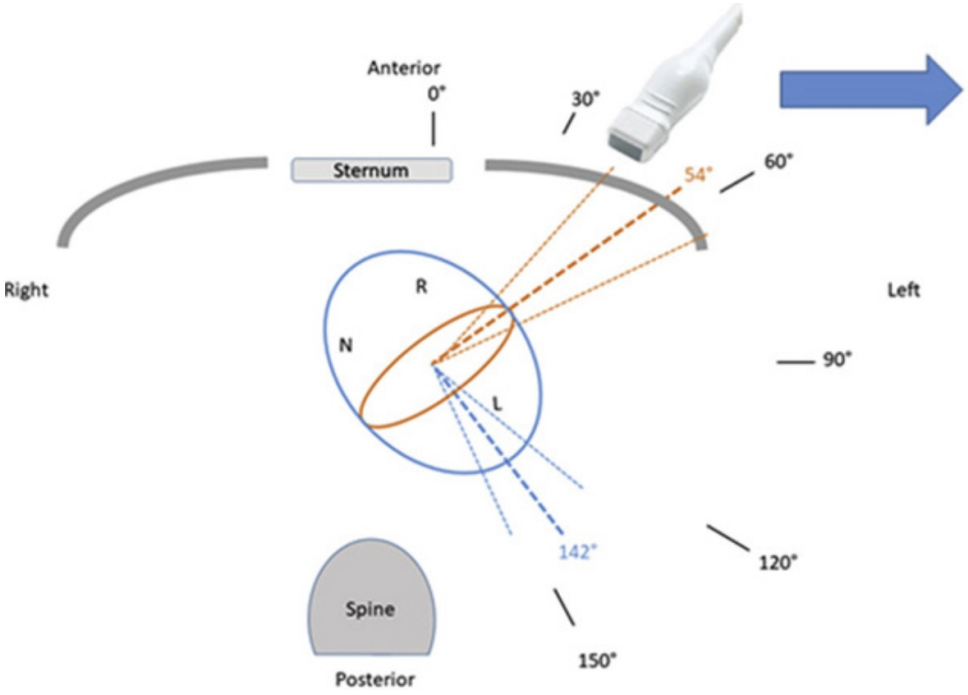
End-systole



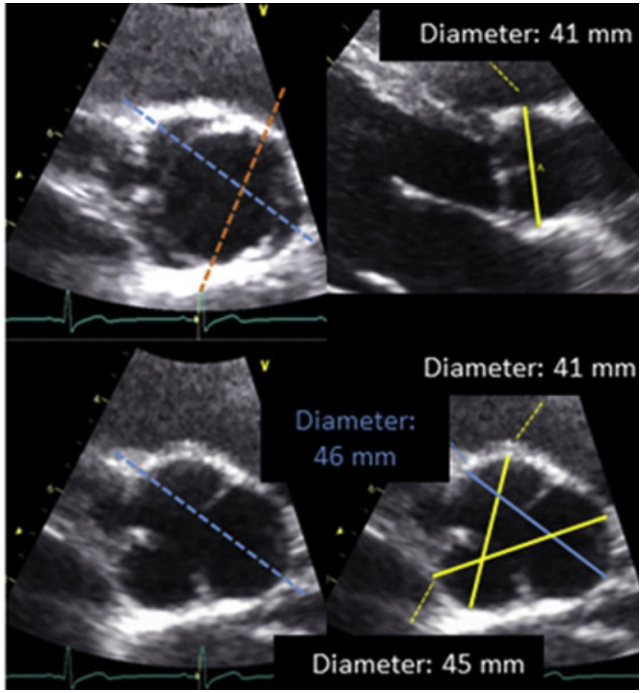
Evangelista A et al. g. Eur Heart J Cardiovasc Imaging 2023

PLAX podhodnocuje rozměr kořene u BAV

- **RCC+NCC −6.1±0.96**
- **RCC+LCC −2.3±0.47 mm**



RCC+NCC o 5 mm



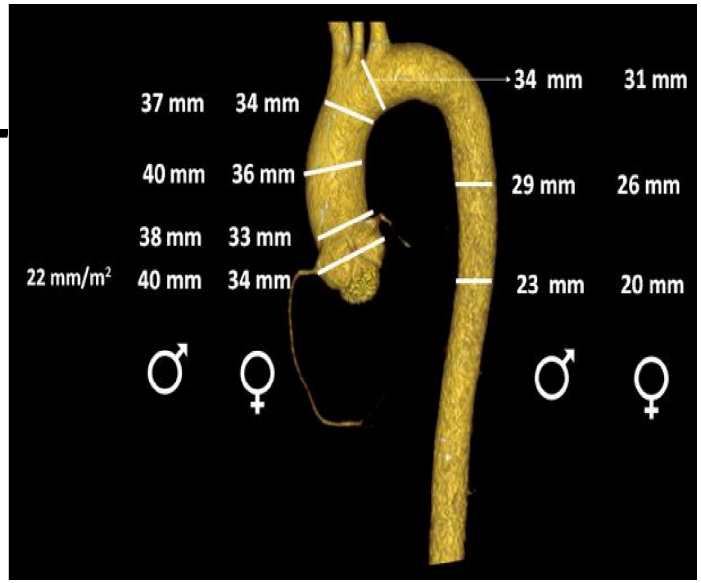
Milleron A et al. JASE 2022

Rozměry aorty

Normální rozměry hrudní aorty:

* **Z-score ≤2** ***(limitací je obezita, atd.***
* **≤ 35 mm ♀**

  ≤ 40 mm ♂ nebo <22 mm/m2



(normální růst aorty u dospělých 0.7-0.9 mm/10 let)

Signifikantní dilatace k došetření:

- **Hrudní aorta > 45 mm**
- **Břišní aorta > 30 mm**

Evangelista A et al. g. Eur Heart J Cardiovasc Imaging 2023

Indexace a Z-score aorty

https://csecho.ca/mdmath

MDMath

Inputs

Gender	Male	
Height	180	cm
Weight	80	kg
Location	Sinus of Valsalva	
Aorta O	45	mm

Clear Calculate

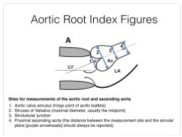
Results

Location	Sinus of Valsalva
BSA	2.0 m^2
ARI (BSA)	22.50 mm/m^2
Aorta E	34.00 mm
O-E ARR	1.32
Z Score	+3.67

Powered by medsquares

Author: Chi-Ming Chow MD MSc FRCPC
Developer: Edward Brawer BSc (Hons)
Illustrator: Ellen Ho BFA

Illustrations



Information

The aortic root index (ARI) can be calculated by dividing the observed aortic root dimension (Aorta O) by the BSA.

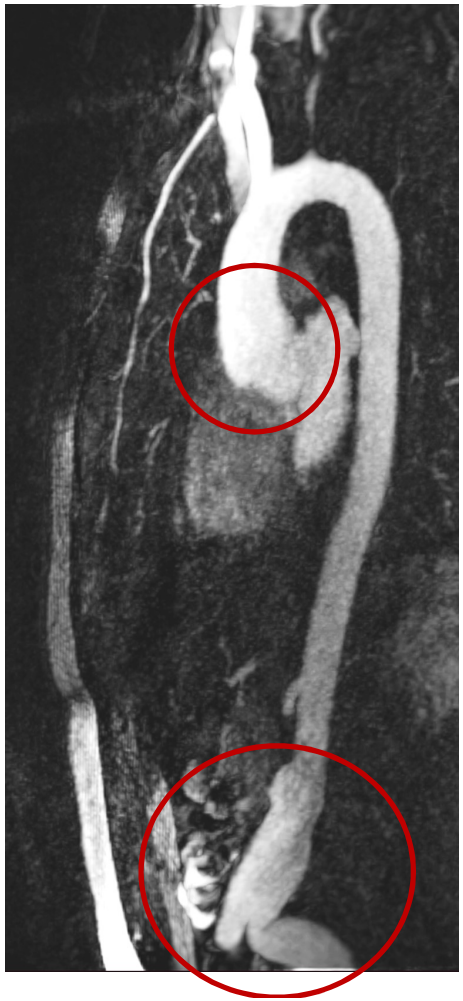
The aortic root ratio (ARR) of observed (Aorta O) to expected (Aorta E) aortic root diameters can be calculated by dividing the observed by the expected diameter.

$$ARI = \frac{AortaO}{BSA}$$

$$\text{O-E ARR} = \frac{\text{Aorta O}}{\text{Aorta E}}$$

$$\text{Z Score} = \frac{\text{Aorta O} - \text{Aorta E}}{SD}$$

Vyšetřit celou aortu!!!



Syndromy spojené s dilatací/disekcí hrudní aorty

Table 7. TAA Syndromes and Conditions Attributable to a Heritable or Genetic Cause

Condition	Gene	Clinical Features
Syndromic HTAD*		
Marfan syndrome	*FBN1*	Aortic root aneurysm, aortic dissection, TAA, MVP, long bone overgrowth, arachnodactyly, dolichostenomelia, scoliosis, pectus deformities, ectopia lentis, myopia, tall stature, pneumothorax, dural ectasia
Loeys-Dietz syndrome	*TGFBR1, TGFBR2, SMAD3,† TGFB2, TGFB3*	TAA, branch vessel aneurysms, aortic dissection, arterial tortuosity, MVP, craniosynostosis, hypertelorism, bluish sclera, bifid/broad uvula, translucent skin, visible veins, club feet, dural ectasia, and premature osteoarthritis and peripheral neuropathy†
Vascular Ehlers-Danlos syndrome	*COL3A1*	TAA, AAA, arterial rupture, aortic dissection, MVP, bowel and uterine rupture, pneumothorax, translucent skin, atrophic scars, small joint hypermobility, easy bruising, carotid-cavernous fistula
Arterial tortuosity syndrome	*SLC2A10*	Tortuous large and medium sized arteries, aortic dilation, craniofacial, skin and skeletal features
Shprintzen-Goldberg syndrome	*SKI*	Craniosynostosis, skeletal features, aortic dilation
Ehlers-Danlos syndrome with periventricular nodular heterotopia	*FLNA*	X-linked, periventricular nodular heterotopia, TAA, BAV, MV disease, PDA, VSD, seizures, joint hypermobility
Meester-Loeys syndrome	*BGN*	X-linked, TAA, aortic dissection, MV disease
LOX-related TAA	*LOX*	TAA, BAV, aortic dissection, Marfanoid habitus in some
Smooth muscle dysfunction syndrome	*ACTA2*	TAA, moyamoya-like cerebrovascular disease, pulmonary hypertension, pulmonary disease, hypoperistalsis, hypotonic bladder, congenital mydriasis[11]

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Syndromy spojené s dilatací/disekcí hrudní aorty

Condition	Gene	Clinical Features
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Marfan syndrome	*FBN1*	Aortic root aneurysm, aortic dissection, TAA, MVP, long bone overgrowth, arachnodactyly, dolichostenomelia, scoliosis, pectus deformities, ectopia lentis, myopia, tall stature, pneumothorax, dural ectasia
Loeys-Dietz syndrome	*TGFBR1, TGFBR2, SMAD3,† TGFB2, TGFB3*	TAA, branch vessel aneurysms, aortic dissection, arterial tortuosity, MVP, craniosynostosis, hypertelorism, bluish sclera, bifid/broad uvula, translucent skin, visible veins, club feet, dural ectasia, and premature osteoarthritis and peripheral neuropathy†
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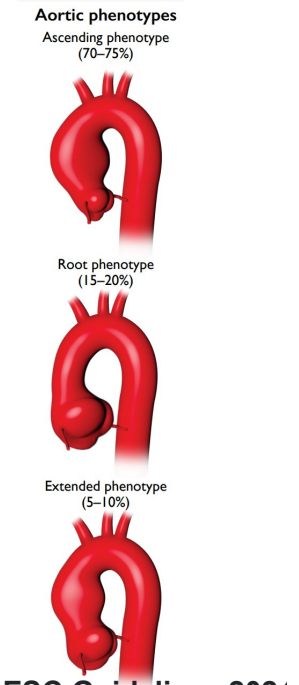
Bikuspidální aortální chlopeň

- 1% populace (♂2%, ♀ 0.5%), ♂:♀ = 2:1 nebo 3:1
- V.s. vazba na X chromozóm
- Riziko výskytu v rodině – 10% pravděpodobnost
- Screening pokrevních příbuzných !!
- Dysfunce chlopně ± Progresívní dilatace asc. aorty
- Riziko disekce 1.5 vs. riziko IE 6% v průběhu života



ESC Guidelines 2024

Indikace preventivní operace:

- **≥55 mm** *(I, B-NR)*
- **≥10 cm2/m (plocha aorty/výška)** *(II, B-NR)*
- **50-54 a rizikové faktory** *(II, B-NR)*
- **≥45 mm při operaci AV** *(II, B-NR)*

RA dissekce
Růst aorty ≥ 3 mm/rok
Koarktace
Dilatace kořene aorty
± aortální regurgitace (ESC 2021)

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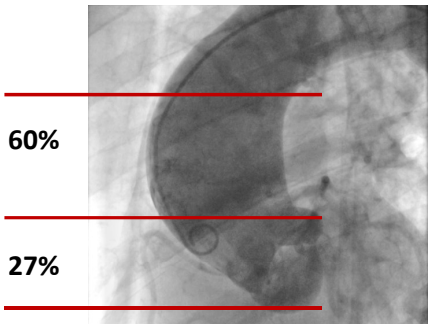
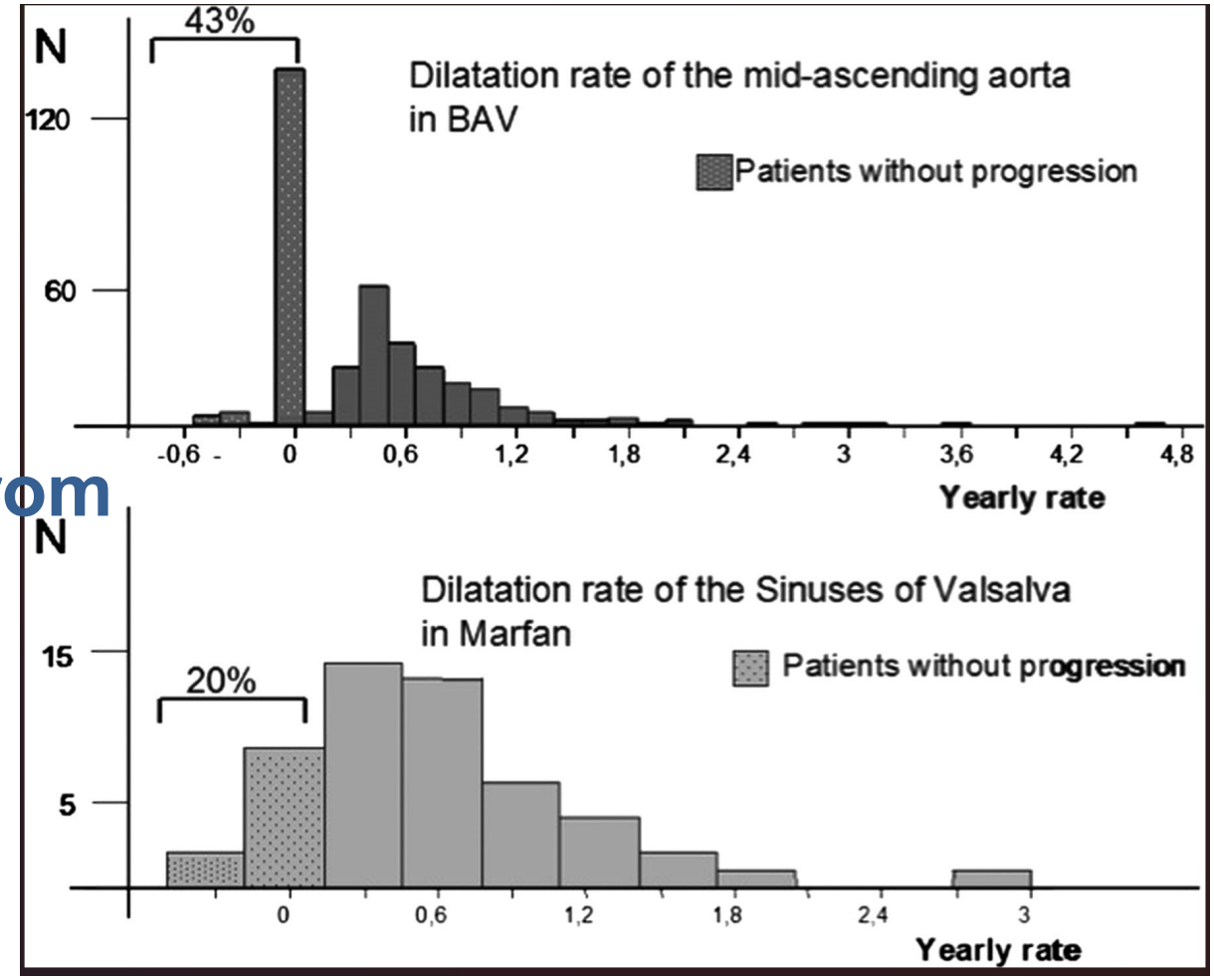
Rychlost růstu prox. asc. aorty

- **Bikuspidální aortální chlopeň**





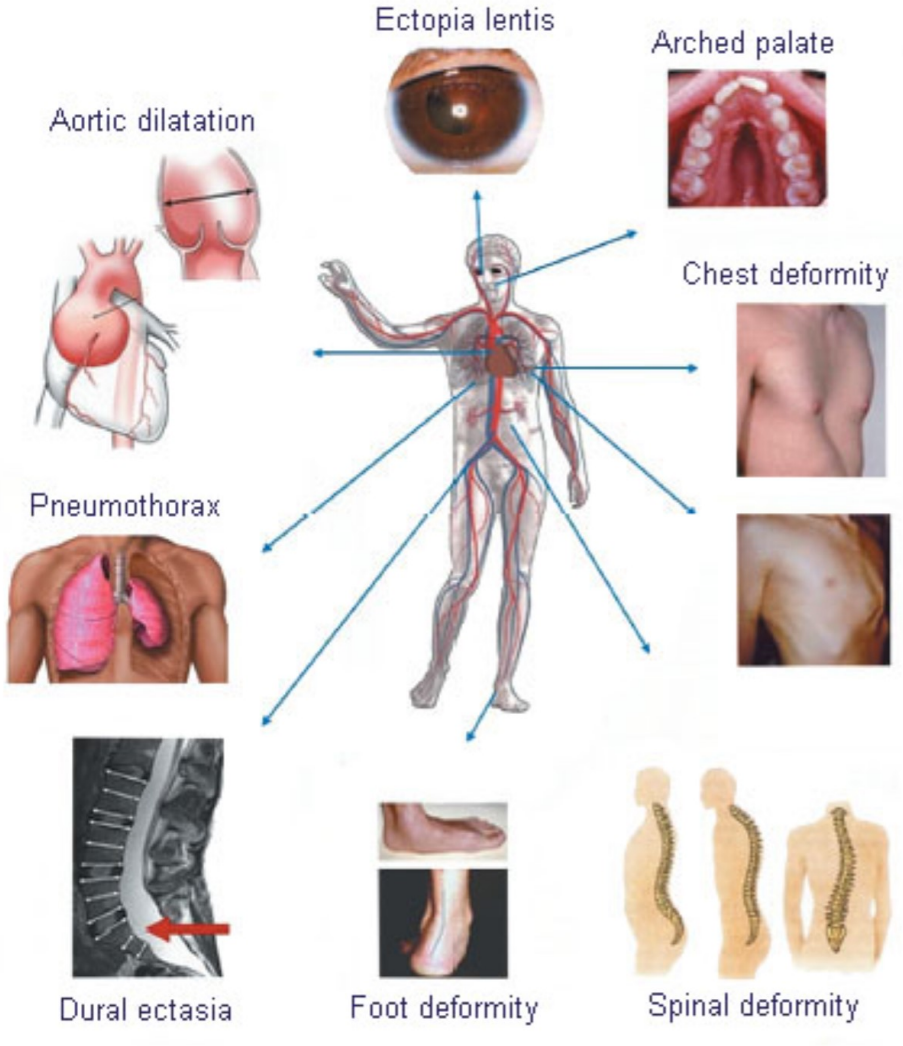
- **Marfanův syndrom**

Rychlost růstu aorty
Norm 0.08 mm/rok
Deg. 0.20 mm/rok
BAV 0.42 mm/rok
MS 0.49 mm/rok

Detaint et al. Heart 2014

Marfanův syndrom

- **Prevalence 1:5000**
- **Mutace ve FBN 1**



https://marfan.sk/en/marfanov-syndr%C3%B3m/symptoms

Marfanův syndrom

- **Klinická diagnostika – Ghent kritéria a kalkulátor**

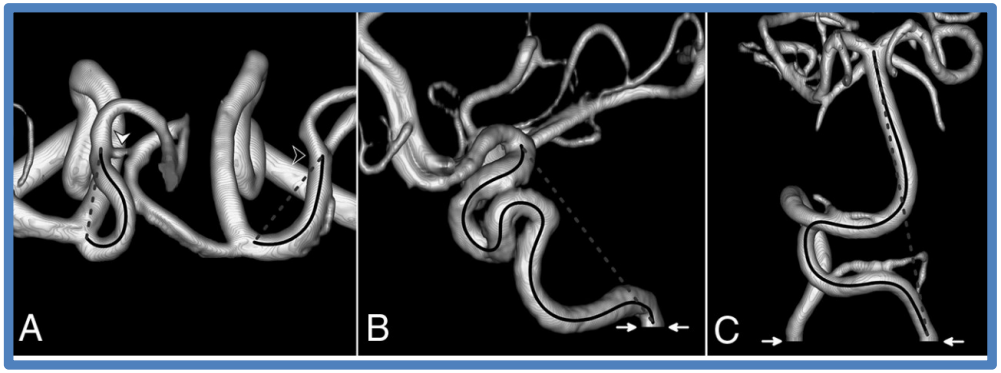
Scoring of systemic features in Marfan syndrome (Loeys et al., 2010).

Systemic feature	Score
● Wrist sign	1
● Thumb sign	1
● Wrist AND thumb signs	3
● Pectus carinatum deformity	2
● Pectus excavatum or chest asymmetry	1
● Hindfoot deformity	2
● Pes planus	1
● Pneumothorax	2
● Dural ectasia	2
● Protrusio acetabuli	2
● Reduced upper segment/lower segment ratio AND increased arm span/height AND severe scoliosis	1
● Scoliosis OR thoracolumbar kyphosis	1
● Reduced elbow extension	1
● Facial features (at least 3 of 5): dolichocephaly, enophthalmos, downslanting palpebral fissures, malar hypoplastia, retrognathia	1
● Skin striae	1
● Myopia >3 diopters	1
● Mitral valve prolapse (all types)	1

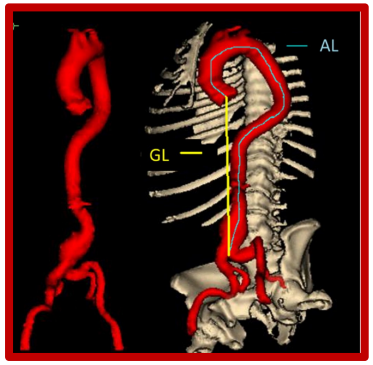
https://marfan.org/dx/score/

Marfanův syndrome

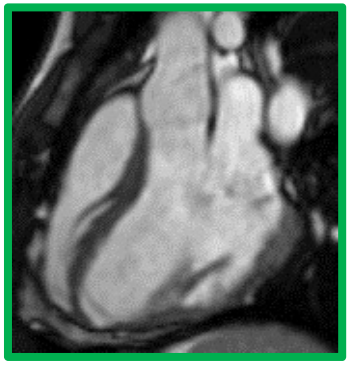
- Mitrální prolaps
- Dilatovaná kardiomyopatie
- Extraaortální cévní malformace



MRI - LDS LDS MS



MRI - MS



MAD u MS

AJNR Am J Neuroradiol 41:1916–22 Oct 2020

R. Franken et al. Int J Card 2015

Follow-up u MS

TTE – klíčová metoda

2. vyšetření za 6 měsíců, TTE dále po 6-12M

MRI (nebo CT) celé aorty vstupně a dále za 1-2(5) roky

- **BB a/nebo ARB – v maximální tolerované dávce**
- **Kontrola TK ≤120/80 – self-monitoring**
- **Profylaktický chirurgický výkon**

  ≥50 mm ***(I, B-NR)***

  ≥45 mm a rizikové faktory ***(II, B-NR)***

  ≥10 cm2/m (plocha aorty/výška) ***(II, B-NR)***

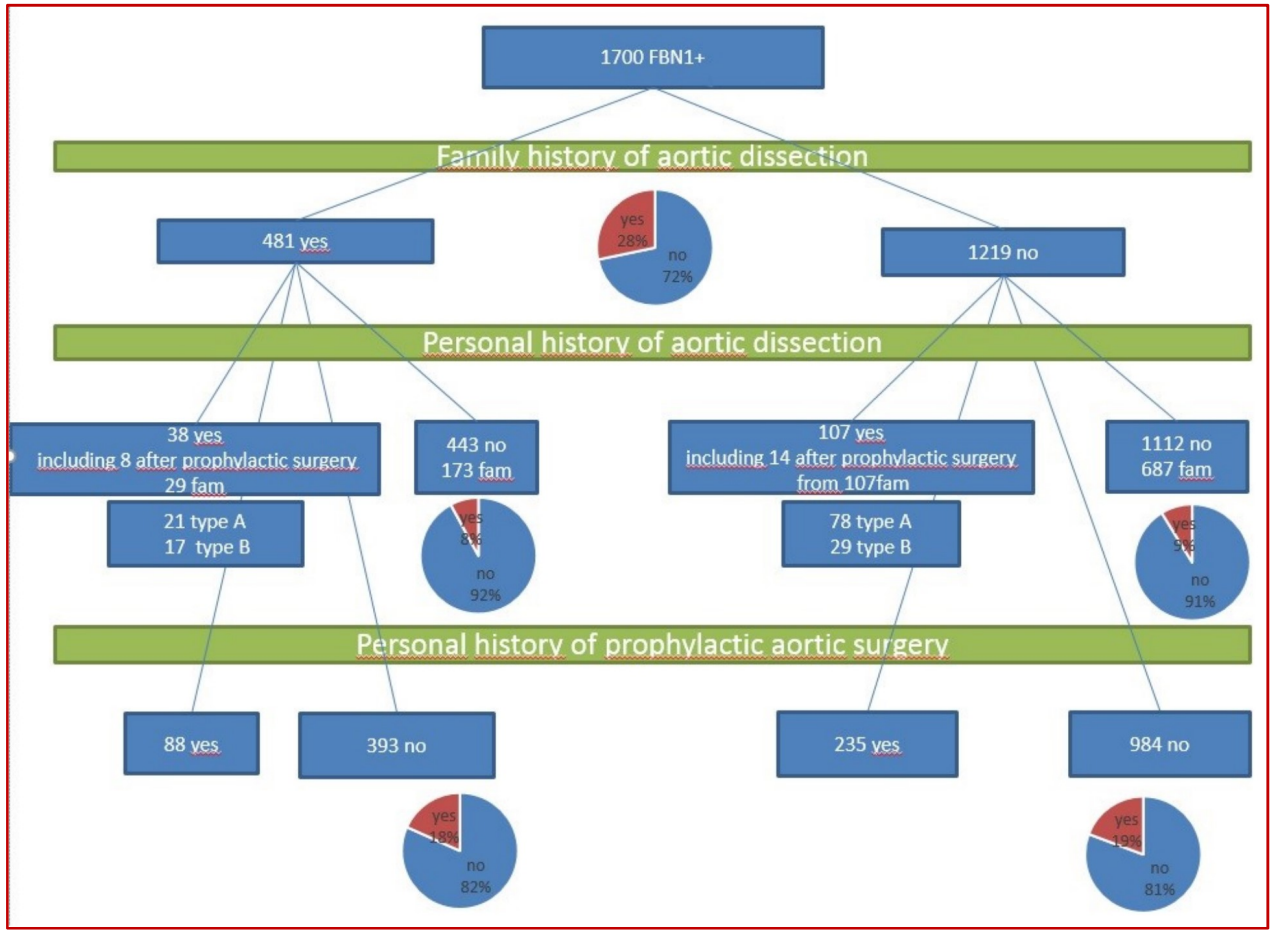
Table 10. Features Associated With Increased Risk of Aortic Complications in Marfan Syndrome

Family history of aortic dissection **Při rozměru <50mm**
Rapid aortic growth (≥0.3 cm/y)
Diffuse aortic root and ascending aortic dilation[14]
Marked vertebral arterial tortuosity[15]

Rezistentní art. hypertenze

2022 ACC/AHA Aortic Disease Guideline, Circulation 2022
ESC Guidelines 2024

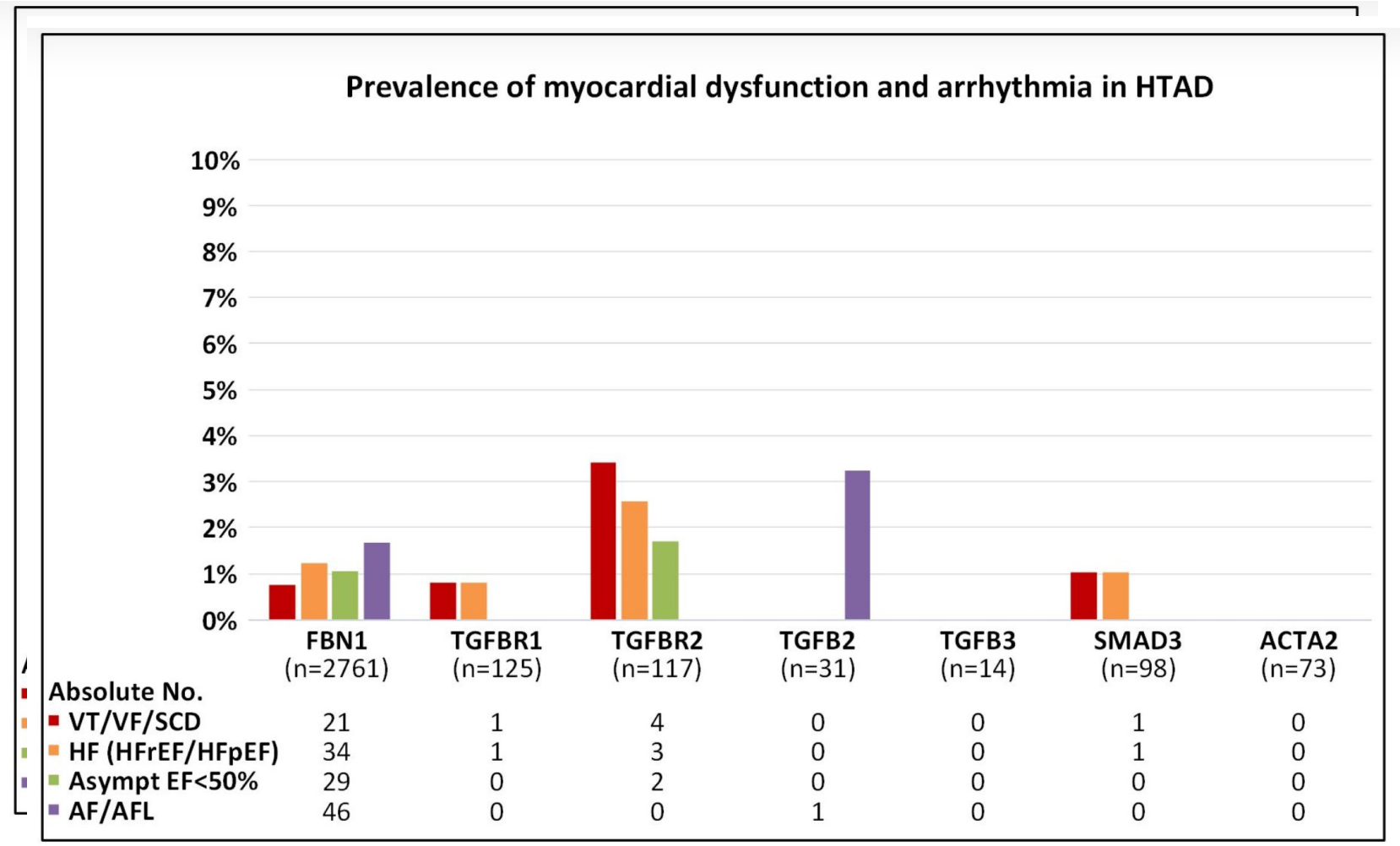
RA dissekce není rizikovým faktorem dissekce aorty u pacientů s mutací FBN 1



M Tchitchinadze, G Jondeau et al.Hospital Bichat-Claude Bernard - Paris - France 2021

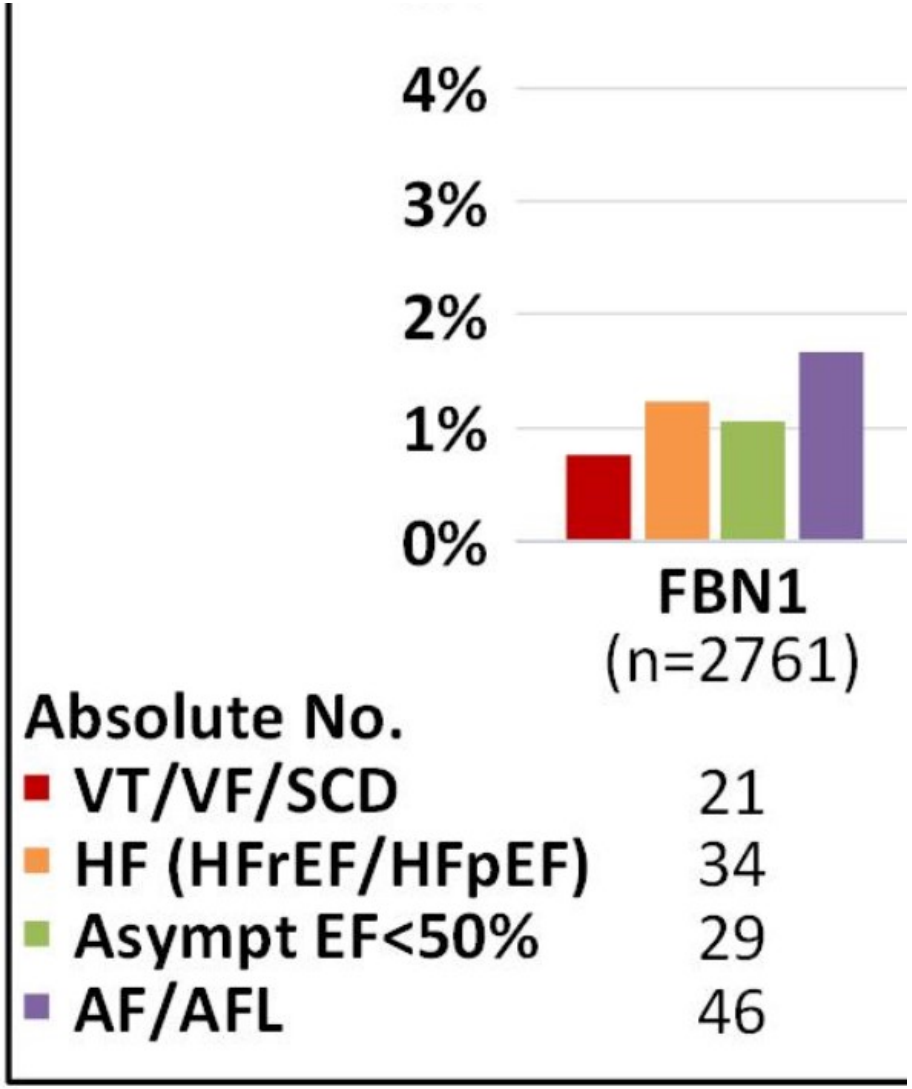
Dysfunkce myokardu a arytmie u HTAD

- 3219 pacientů v 9ti centrech



ESC 202

Dysfunkce myokardu a arytmie u HTAD



A. Demolder et al. ESC 202

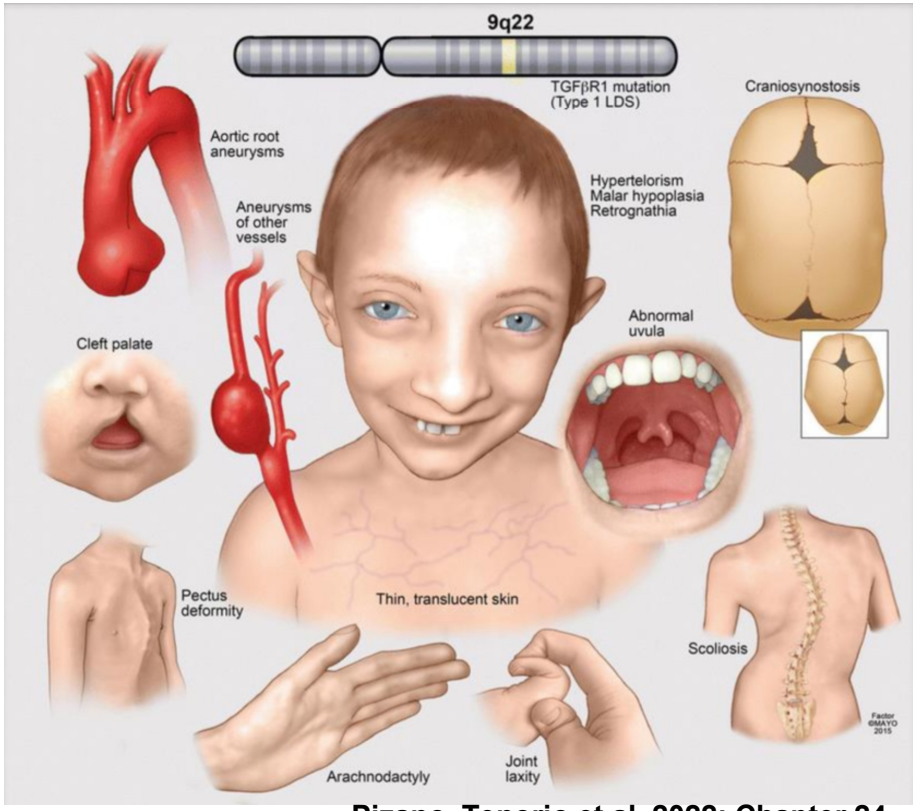
Loeys-Dietz syndrom

- **Cca 1:100 000**
- **Dilatace/disekce aorty**
- **Výrazná točitost tepen**

Table 1 LDS classification

LDS type (proposed)	Gene symbol	Other disorders reported
LDS 1	*TGFBR1*	TAAD (previously, LDS 1a, 1b, 2a, 2b)
LDS 2	*TGFBR2*	TAAD, MFS2 (previously LDS 1a, 1b, 2a, 2b)
LDS 3	*SMAD3*	Aneurysms-osteoarthritis syndrome
LDS 4	*TGFB2*	Aneurysm, aortic and cerebral, with arterial tortuosity and skeletal manifestations

MacCarrick G et al. Genet Med 2014



Pizano, Tenorio et al. 2022: Chapter 24

Follow-up u LDS

TTE a MRI hrudník-pánev (CT)

- **2. vyšetření za 6M, dále á 6-12M při dilataci**
- **MRI (nebo CT) hrudník-pánev á 24M u normálního nálezu.**
- **MRI (nebo CT) krčních a intrakr. tepen á 12M až 36M**

- **<u>BB a/nebo ARB</u> – v maximální tolerované dávce**

- **<u>Profylaktický chirurgický výkon</u>**
- **≥45 mm** ***(I, B-NR)***

COR	LOE (references)	Genetic Variant	Presence of High-Risk Features*	Aortic Diameter (cm)
1	C-LD[2]	*TGFBR1*	No	≥4.5
1	C-LD[2]	*TGFBR2*	No	≥4.5
2b	C-EO[2]	*TGFBR1*	Yes	≥4.0
2a	C-LD[1,2]	*TGFBR2*	Yes	≥4.0
2a	C-EO[13,16]	*SMAD3*	–	≥4.5†
2b	C-EO[5-7]	*TGFB2*‡	–	≥4.5†
2b	C-EO[9,23]	*TGFB3*	–	≥5.0†

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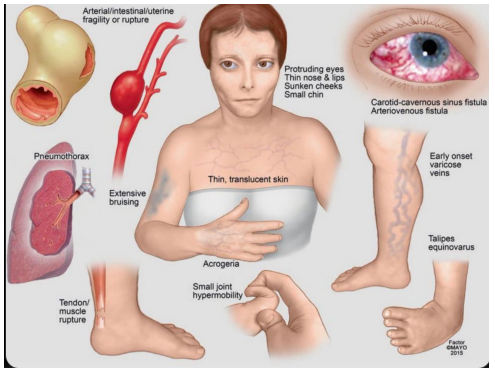
Ehlers-Danlos syndrome

- 1:50-100 000
- Mutace v COL3A1
- Vaskulární forma – křehkost tepen



X.com

TTE a MRI hrudník-pánev (CT)

2. vyšetření za 6M, dále á 6-12M při dilataci

MRI (nebo CT) hrudník-pánev á 24M u normálního nálezu

- BB (celiprolol) a/nebo ARB – v maximální tolerované dávce

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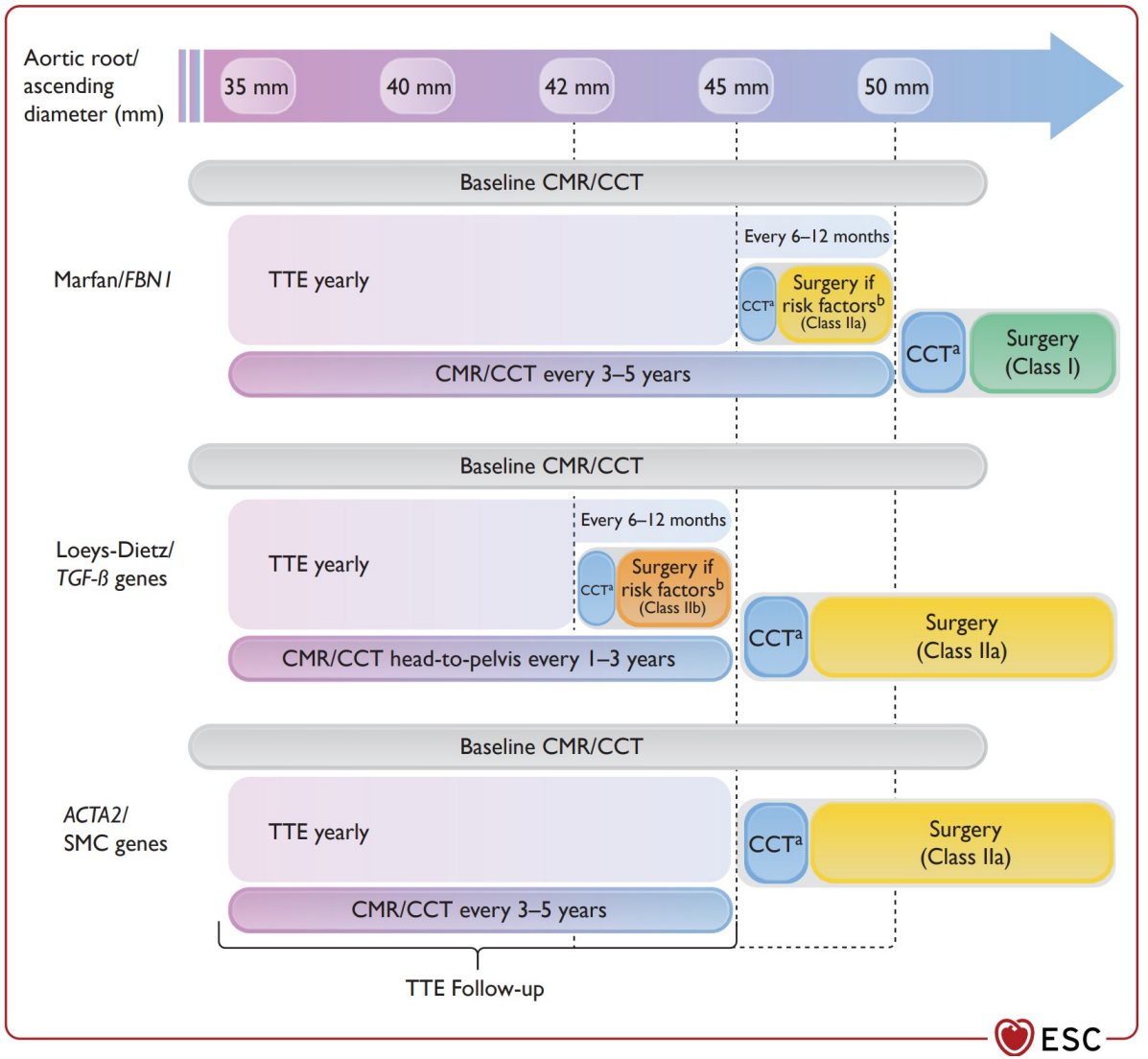
Imaging follow-up



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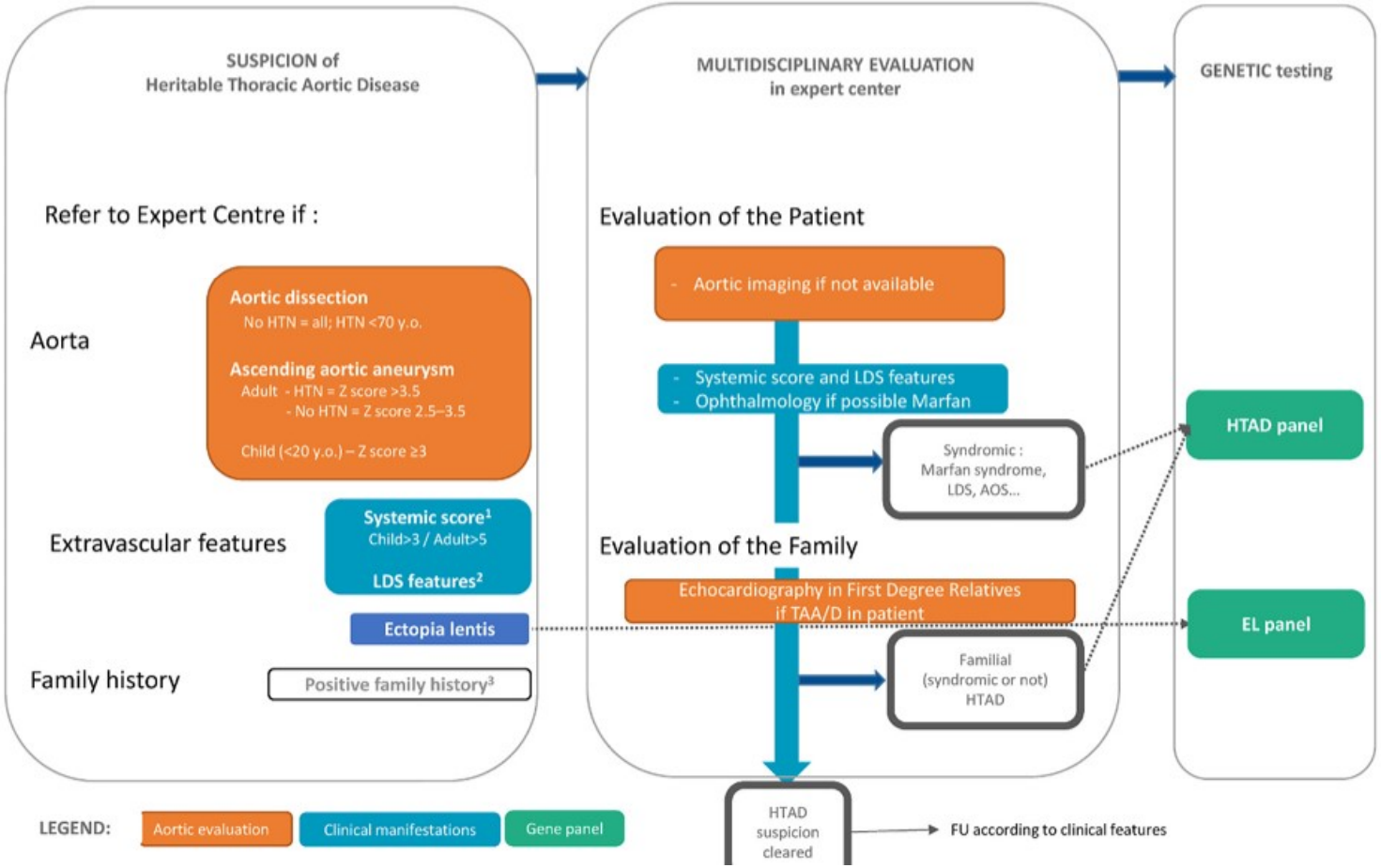
Specializovaná centra dětské a dospělé medicíny



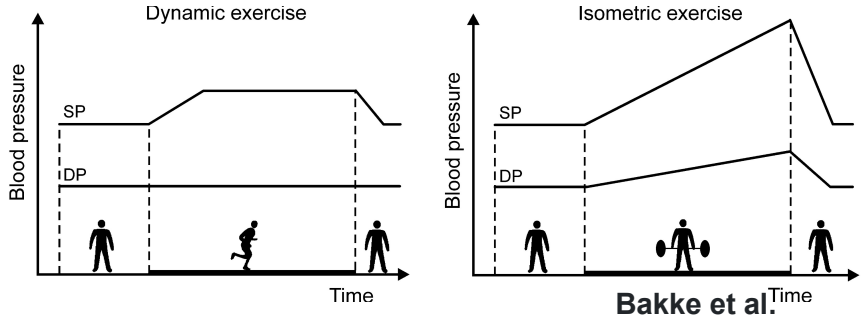
VASCERN. European Journal of Medical Genetics 2022

Režimová opatření

- Přísná kontrola TK (≤120/80) self-monitoring
- Betablokátory a/nebo ARB
- Lépe se vyhnout: ca blokátorům, dekongestia, laxativa, sumatriptan, amfetamin, fluorochinolony
- Vhodná pravidelná dynamická zátěž (lehká až střední)
- NE!! těžká břemena, silové a kontaktní sporty, skoky

♀

- Plánované těhotenství
- Sledování v těhotenství
- Možnost asistované reprodukce
- BB po nepřetržitě, ARB vysadit ihned



Bakke et al. 2007

2022 ACC/AHA Aortic Disease Guideline, Circulation 2022

ESC Guidelines 2024

Děkuji za pozornost

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&
Centrum pro vrozené vady v dospělosti
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