



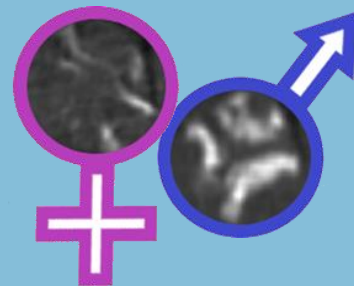
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Molecular & biological mechanisms in valvular heart diseases: insights, innovations & future directions

Marie-Annick Clavel, DVM, PhD, FACC, FAHA, FCCS

Professor – Université Laval (Quebec, Canada)



Disclosures



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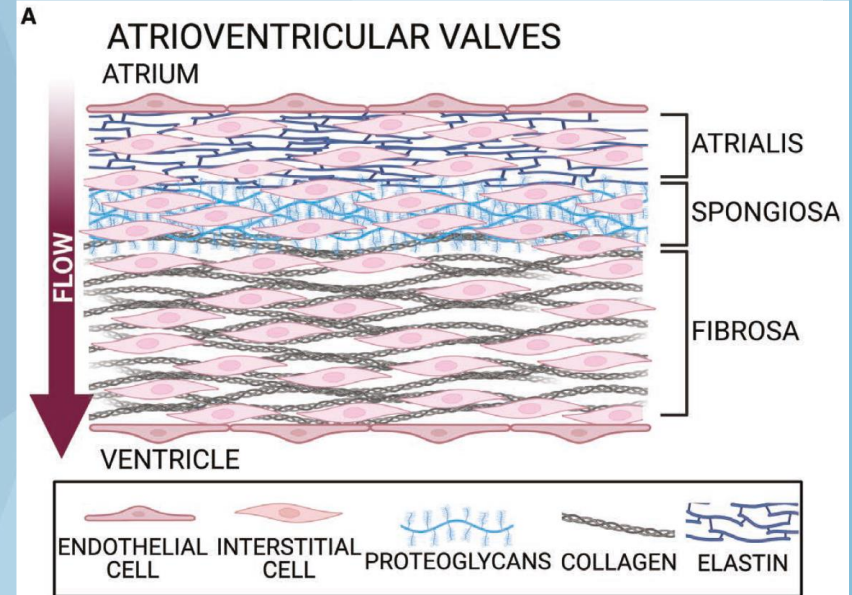
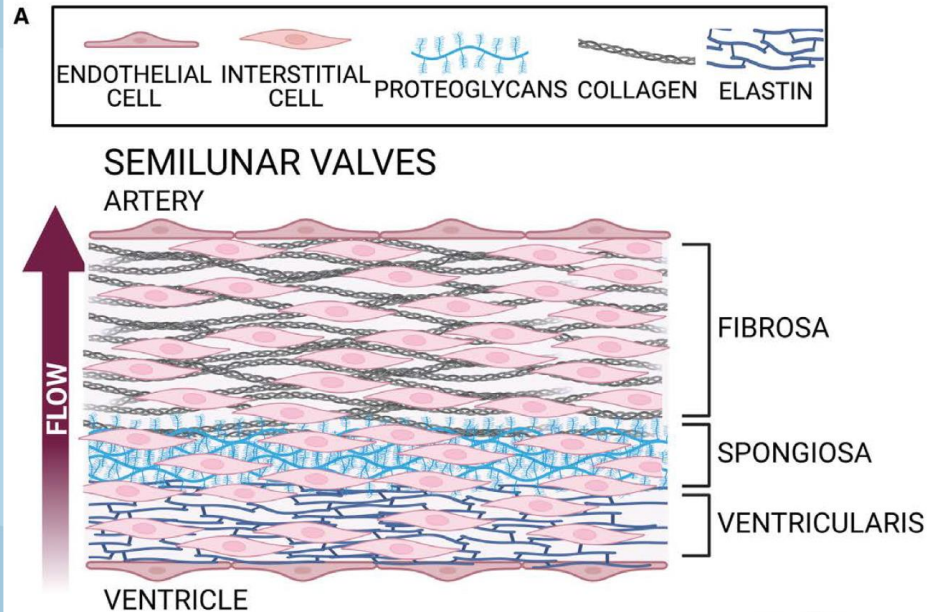
- CT - Core laboratory contract: Edwards Lifesciences; Novartis
- Research grants: Edwards Lifesciences; Medtronic; Pi-Cardiac; Rednvia

VHD are active processes



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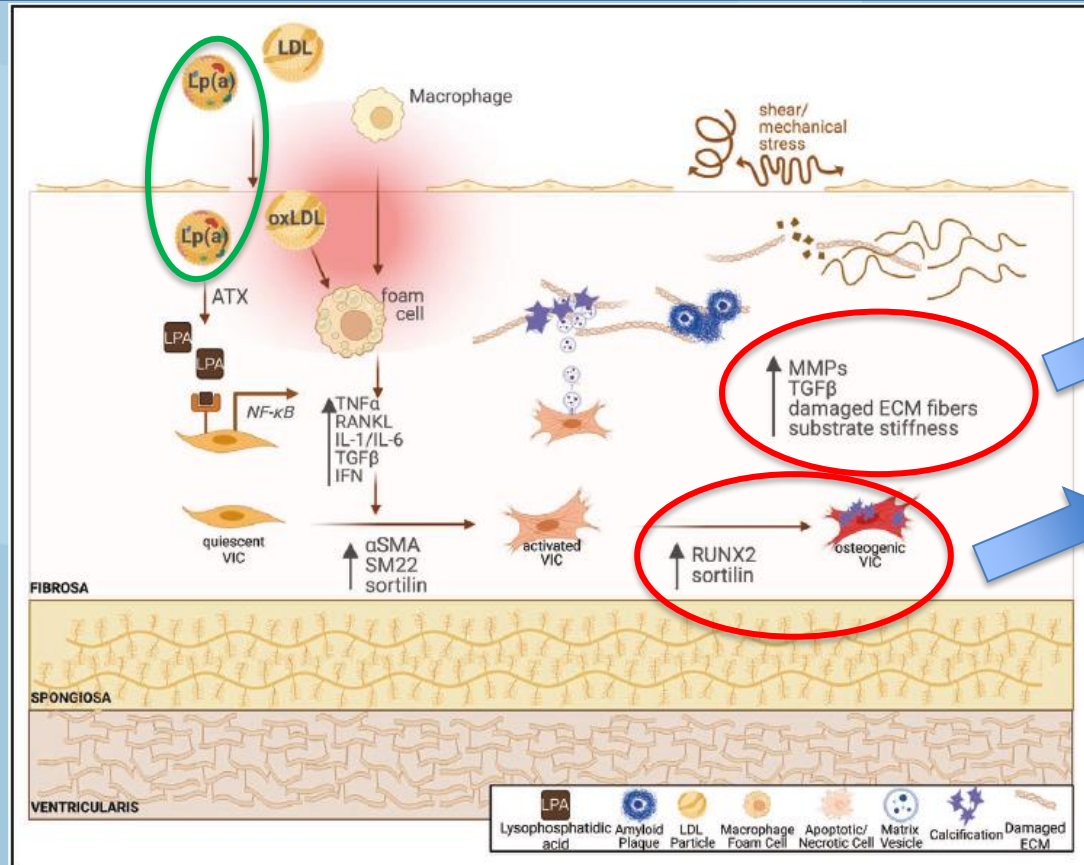


Fibro-calcification in Aortic Valve

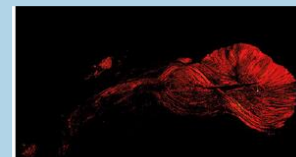


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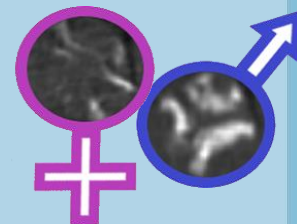
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Women



Men

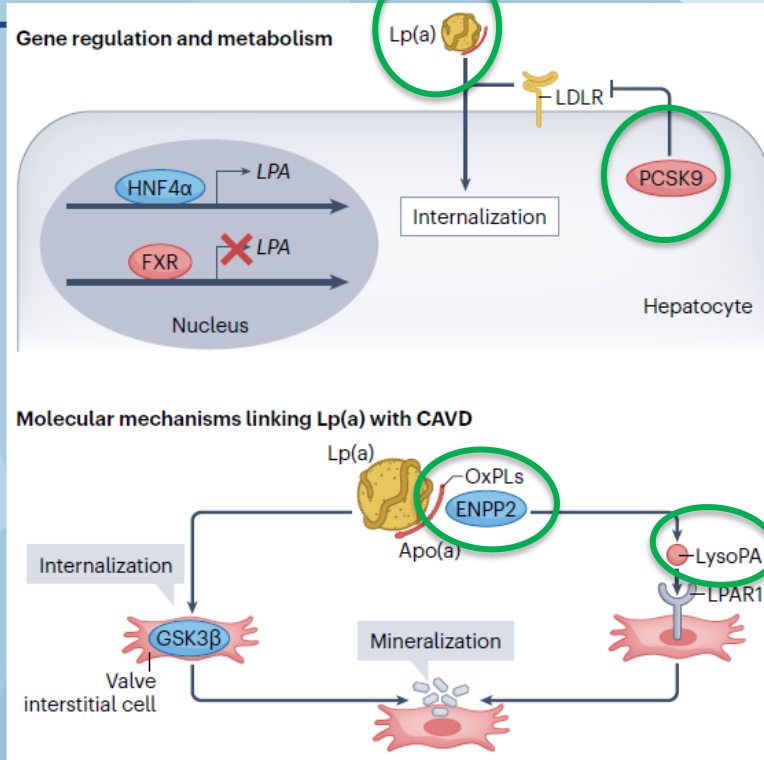


Lipids -Lp(a)



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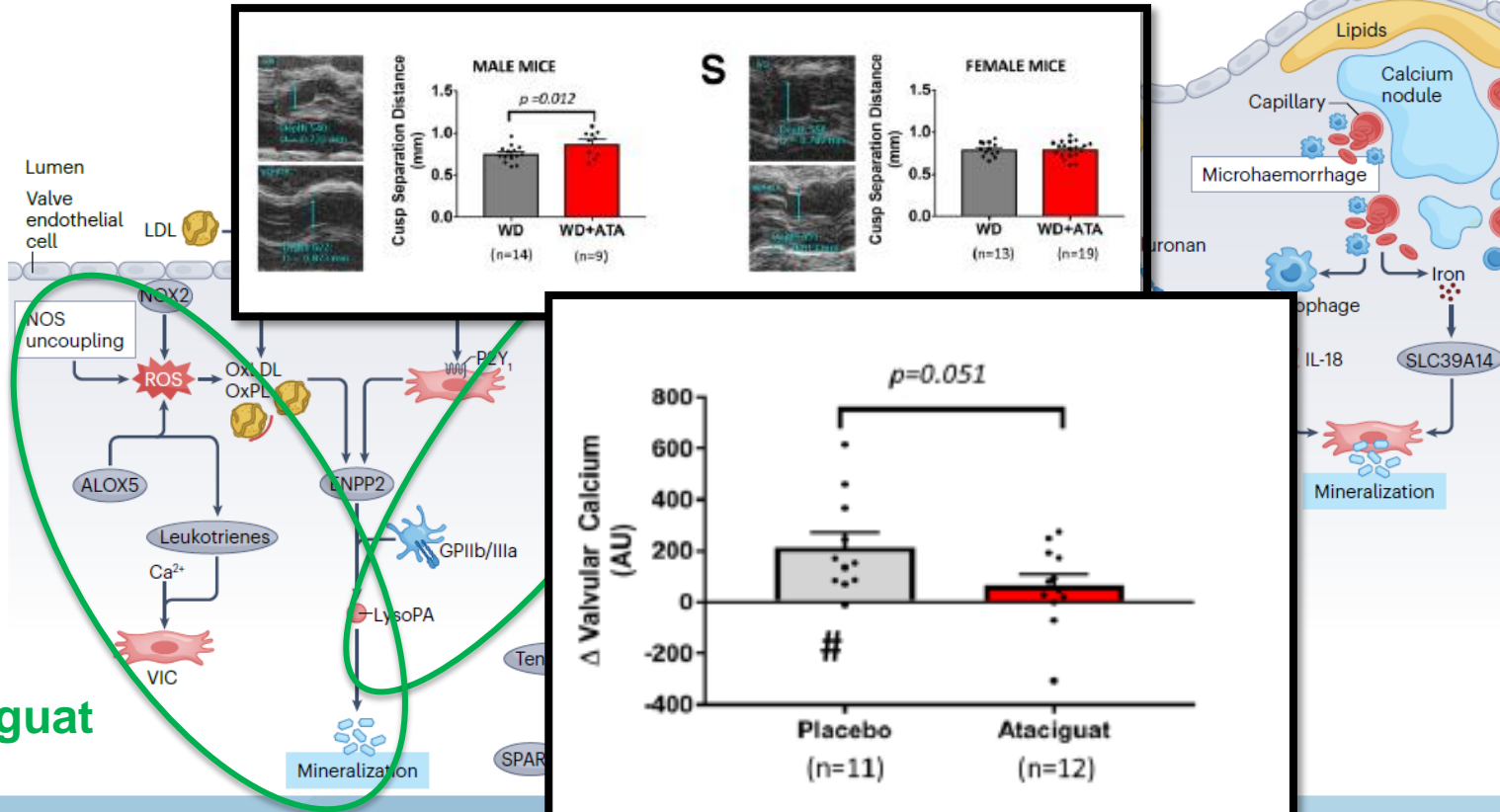
Moncla et al. *Nat Rev Cardiol* . 2023 Aug;20(8):546-559; Thanassoulis et al. *N Engl J Med* 2013;368:503-512; Capoulade et al. *J Am Coll Cardiol* . 2015 Sep 15;66(11):1236-1246

Inflammation, Fibrosis, and Calcification



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Moncla et al. *Nat Rev Cardiol* . 2023 Aug;20(8):546-559; Zhang et al. *Circulation* . 2025 Apr;151(13):913-930

SGLT2i... and also GLP1, Evogliptin...



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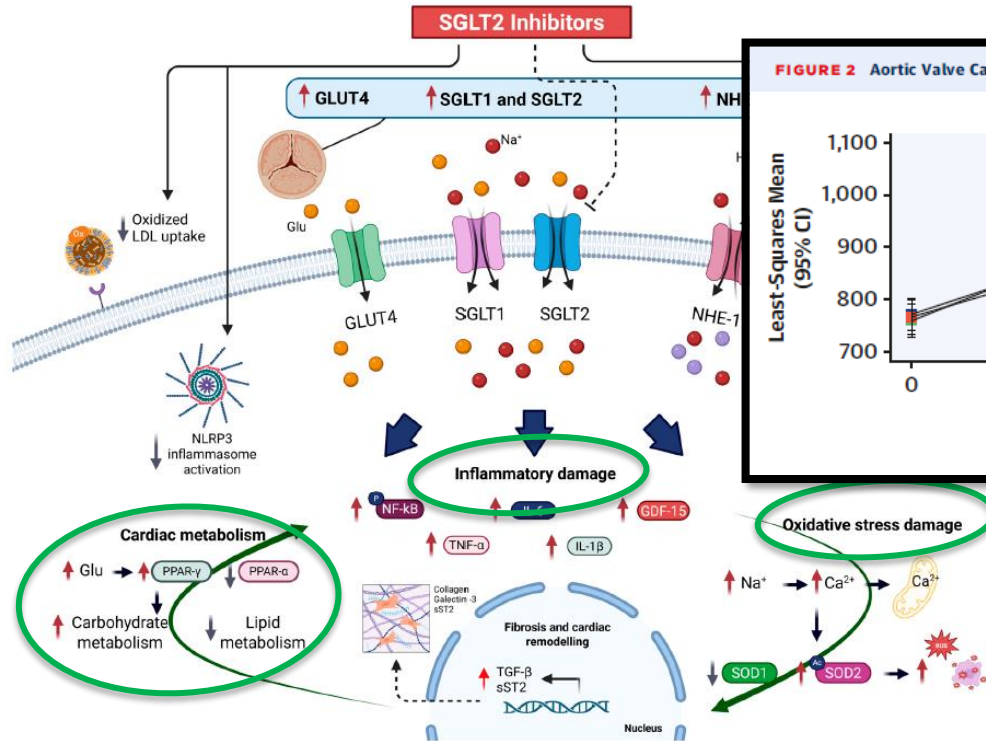
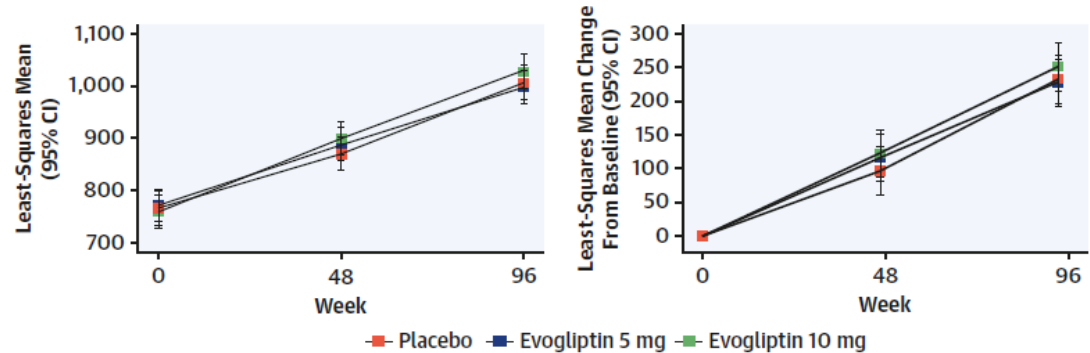


FIGURE 2 Aortic Valve Calcium Volume



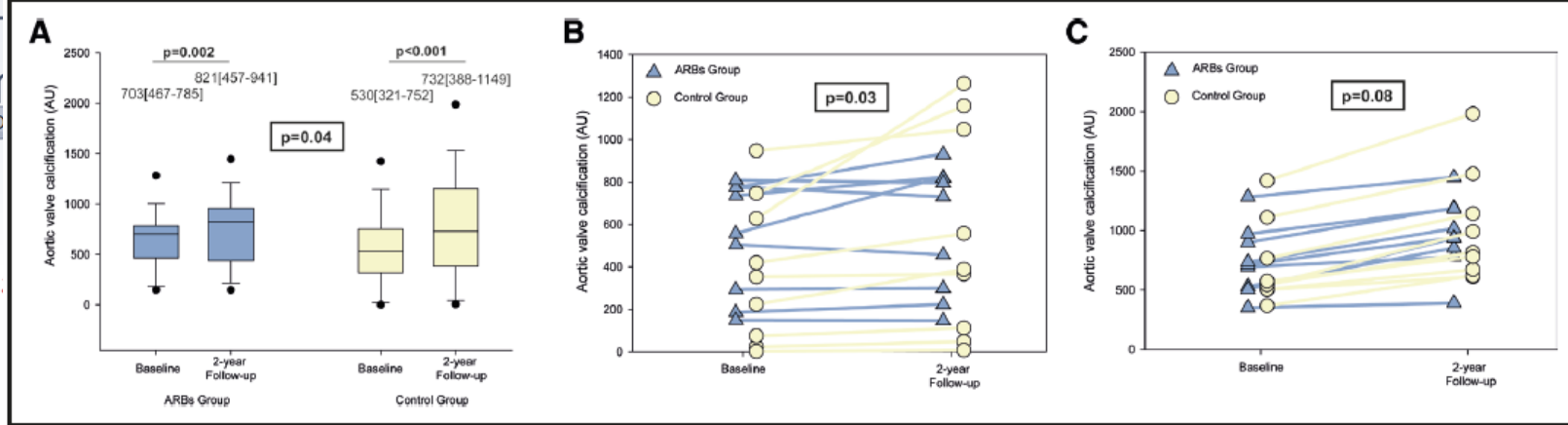
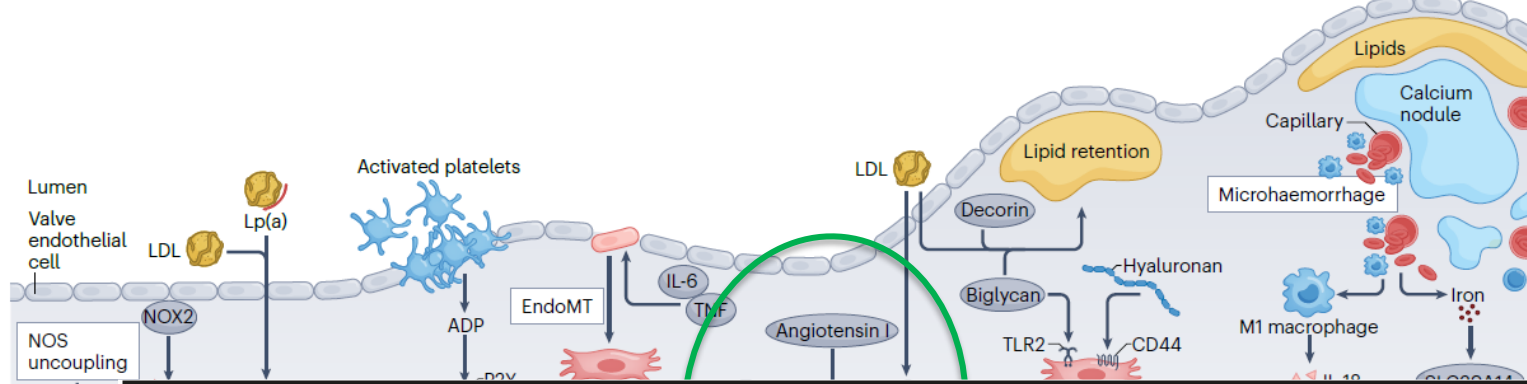
Karakasis et al. *Int J Mol Sci.* 2025 May 8;26(10):4494; Song et al. *J Am Coll Cardiol* . 2024 Sep 17;84(12):1064-1075

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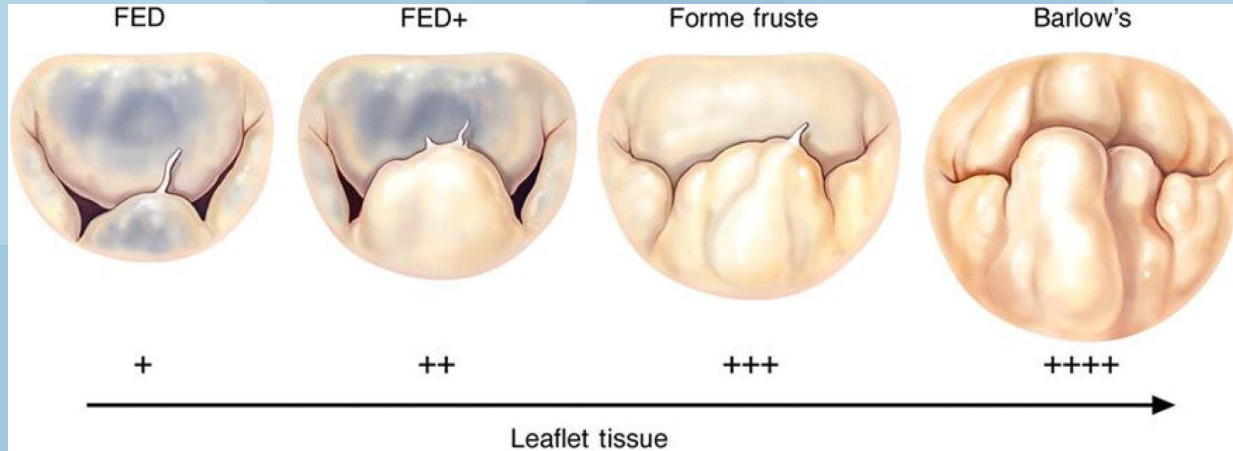
Moncla et al. *Nat Rev Cardiol* . 2023 Aug;20(8):546-559; Demers et al. *Circ Cardiovasc Imaging*. 2025 May;18(5):e017913

Primary Mitral Regurgitation



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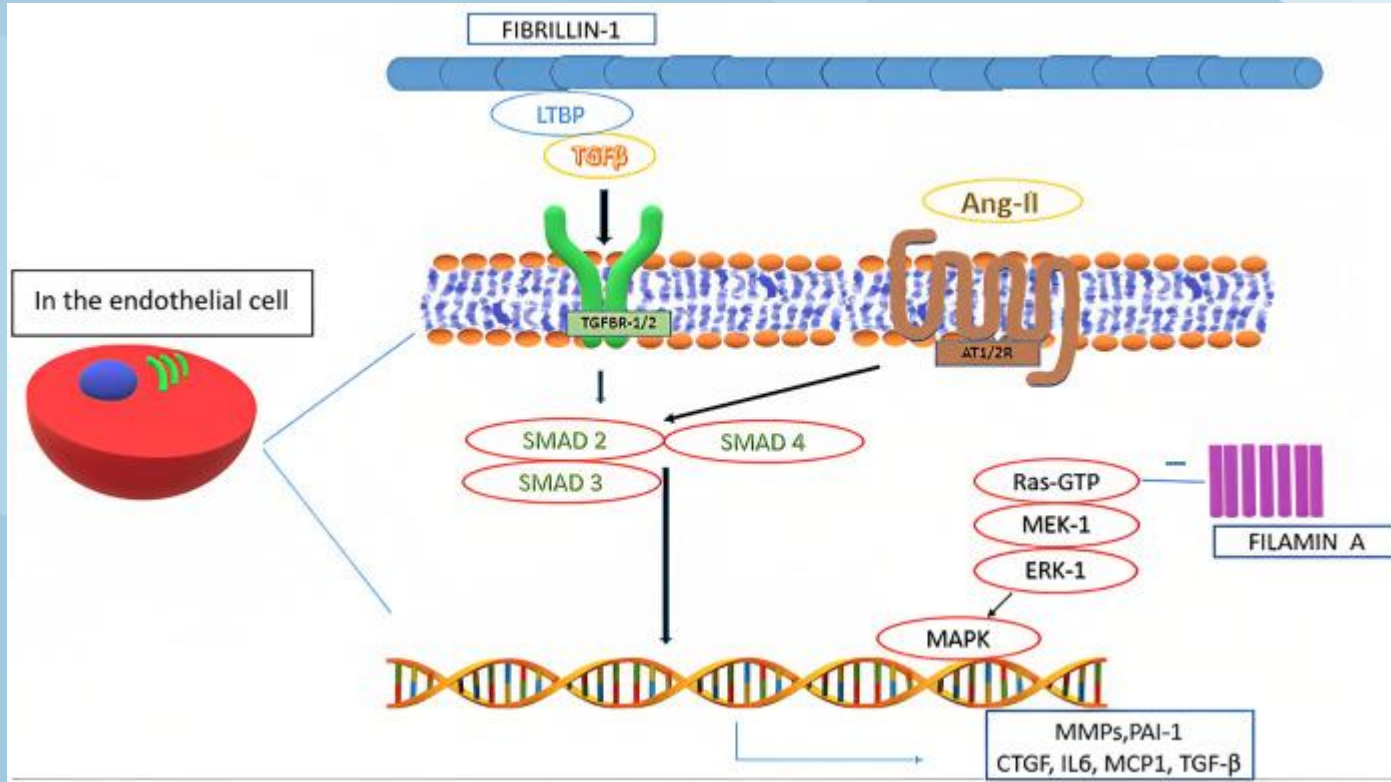


Primary Mitral Regurgitation



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ACE, ARB?

Reduction MR
variable and
inconsistent

Familial Primary Mitral Regurgitation



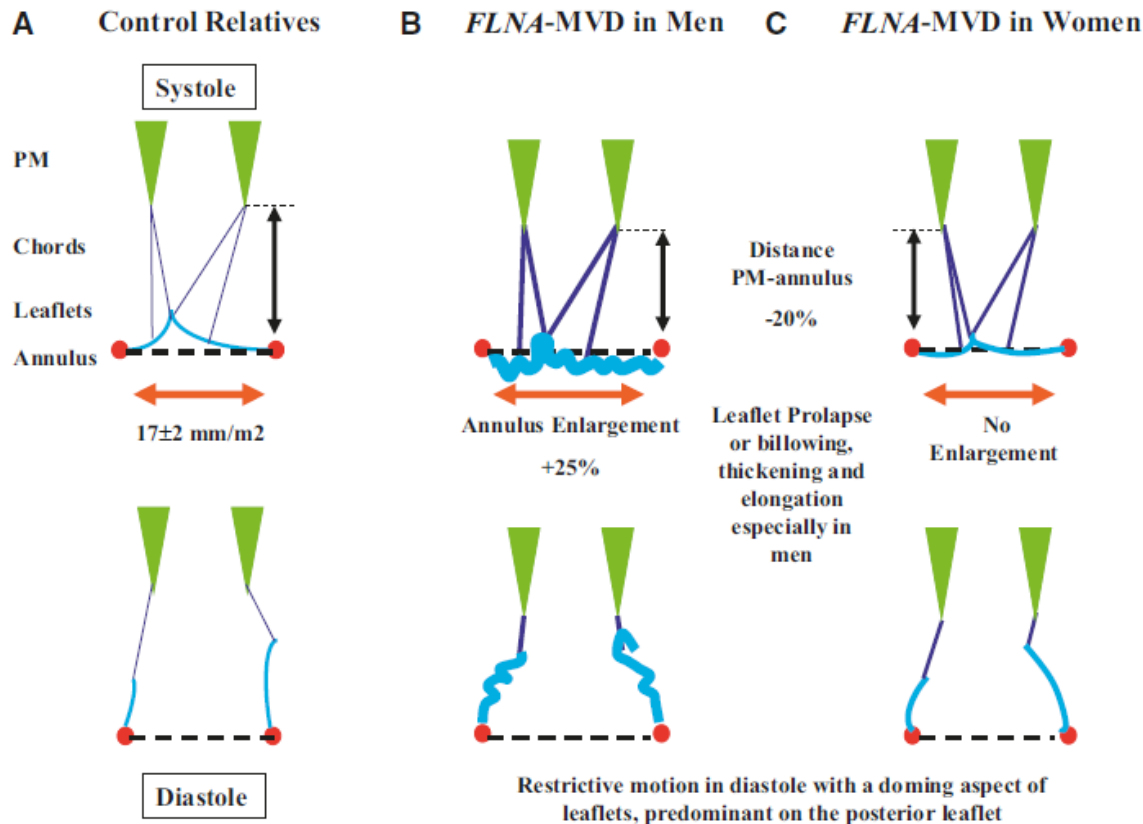
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Filamin-A

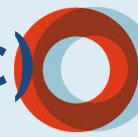
Men: mitral annulus: larger,
mitral leaflets: thickened,
redundant, elongated,
prolapsed in systole

distance papillary muscles
and mitral annulus: lower

Women changes moderate

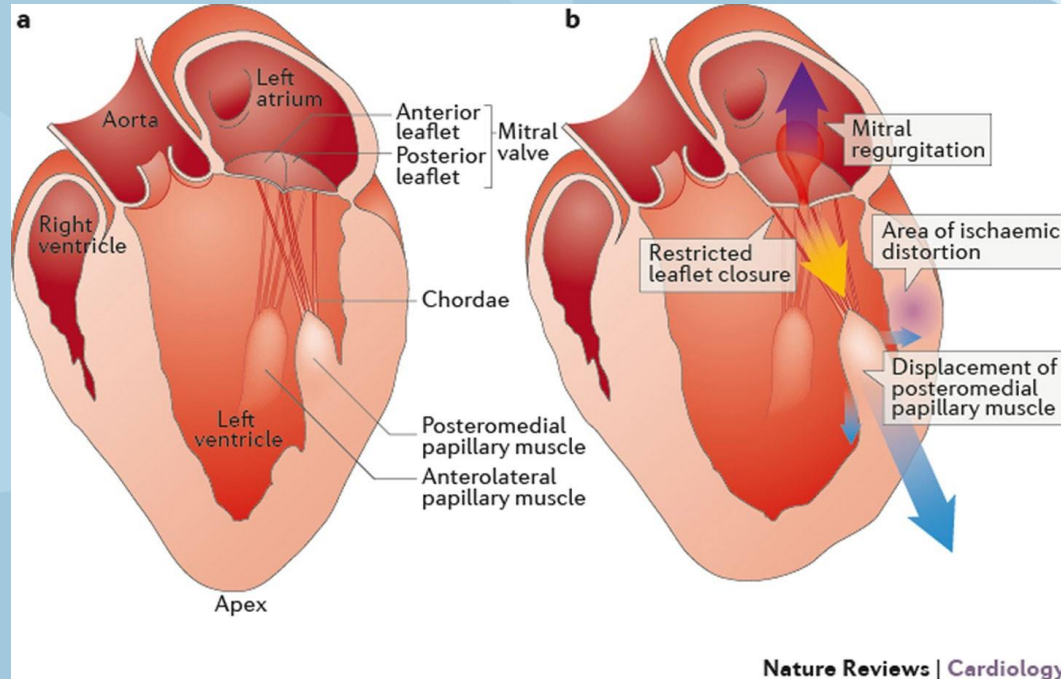


Secondary Mitral Regurgitation (Ischemic)

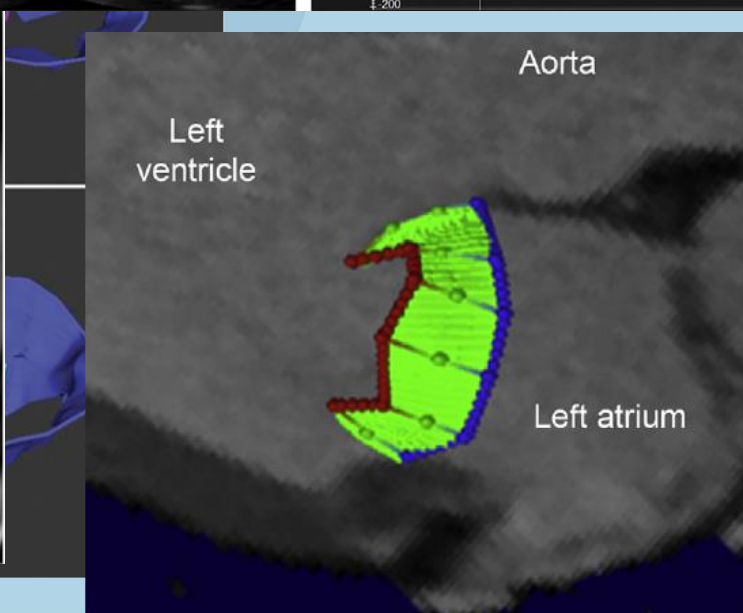
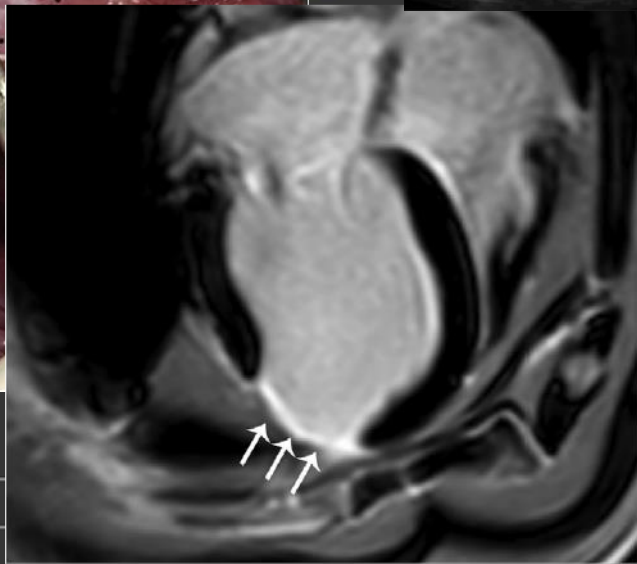
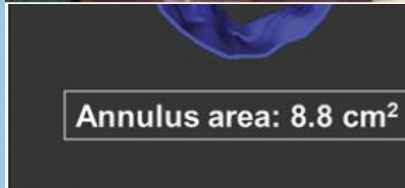
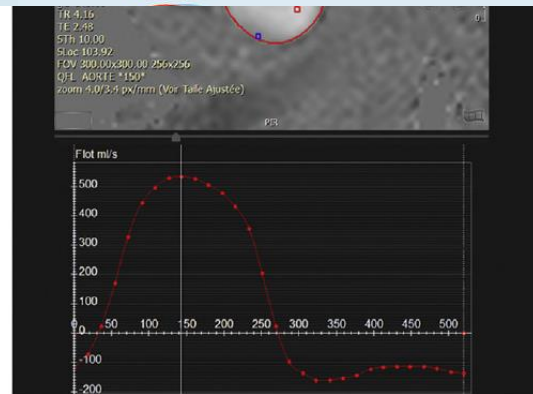
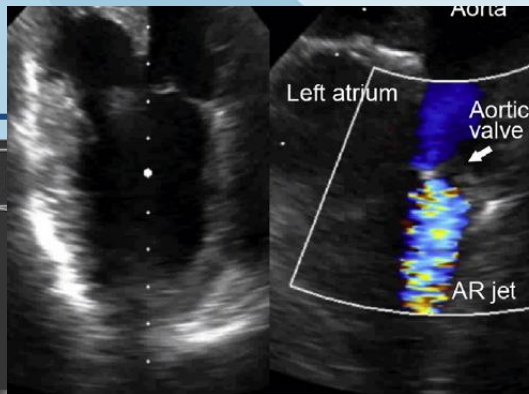
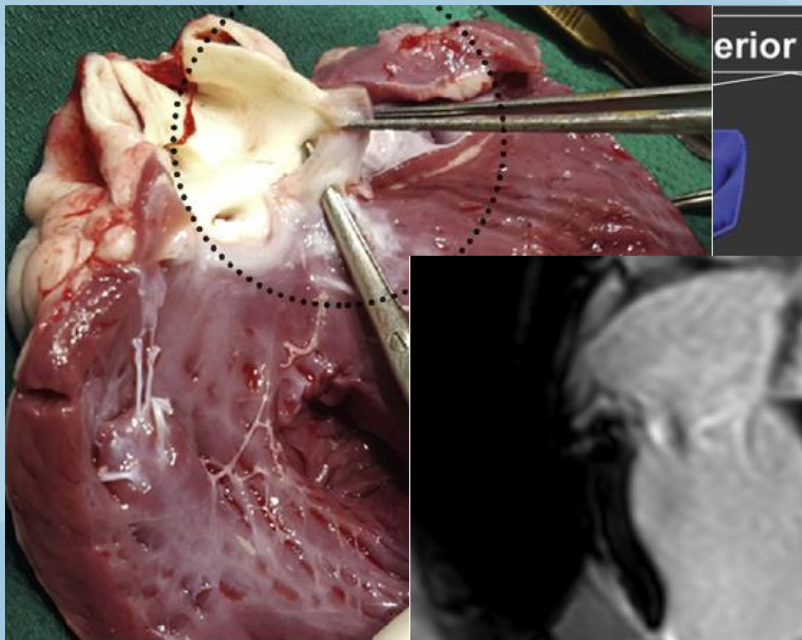


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Only LV... or not?



Impact of MI on mitral leaflet growth



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A

LV End-Diastolic Volume (ml)

300
200
100
0

B

$p = 0.80$

200

$p = 0.69$

C

Mitral Valve Leaflet Area (cm^2)

20
15
10
5

Bas

D

$p = 0.03$

40

$p < 0.01$

E

Leaflet Area/Closure Area

1.6
1.4
1.2
1.0
0.8

Baseline
AR

Follow-Up
AR

Baseline
AR+MI

Follow-Up
AR+MI

$p = 0.02$

F

Leaflet Area/Closure Area
Ratio and Infarct Size

Leaflet Area/Closure Area

1.6
1.4
1.2
1.0
0.8

Infarct Size (g)

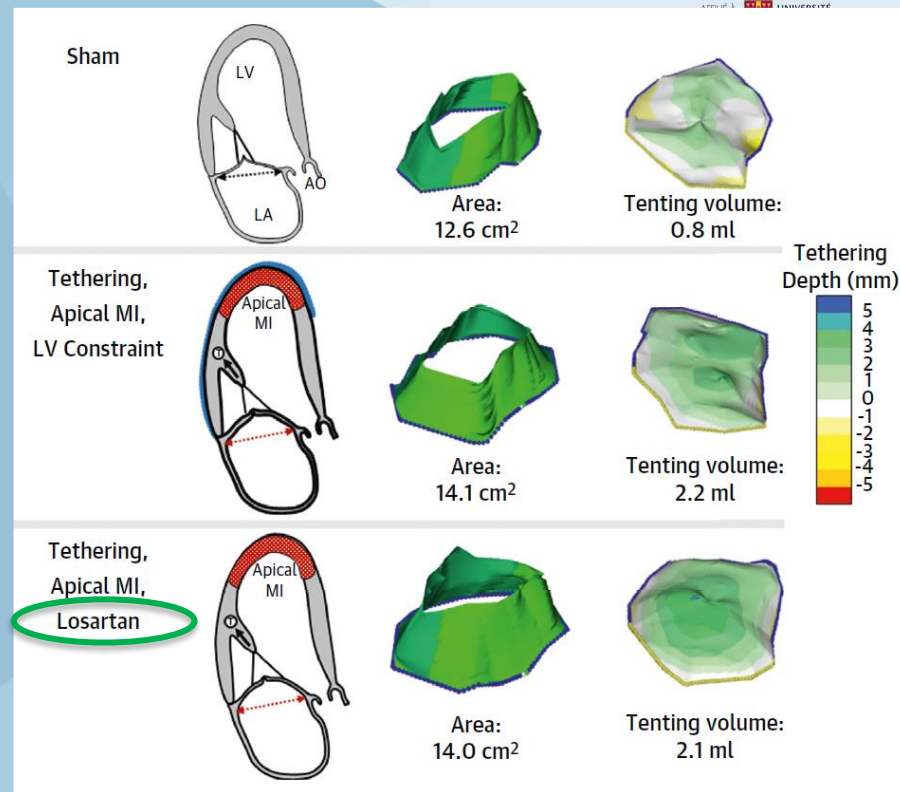
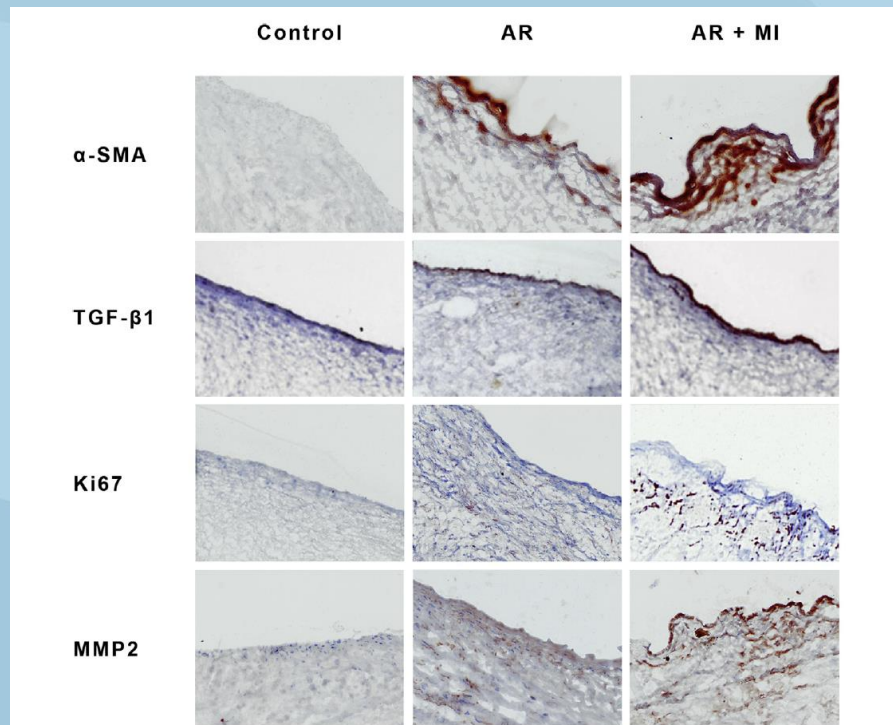
$r = -0.939$
 $p = 0.002$

● CTL ● AR+MI

Impact of MI on mitral leaflet growth



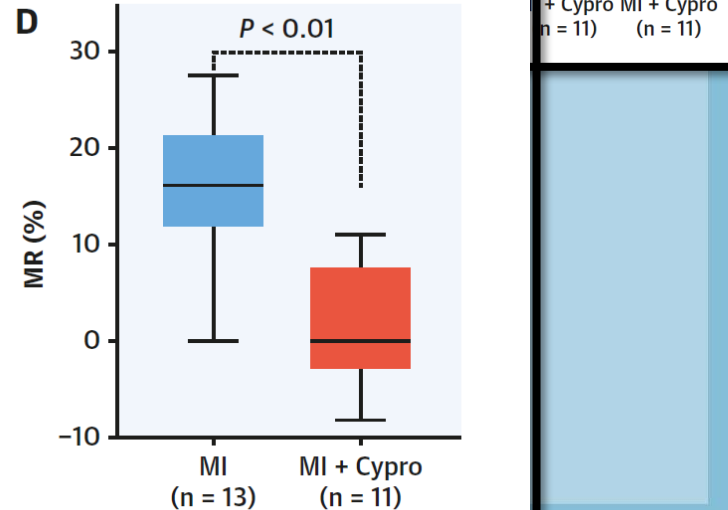
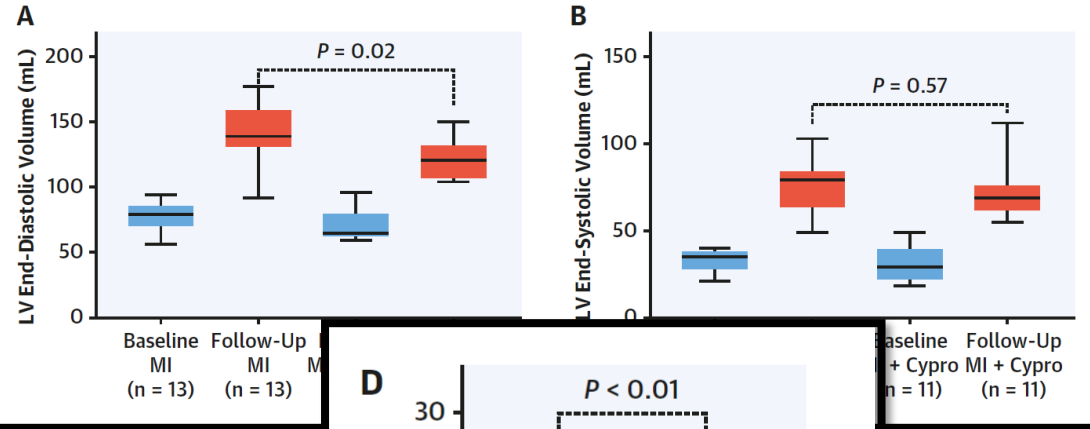
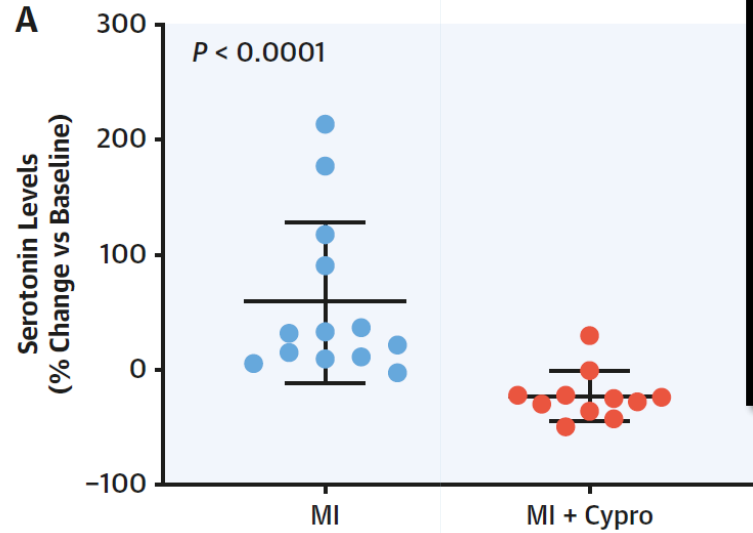
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Medical tx at the time of MI?



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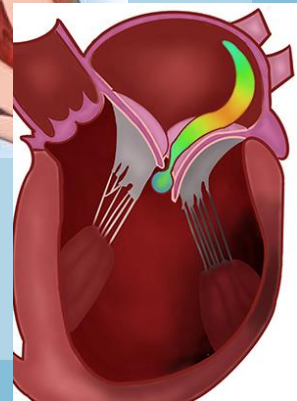
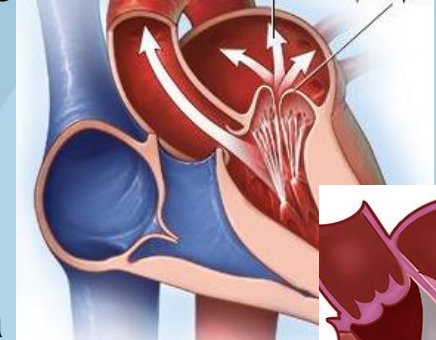
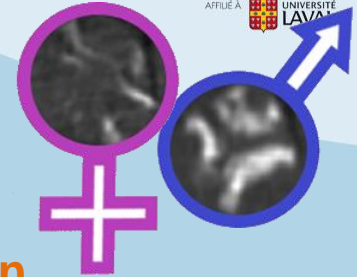


Conclusion: Sex-differences in AS from imaging



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- **Aortic valve calcification is lower** in women for the AS same severity but **fibrosis is higher** - And thus pathophysiology is different
- Several **ongoing trials** (Lp(a); Evogliptin, ARBs, Ataciguat,...) **in Aortic Stenosis**
- **Primary MR present differently** between sexes and **chromosomic defect** have different impact
- **Secondary MR** post myocardial infarction is not only a ventricular disease and **mitral valve leaflets are remodelled**: thus medication at the time of MI could limit MR





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Thank you for your attention