

XXX JORNADA CATALANA DE  
DIAGNÒSTIC PRENATAL ECOGRÀFIC

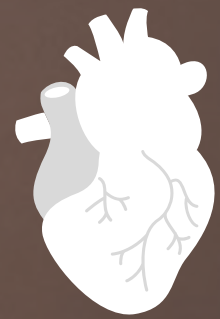
# Polivalvulopatia secundària a mutació del gen de la Filamina A (FLNA)

A propòsit d'un cas

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CAS CLÍNIC



FLNA



CONCLUSIONS



BIBLIOGRAFIA





# 1. CAS CLÍNIC

# 1. CAS CLÍNIC

26 anys

1.0.0.1

Plaquetopènia gestacional



# 1. CAS CLÍNIC



13.6

Marcadors de cromosomopaties negatius  
Triple screening baix risc  
Quatre càmares

# 1. CAS CLÍNIC



22.0

Levocardia, cardiomegàlia, dominància cavitats dretes

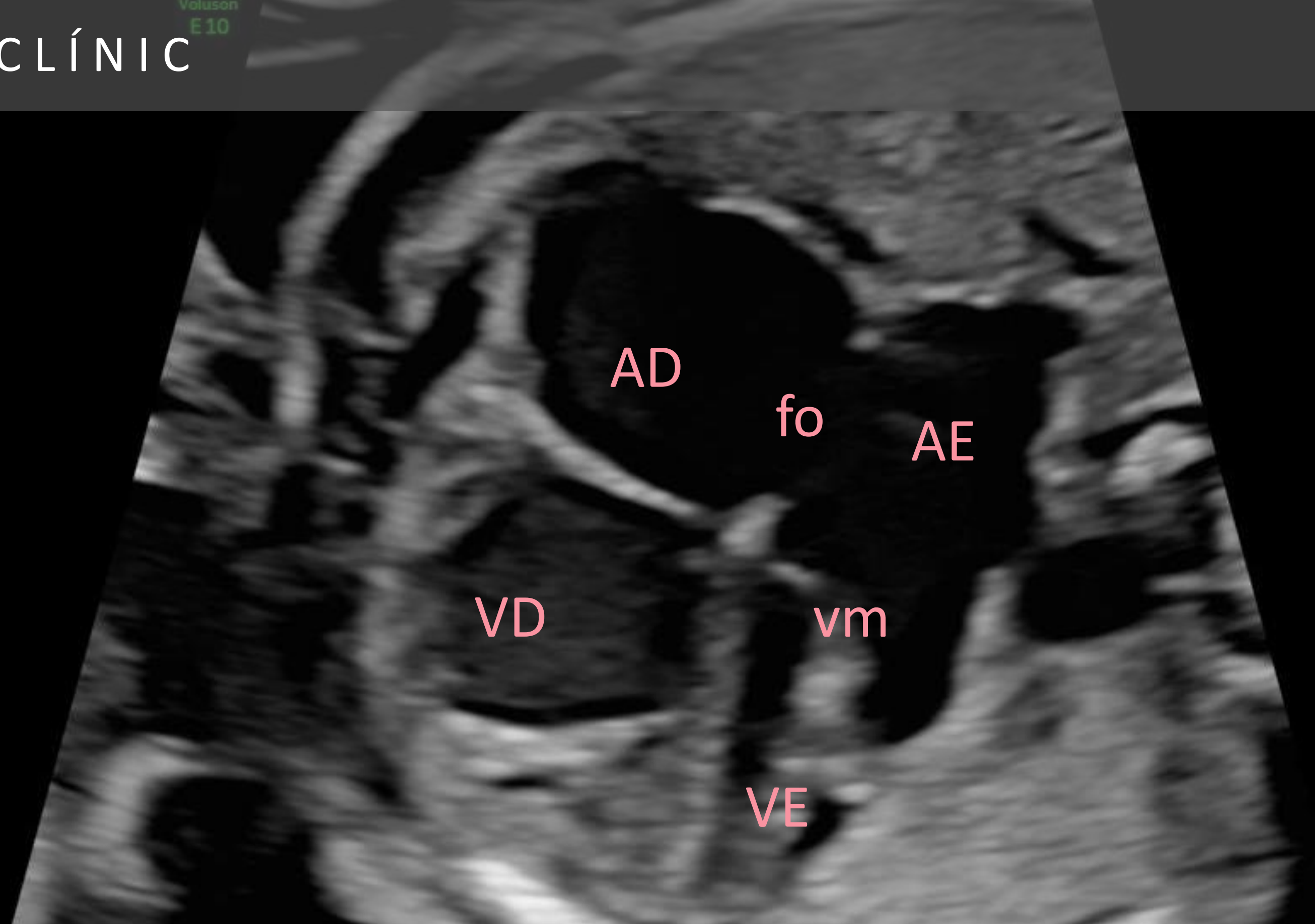
# 1. CAS CLÍNIC

Es remet a BCNatal



# 1. CAS CLÍNIC

2/3 Trim. Cardiac/OB  
HI M 7.90 - 4.50  
Gn -5  
C8/M16  
FF1/E4  
SRI II 4/CRI 2



22.5

Vàlvula mitral displàsica

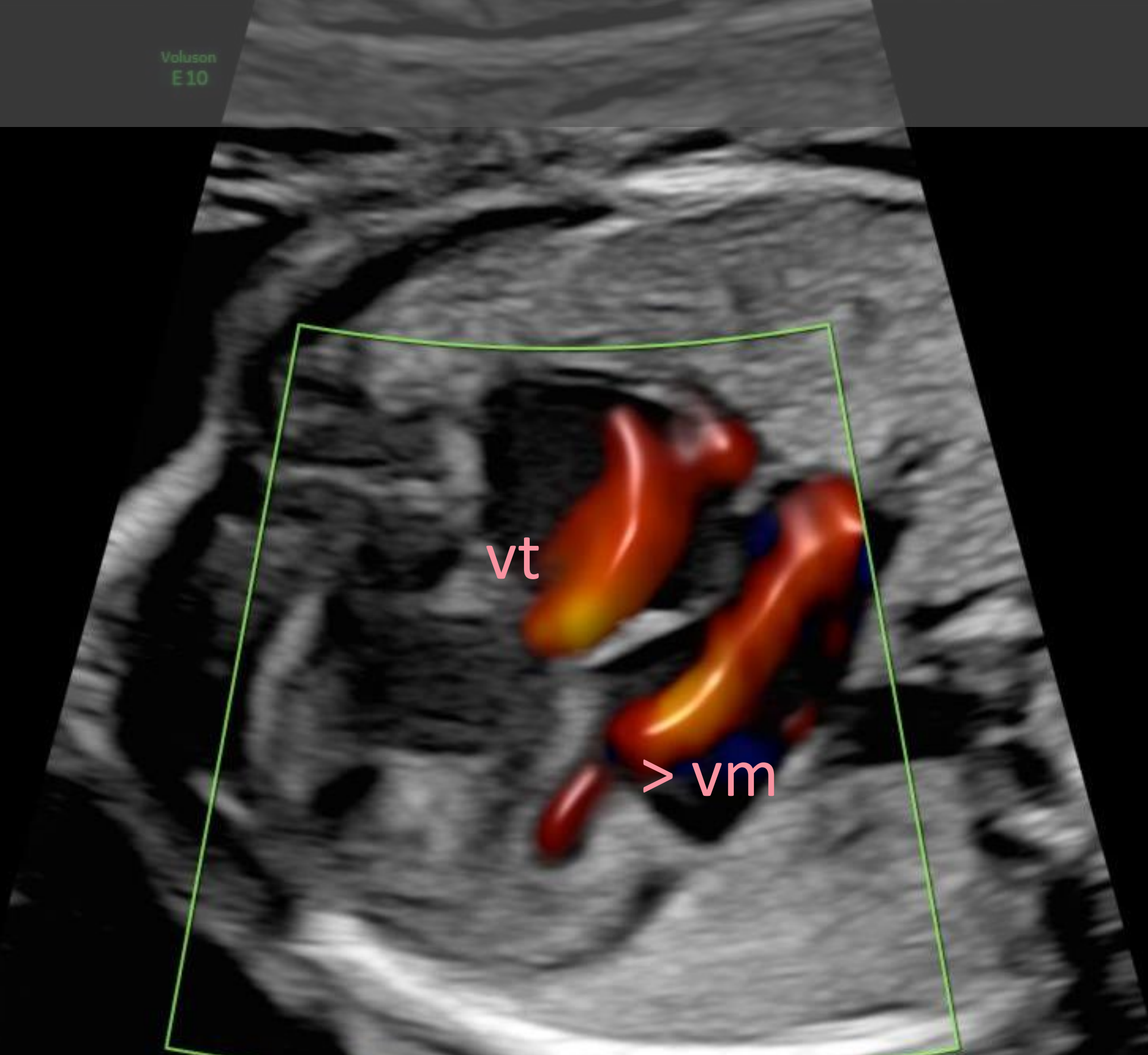


# 1. CAS CLÍNIC



Voluson  
E10

28Hz/ 7.4cm  
30°/1.9  
2/3 Trim. Cardiac/OB  
HI M 7.90 - 4.50  
Gn -5  
C8/M16  
FF1/E4  
SRI II 4/CRI 2  
  
Gn -0.4  
Frq low  
Qual norm  
WMF mid2  
PRF 8.4kHz

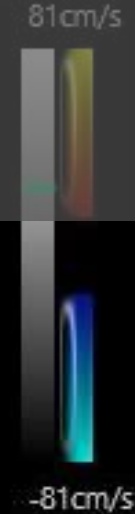


22.5

Insuficiència mitral i tricúspide

# 1. CAS CLÍNIC

Gn 12.0  
WMF 500 Hz  
SV Angl 0  
PRF 13.9kHz

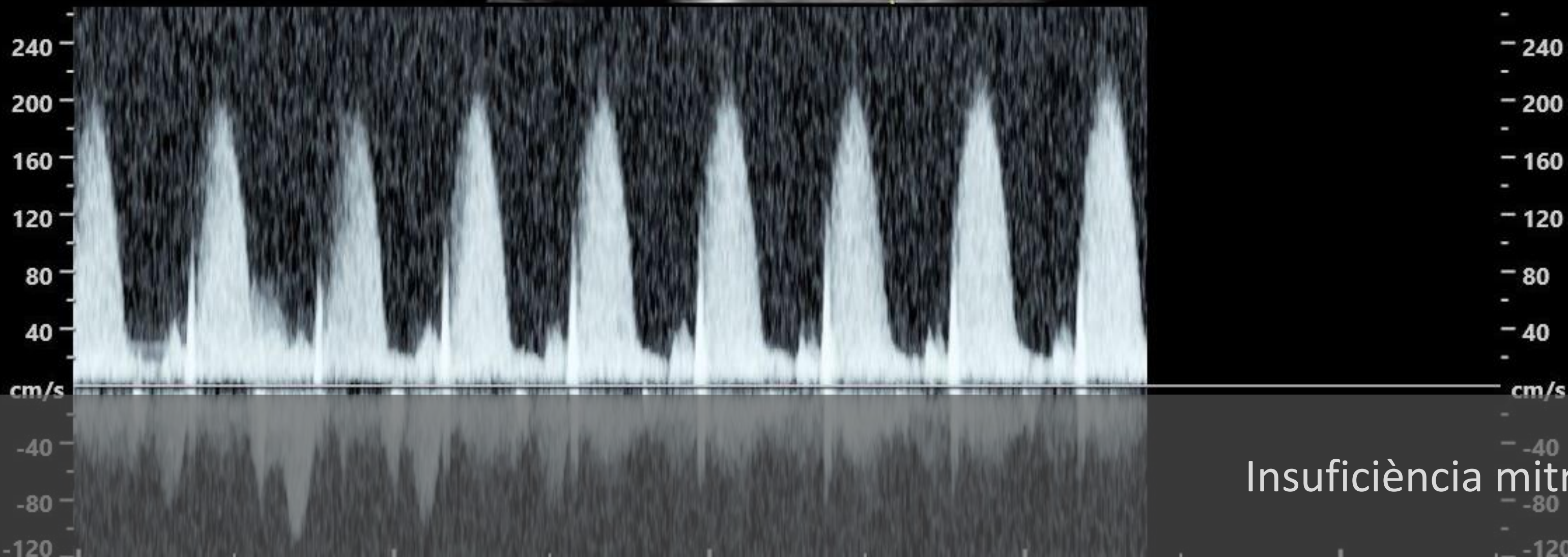


Voluson  
E10



9Hz/ 7.4cm  
30°/1.9  
2/3 Trim. Cardiac/OB  
HI M 7.90 - 4.50  
Gn -5  
C8/M16  
FF1/E4  
SRI II 4/CRI 2

Gn -0.4  
Frq mid  
Qual norm  
WMF mid2  
PRF 8.4kHz

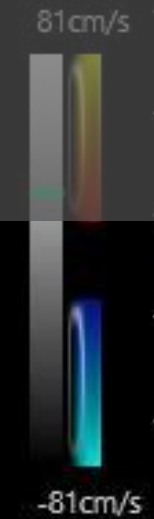


22.5

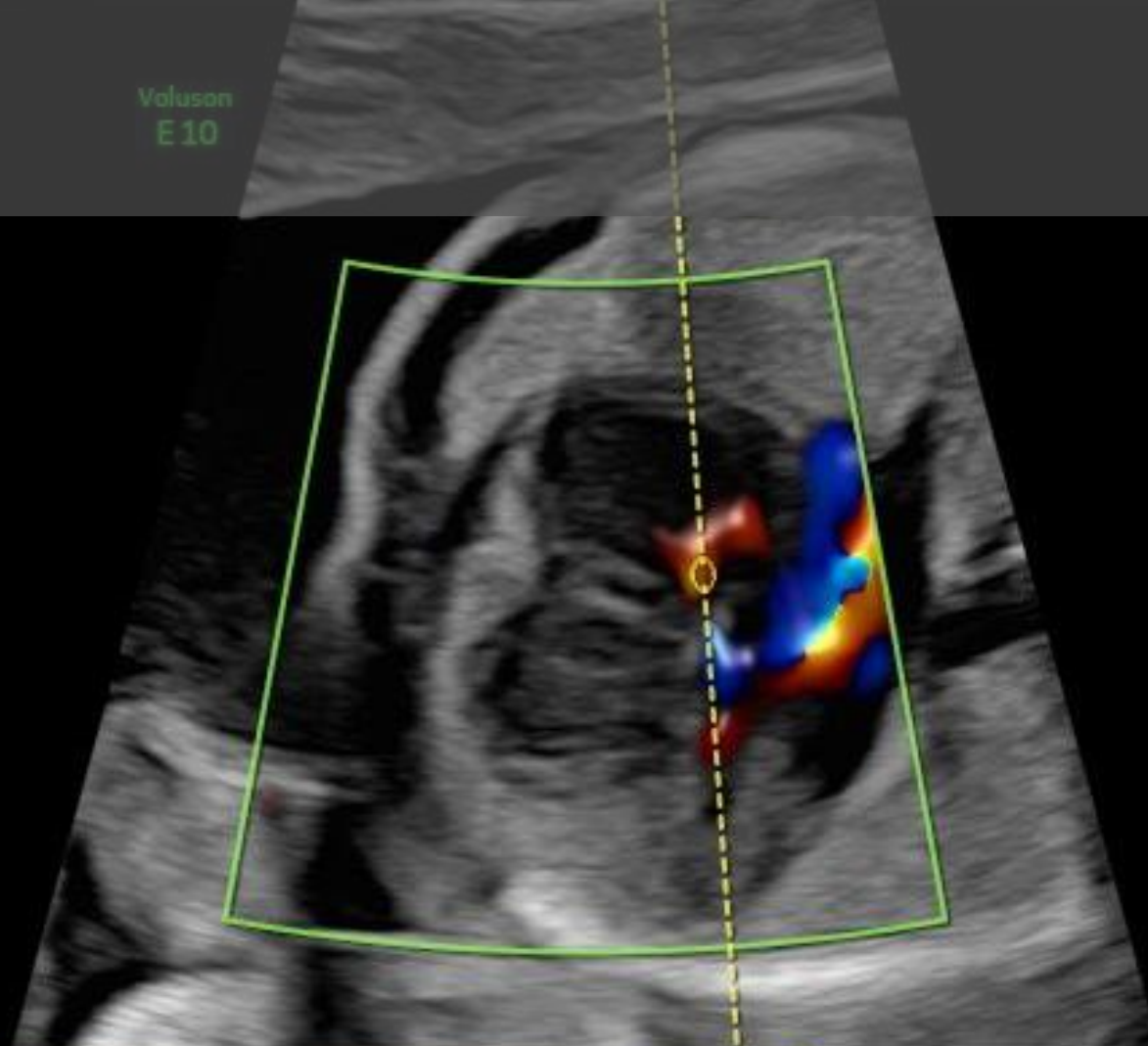
Insuficiència mitral

# 1. CAS CLÍNIC

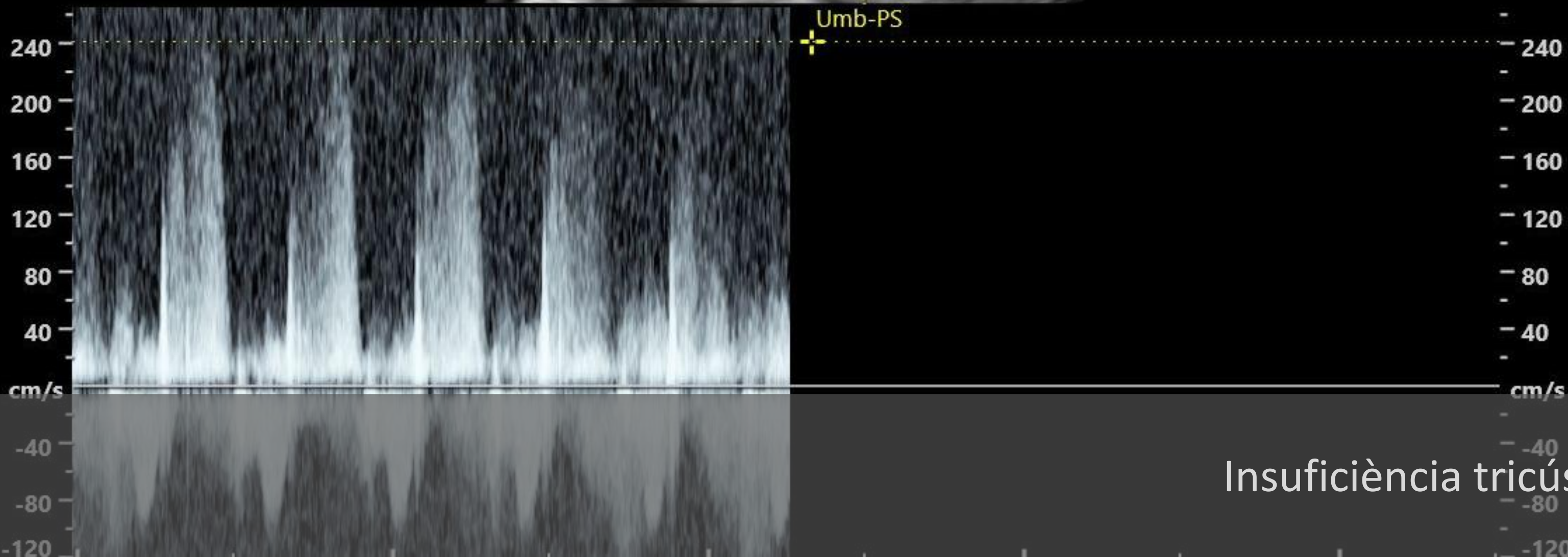
Gn 12.0  
WMF 500 Hz  
SV Angle 0  
PRF 13.9kHz



Valuson  
E10



Umb-PS 240.63cm/s  
30°/1.9  
2/3 Trim. Cardiac/OB  
HI M 7.90 - 4.50  
Gn -5  
C8/M16  
FF1/E4  
SRI II 4/CRI 2  
Gn -0.4  
Frq mid  
Qual norm  
WMF mid2  
PRF 8.4kHz

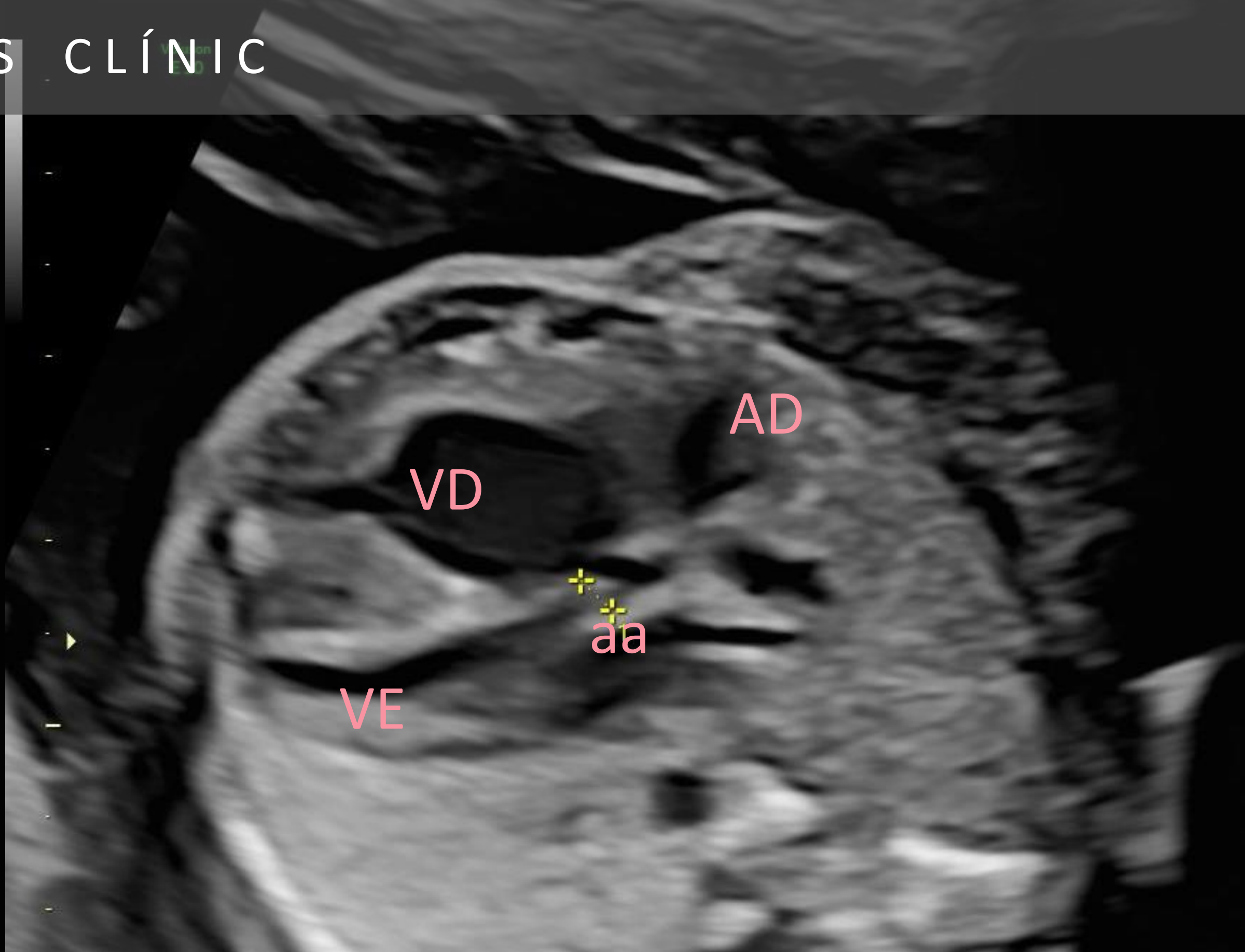


22.5

Insuficiència tricúspide

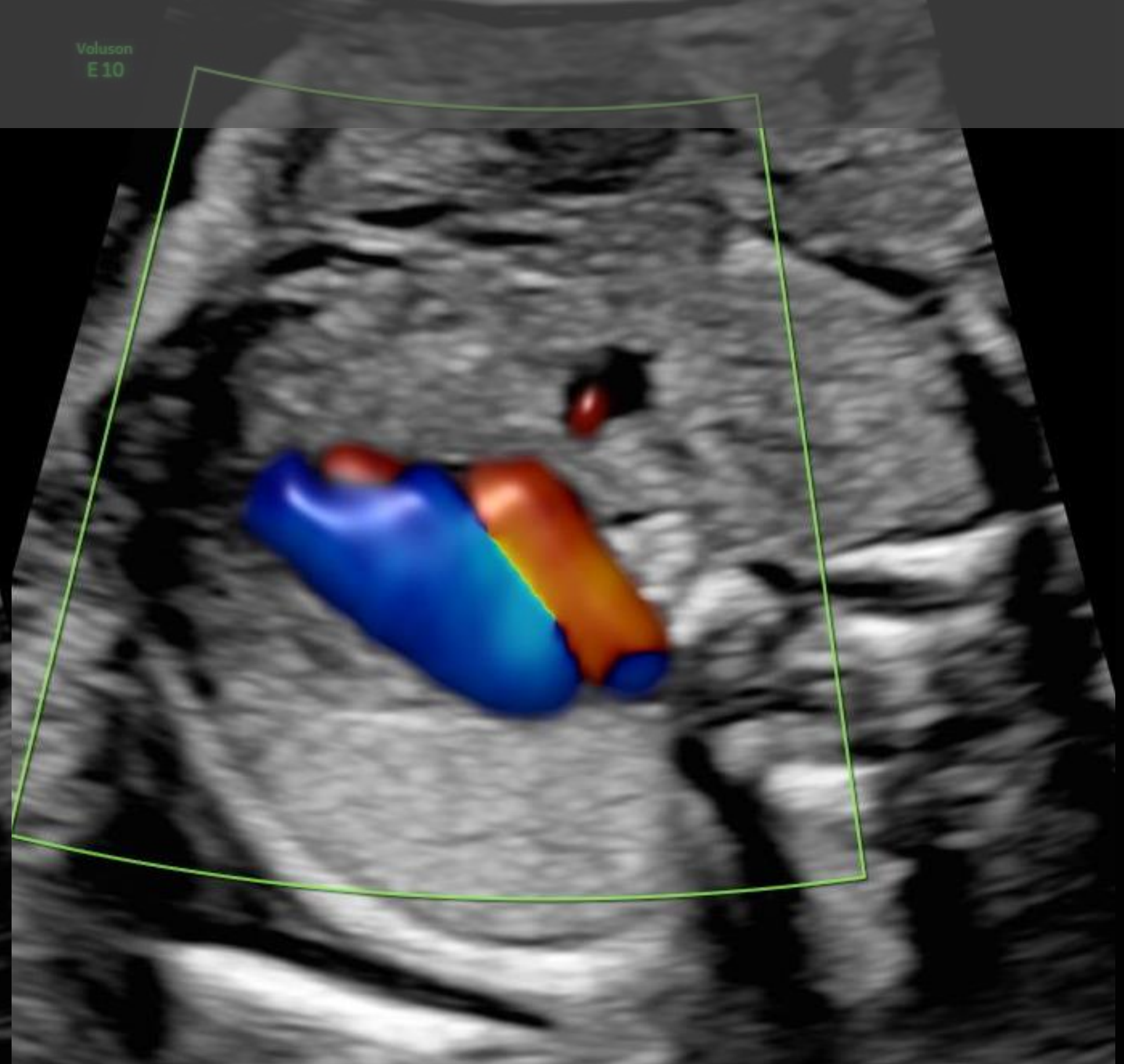
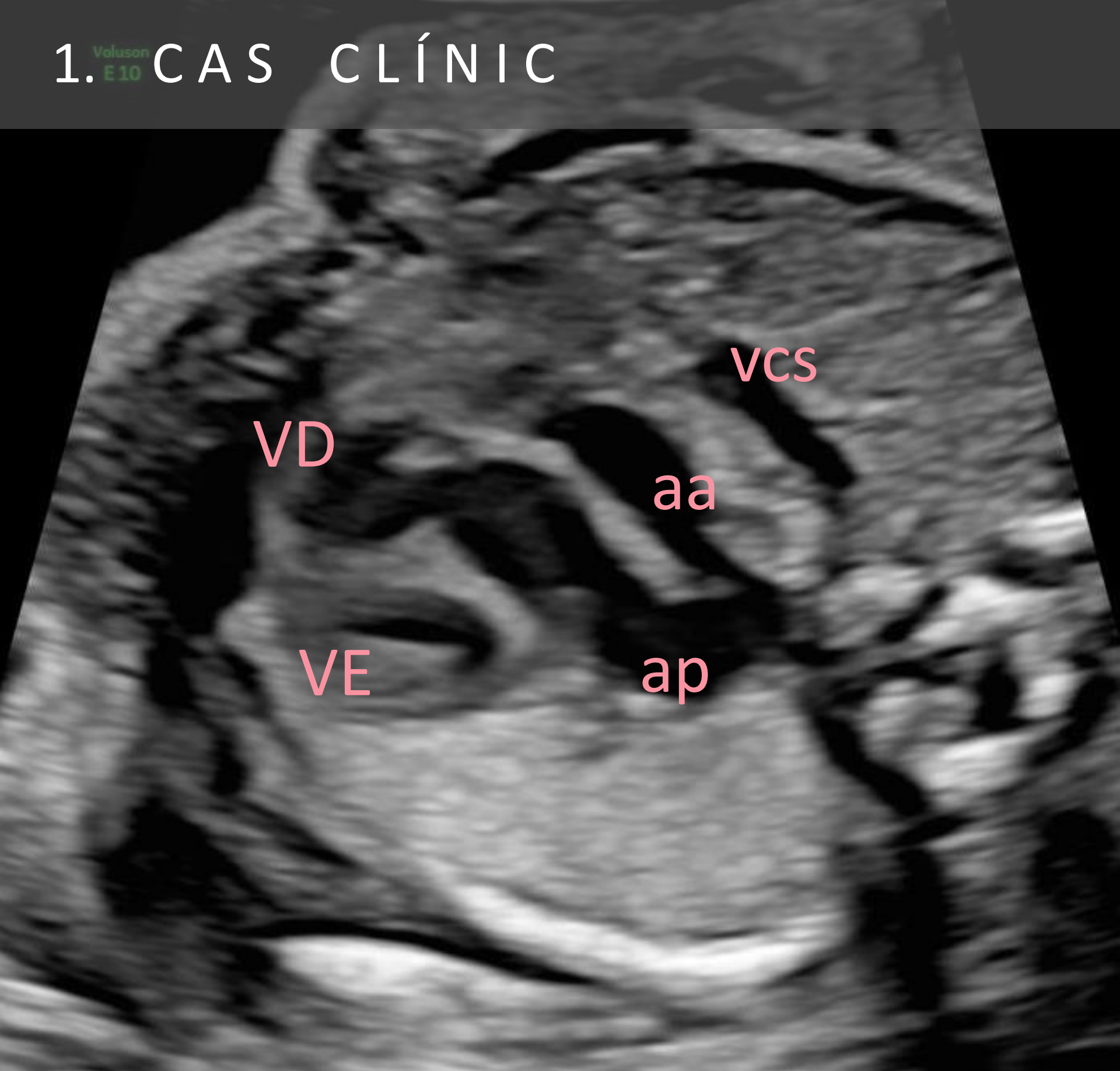
# 1. CAS CLÍNICO

46Hz/ 8.5cm  
50°/2.1  
2/3 Trim. Cardiac/OB  
HI M 7.70 - 4.30  
Gn 3  
C8/M7  
FF3/E1  
SRI II 3/CRI 2



22.5

Estenosi aórtica  
1 D 2.36mm



22.5

3 vasos amb fluxos discordants amb istme aòrtic revers

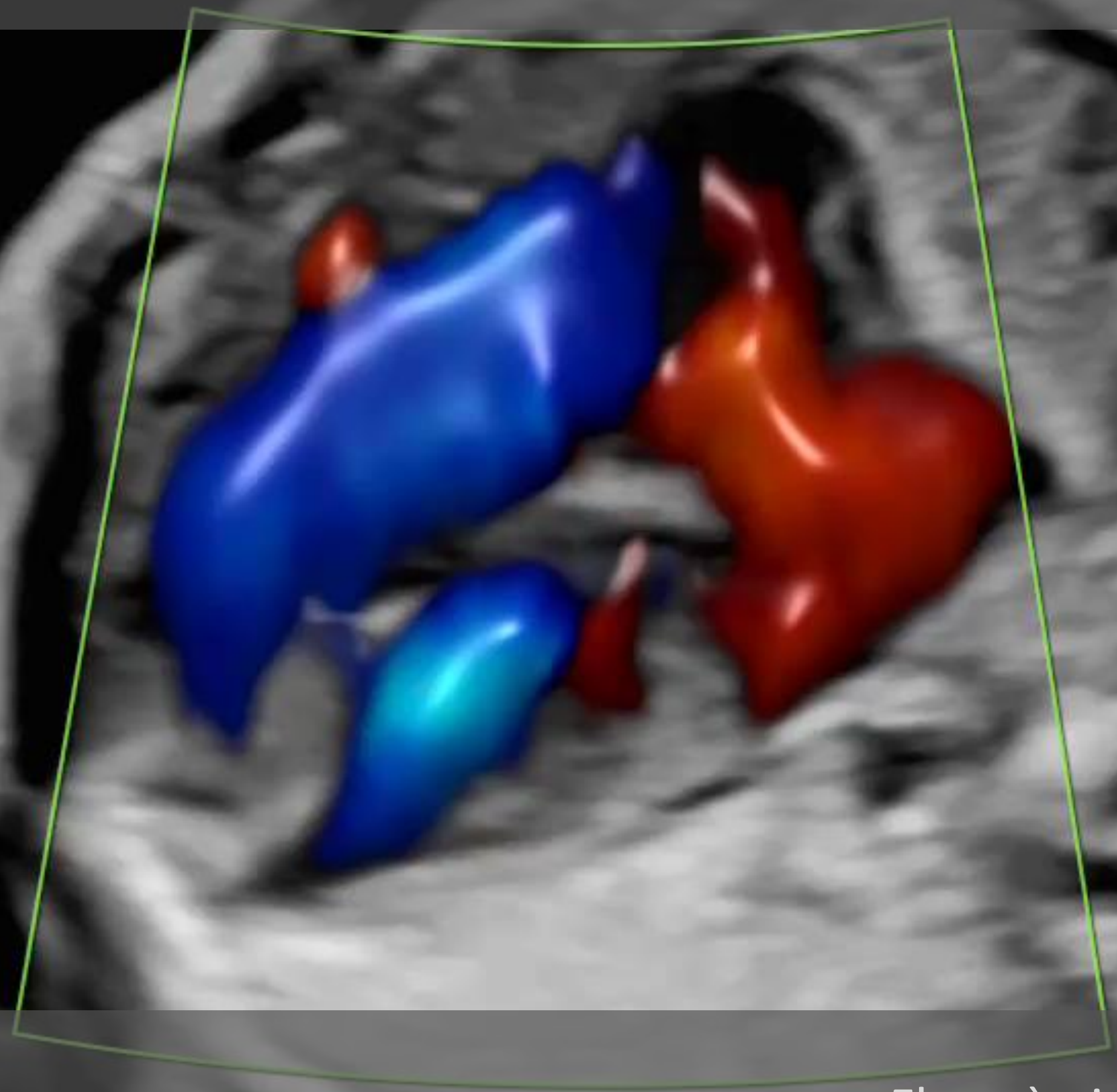
# 1. CAS CLÍNIC

HI M 7.70 - 4.30  
Gn 3  
C8/M7  
FF3/E1

SRI II 3/CRI 2

Gn -4.6  
Frq mid  
Qual norm  
WMF mid1  
PRF 6.4kHz

-71cm/s



22.5

Flux aòrtic estenosi + insuficiència

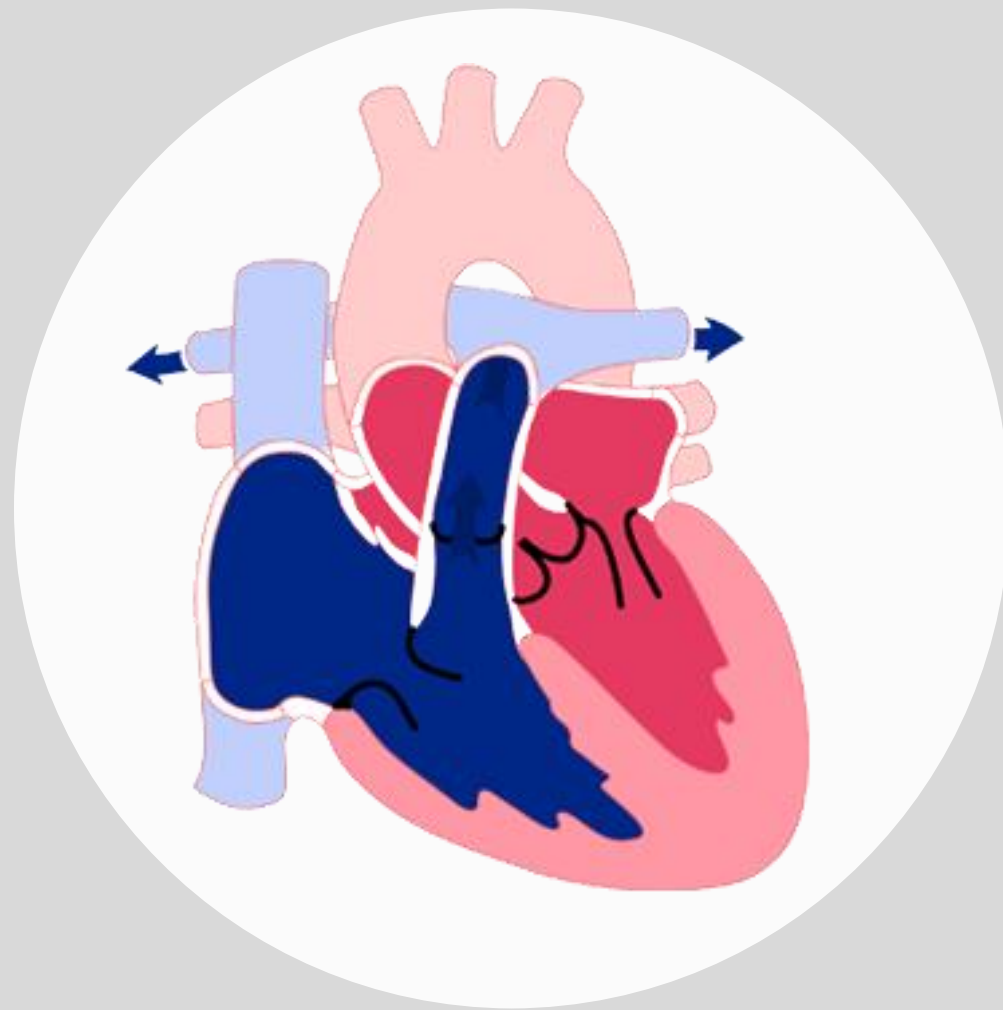
# 1. CAS CLÍNIC

## DIAGNÒSTIC DIFERENCIAL

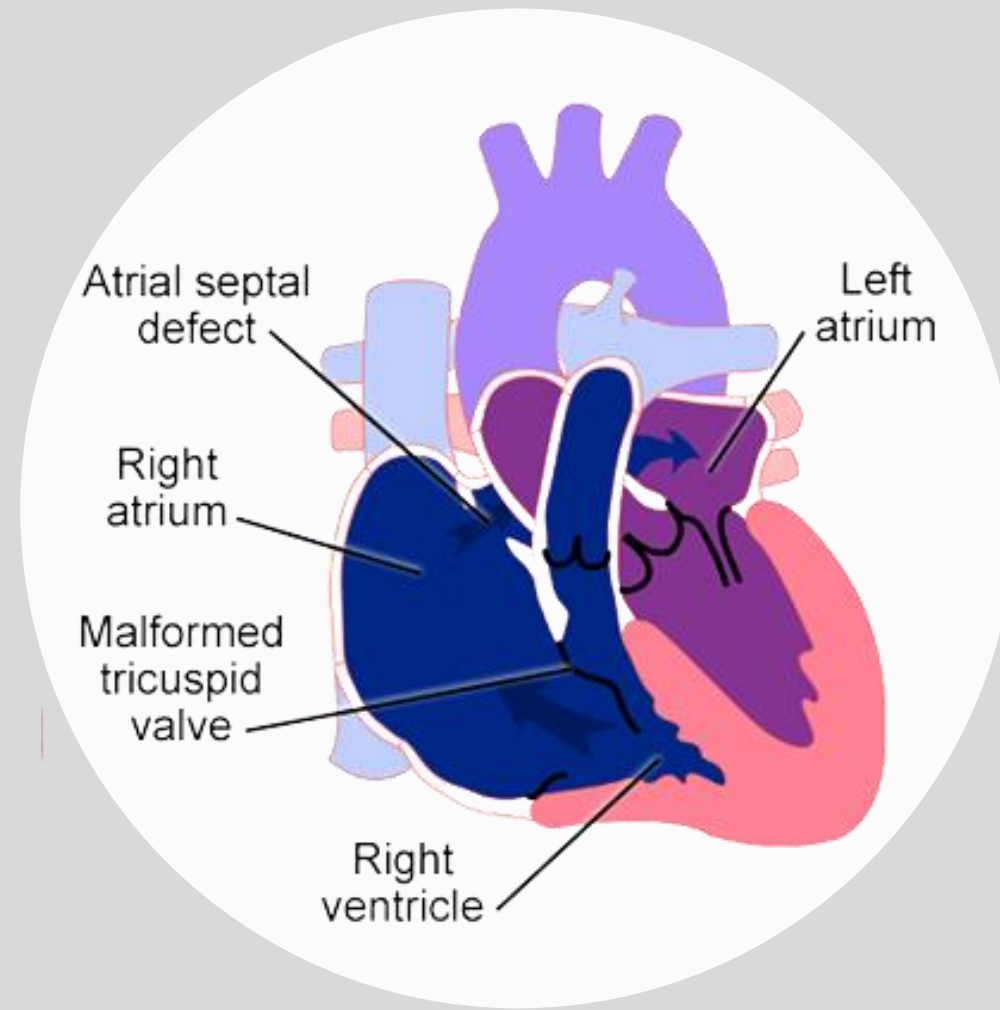


# 1. CAS CLÍNIC

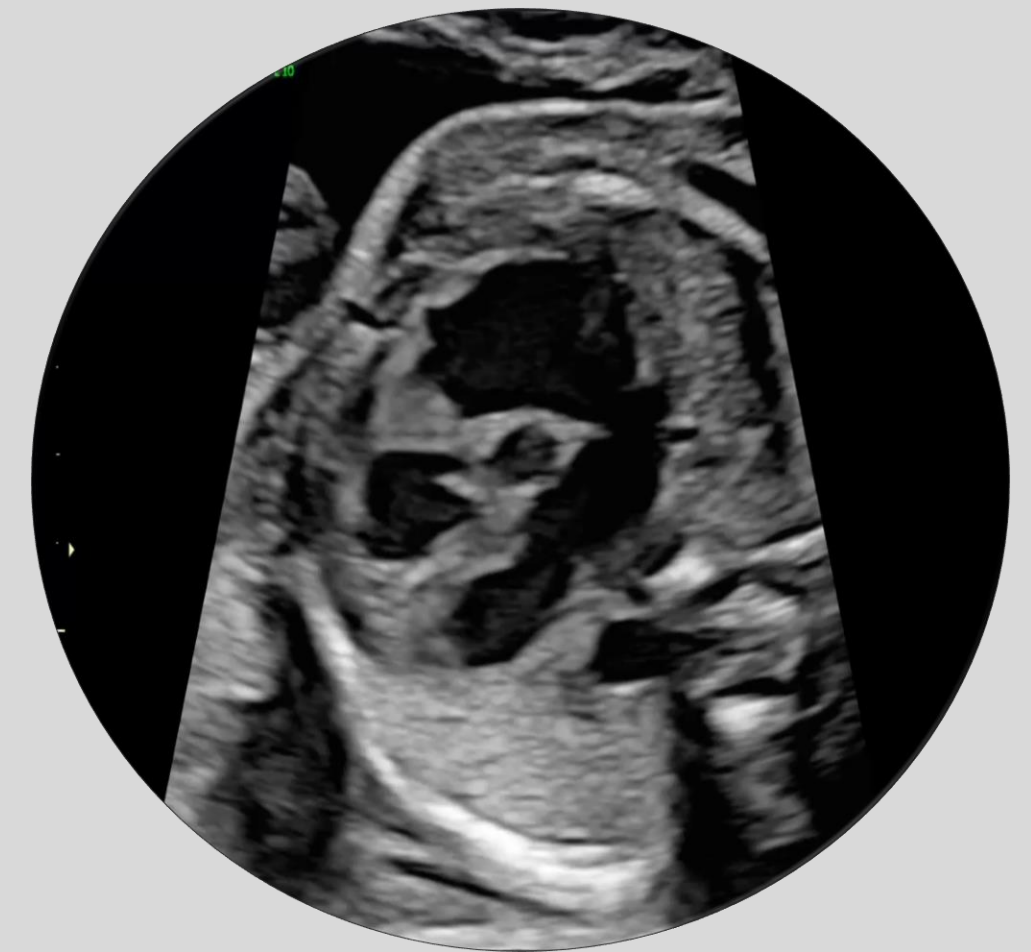
## DIAGNÒSTIC DIFERENCIAL



Cor normal



Ebstein



Ebstein mitral  
vs  
Miocardiopatia polivalvular



# 1. CAS CLÍNIC



AMNIOCENTESI

# 1. CAS CLÍNIC

QF - PCR



ARRAYcGH



# 1. CAS CLÍNIC

Progressió desfavorable  
amb insuficiència polivalvular



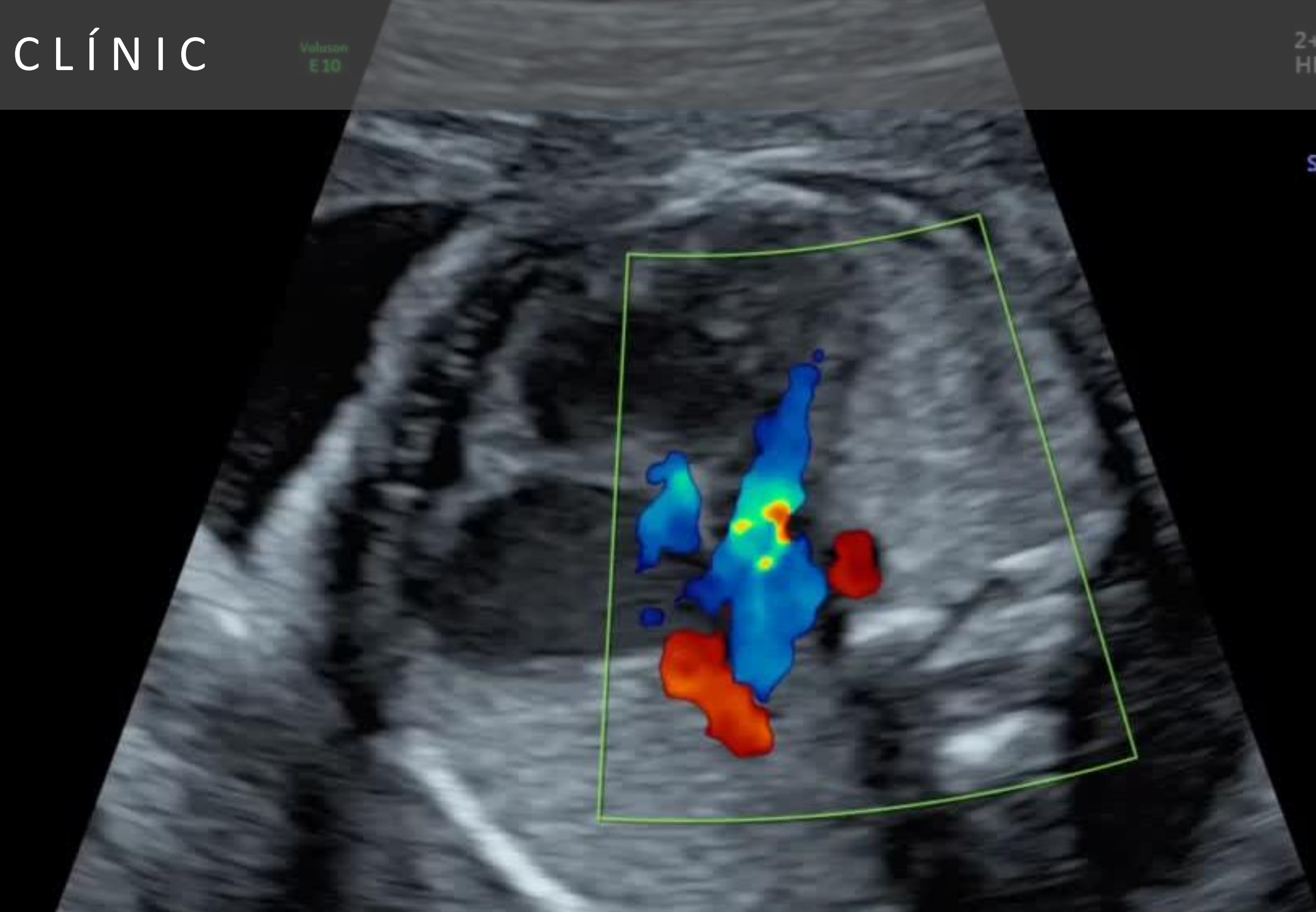
# 1. CAS CLÍNIC



Voluson  
E 10

40° / 32Hz  
2+3 Trim. Card.  
HM 7.30 - 4.50  
Gn 8  
C6 / M7  
FF5 / E3  
**SRI II 2 / CRI 3**

Gn -7.8  
Frq mid  
Qual norm  
WMF low2  
PRF 9.0kHz



## 25.6

Regurgitació mitral  
Foramen oval amb flux invertit esquerra-dreta

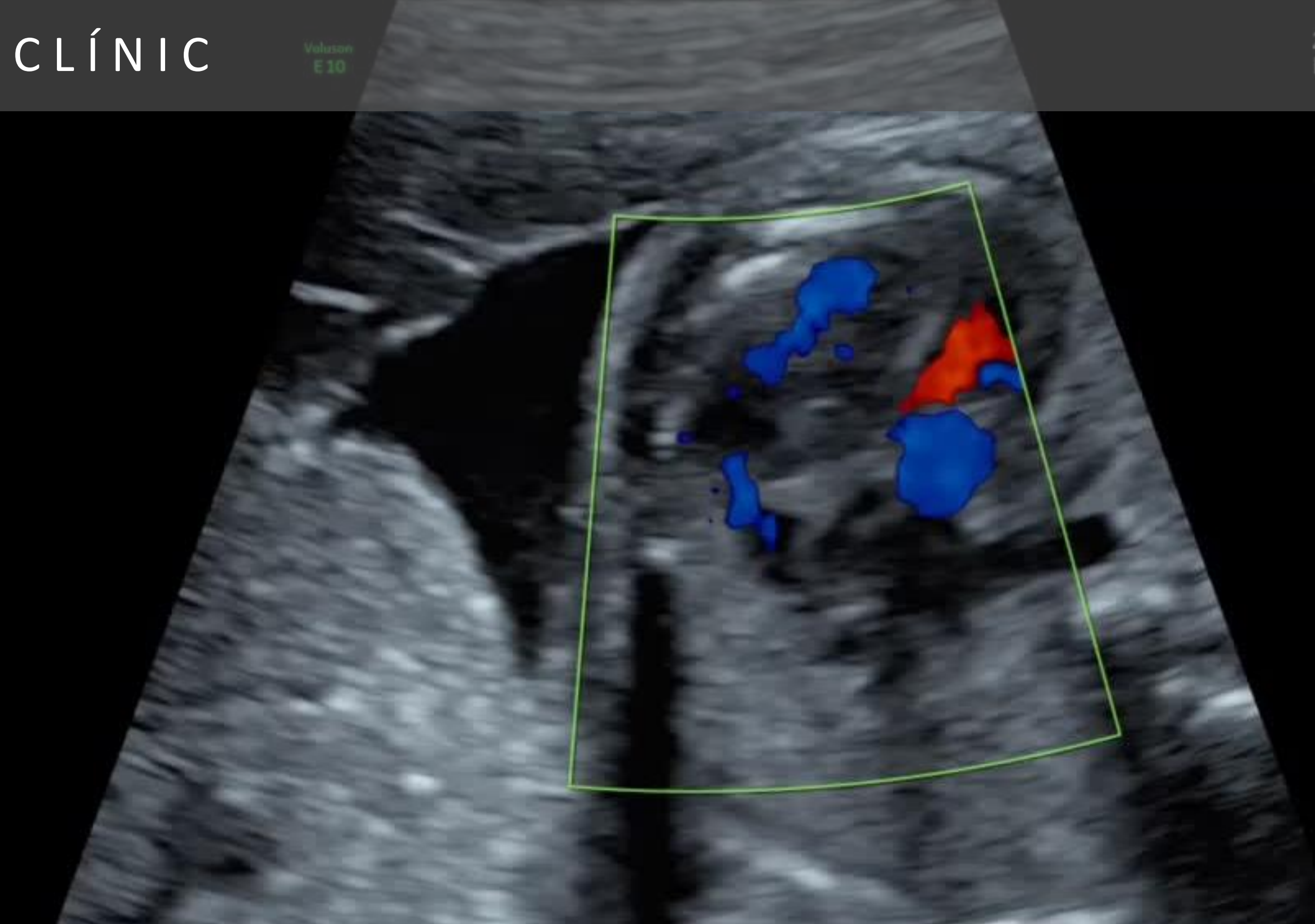
# 1. CAS CLÍNIC



Voluson  
E 10

40° / 30Hz  
2+3 Trim. Card.  
HM 7.30 - 4.50  
Gn 8  
C6 / M7  
FF5 / E3  
SRI II 2 / CRI 3

Gn -7.8  
Frq low  
Qual norm  
WMF low2  
PRF 9.0kHz



25.6

Grans vasos amb fluxos invertits

# 1. CAS CLÍNIC

## EXOMA DIRIGIT

### VARIANT GENÈTICA

**FLNA**

(NM\_001456.3):

c.6401\_6404del/p.Glu2134AlafsTer22

### LOCALITZACIÓ

X-153580994-GCTCT-G

### GENOTIP

Hemicigosi

### CLASSIFICACIÓ

Patogénica:  
PVS1/PM2/PP3

FLNA

(NM\_001456.3):

c.6401\_6404del/p.Glu2134AlafsTer22

X-153580994-GCTCT-G

Heterocigosi

Patogénica:  
PVS1/PM2/PP3





INDUCCIÓ

38.5

**PART  
EUTÒCIC**





# 1. CAS CLÍNIC

Confirma  
insuficiència  
valvular



- HTP
- Ductus arteriós persistent
- CIA ostium secundum amb shunt esquerra-dreta

Tancament percutani del ductus  
Diürètics + hipotensors



- Retard ponderal
- Retard psicomotor
- RM: heterotípia periventricular i aprimament del cos callós
- Infeccions respiratòries de repetició en context d'insuf cardíaca

Correcció de  
vàlvula mitral



Exitus

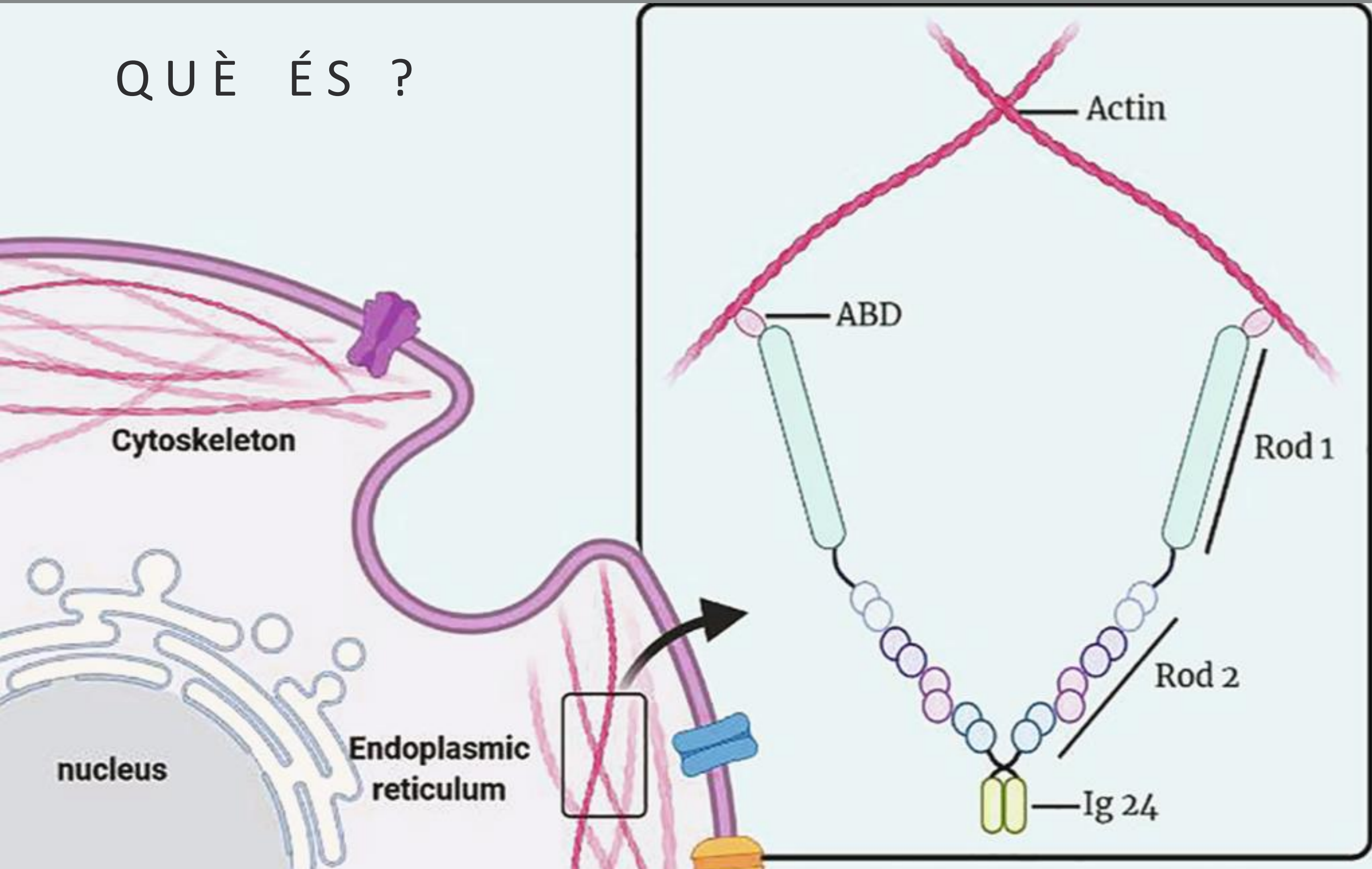


A close-up photograph of a pregnant woman's belly, which is being gently held by her hand. The woman is wearing a black top and black shorts. The background is a solid, light beige color.

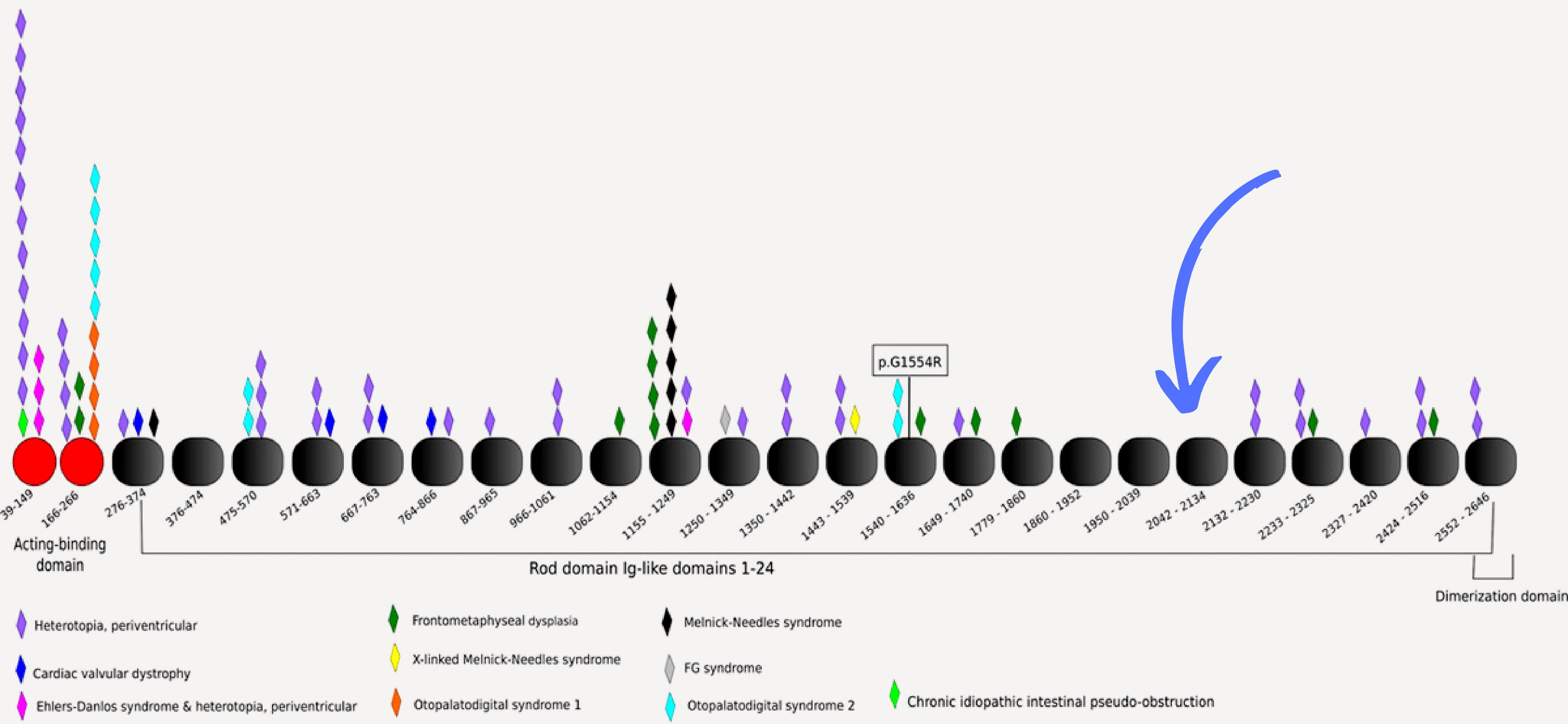
## 2. LA FILAMINA A (FLNA)

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QUÈ ÉS ?



# 2. FILAMINA A (FLNA)



## 2. FILAMINA A (FLNA)

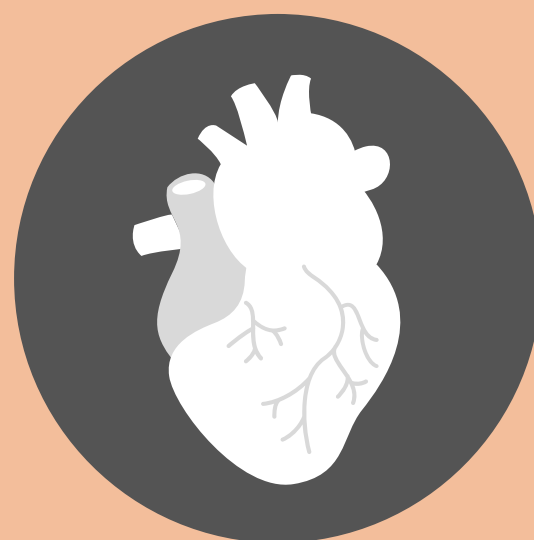
### CONSEQÜÈNCIES



- Heteròtopia nodular periventricular
- Síndrome Ehlers Danlos
- Síndrome Melnick Needles
- Síndrome otopalatodigital
- Displàsia frontometafisarea



- Prolapse vàlvula mitral
- Ductus arteriós persistent
- Aneurisma aòrtic
- IAM
- HTA
- Distròfia valvular mixomatosa lligada al X



- Insuficiència respiratòria crònica
- Malaltia pulmonar emfisematosa
- Síndrome de distret respiratori agut



- Macrotrombocitopenia



### 3. CONCLUSIONS

### 3. CONCLUSIONS

- Mutació del gen de la Filamina A (FLNA) extremadament infreqüent
- Poc reportada en vida fetal
- Pronòstic desfavorable
- Necessitat de consell interdisciplinari
- Hem de pensar-hi en context de patologia polivalvular cardíaca



# 4. BIBLIOGRAFIA

Bandaru S, Ala C, Zhou AX, Akyürek LM. Filamin A Regulates Cardiovascular Remodeling. *Int J Mol Sci*. 2021 Jun 18;22(12):6555.

Deng X, Li S, Qiu Q, Jin B, Yan M, Hu Y, Wu Y, Zhou H, Zhang G, Zheng X. Where the congenital heart disease meets the pulmonary arterial hypertension, FLNA matters: a case report and literature review. *BMC Pediatr*. 2020 Nov 3;20(1):504.

Fernández L, Tenorio J, Polo-Vaquero C, Vallespín E, Palomares-Bralo M, García-Miñaúr S, Santos-Simarro F, Arias P, Carnicer H, Giannivelli S, Medina J, Pérez-Piaya R, Solís J, Rodríguez M, Villagrà A, Rodríguez L, Nevado J, Martínez-Glez V, Heath KE, Lapunzina P. In-frame Variants in FLNA Proximal Rod 1 Domain Associate With a Predominant Cardiac Valvular Phenotype. *Rev Esp Cardiol (Engl Ed)*. 2018 Jul;71(7):545-552. English, Spanish.

Kyndt F, Gueffet JP, Probst V, Jaafar P, Legendre A, Le Bouffant F, Toquet C, Roy E, McGregor L, Lynch SA, Newbury-Ecob R, Tran V, Young I, Trochu JN, Le Marec H, Schott JJ. Mutations in the gene encoding filamin A as a cause for familial cardiac valvular dystrophy. *Circulation*. 2007 Jan 2;115(1):40-9.

Lardeux A, Kyndt F, Lecointe S, et al. Filamin-a-related myxomatous mitral valve dystrophy: genetic, echocardiographic and functional aspects. *J Cardiovasc Transl Res*. 2011;4:748–756.

Le Tourneau T, Le Scouarnec S, Cueff C, Bernstein D, Aalberts JJJ, Lecointe S, Mérot J, Bernstein JA, Oomen T, Dina C, Karakachoff M, Desal H, Al Habash O, Delling FN, Capoulade R, Suurmeijer AJH, Milan D, Norris RA, Markwald R, Aikawa E, Slaughter SA, Jeunemaitre X, Hagege A, Roussel JC, Trochu JN, Levine RA, Kyndt F, Probst V, Le Marec H, Schott JJ. New insights into mitral valve dystrophy: a Filamin-A genotype-phenotype and outcome study. *Eur Heart J*. 2018 Apr 14;39(15):1269-1277.

Meliota G, Vairo U, Ficarella R, Milella L, Faienza MF, D'Amato G. Cardiovascular, Brain, and Lung Involvement in a Newborn With a Novel FLNA Mutation: A Case Report and Literature Review. *Adv Neonatal Care*. 2022 Apr 1;22(2):125-131.

Mercer CL, Androletti G, Carroll A, Salmon AP, Temple IK, Ennis S. Familial Ebstein Anomaly: Whole Exome Sequencing Identifies Novel Phenotype Associated With FLNA. *Circ Cardiovasc Genet*. 2017 Dec;10(6):e001683.

Reinstein E, Frentz S, Morgan T, Garcia-Minaur S, Leventer RJ, McGillivray G, et al. Vascular and connective tissue anomalies associated with X-linked periventricular heterotopia due to mutations in Filamin A. *Eur J Hum Genet* 2013;21:494–502.

Robertson SP, Jenkins ZA, Morgan T, Adès L, Aftimos S, Boute O, et al. Frontometaphyseal dysplasia: mutations in FLNA and phenotypic diversity. *Am J Med. Genet A*. 2006;140:1726–1736.

Robertson SP, Twigg SR, Sutherland-Smith AJ, Biancalana V, Gorlin RJ, Horn D, Kenwrick SJ, Kim CA, Morava E, Newbury-Ecob R et al.: Localized mutations in the gene encoding the cytoskeletal protein filamin A cause diverse malformations in humans. *Nat Genet* 2003, 33:487-491.

Robertson SP. Filamin A: phenotypic diversity. *Curr Opin Genet Dev*. 2005 Jun;15(3):301-7.

Zhou J, Kang X, An H, Lv Y, Liu X. The function and pathogenic mechanism of filamin A. *Gene*. 2021 Jun 5;784:145575.



An aerial photograph of a rugged coastline. The left side shows steep, rocky cliffs covered in dense green pine trees. The right side shows a rocky shoreline with waves crashing against the rocks, creating white foam. The water in the center is a deep, clear turquoise color. The overall scene is bright and scenic.

MOLTES GRÀCIES !

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