



Case Presentation

A family with LVH

Θωμάς Γκόσιος

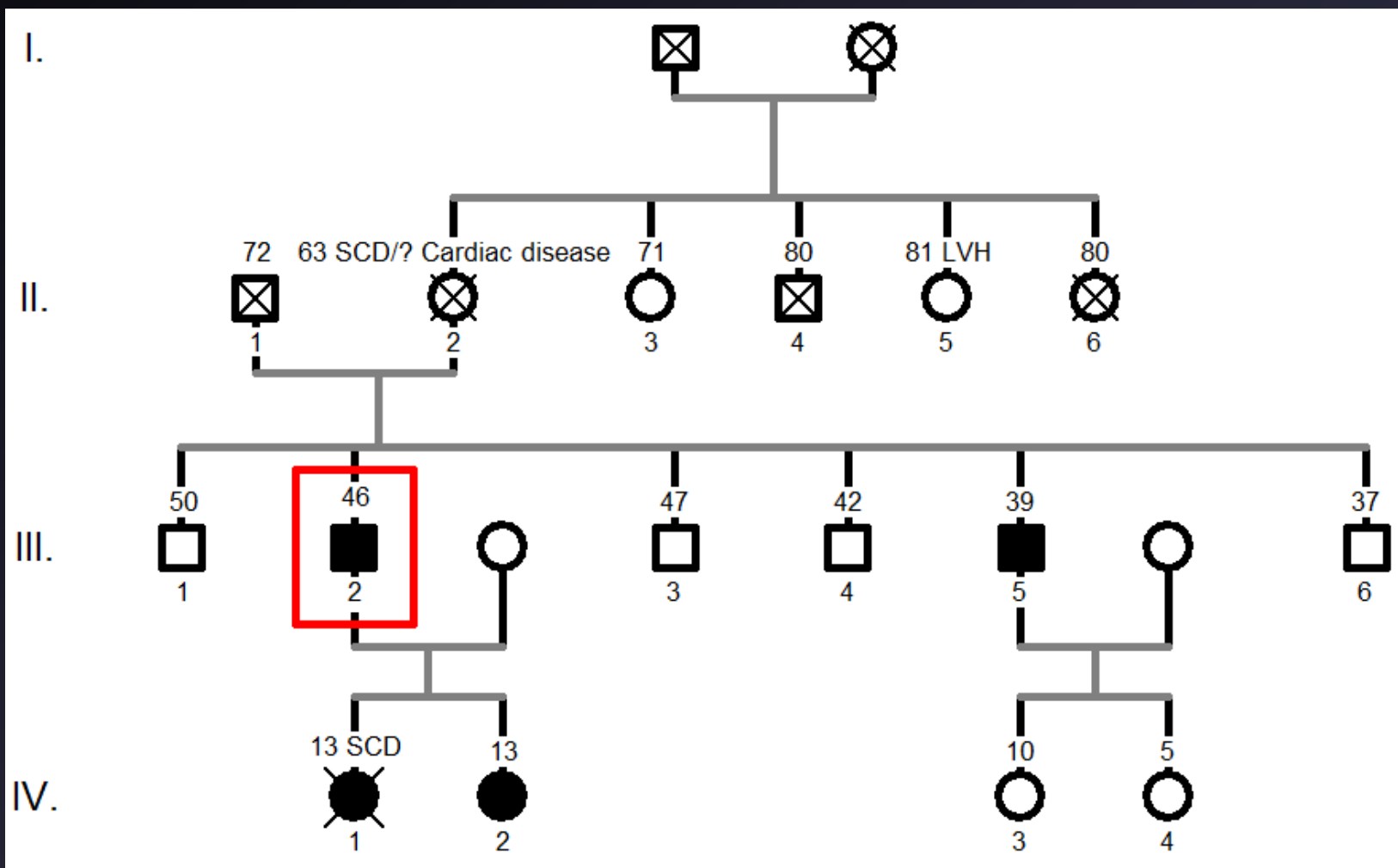
Ειδικευόμενος Καρδιολογίας

Ιατρείο Μυοκαρδιοπαθειών

Α' Καρδιολογική Κλινική ΑΧΕΠΑ

Αριστοτέλειο Πανεπιστήμιο Θεσ/νίκης

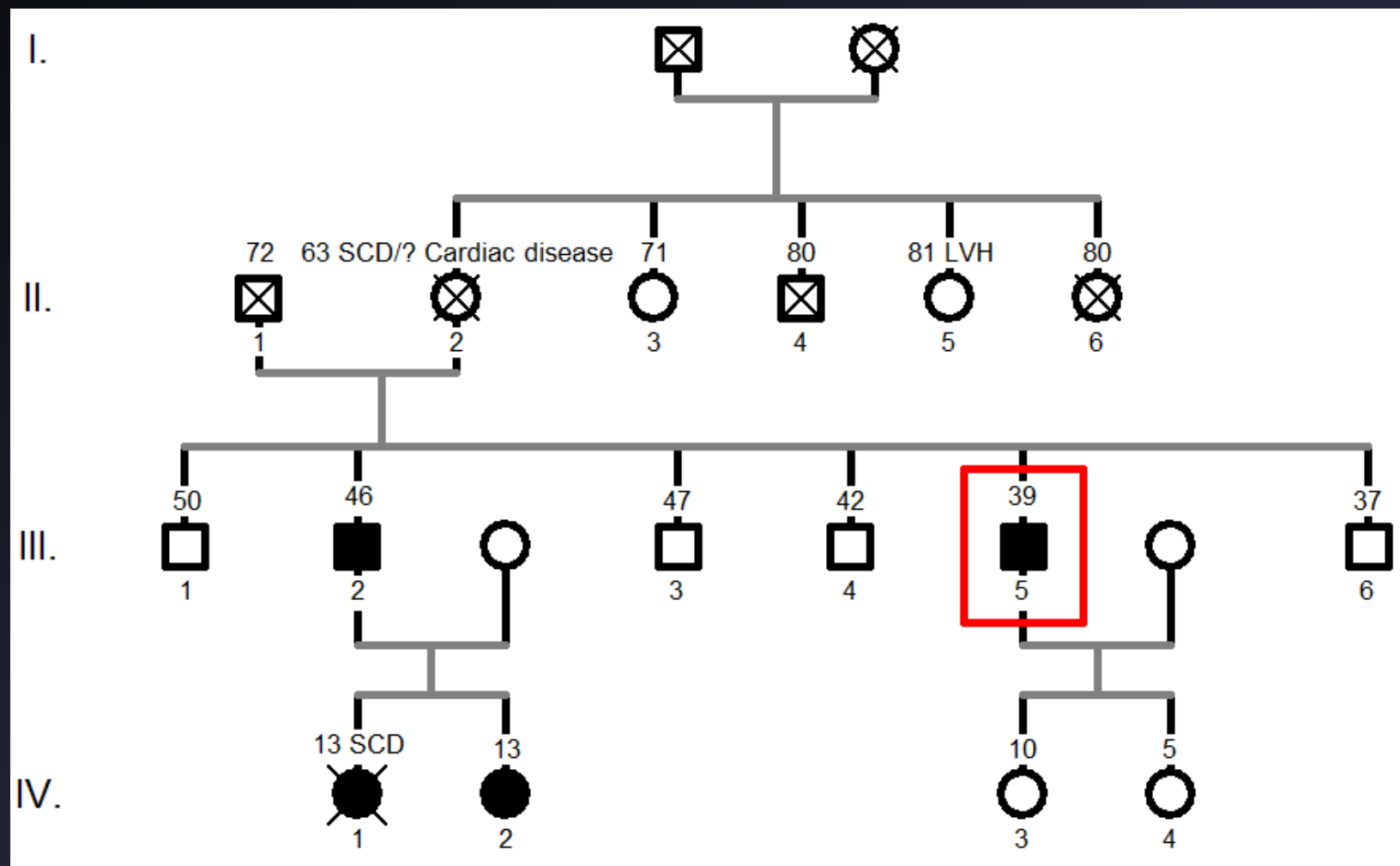
Family Pedigree



Proband: Index pt III 2

- 46-y
- Age at first diagnosis 33-y
- NYHA Class II
- Syncope (2008, neurally mediated)
- ECG LVH-strain
- Echo LV asymmetric hypertrophy, Max thickness 1.7cm, no resting or provokable gradient
- 24-h Holter no episodes of NSVT
- Normal BP response to exercise
- MRI 30% LGAD enhancement
- Genetic test for Anderson Fabry's negative

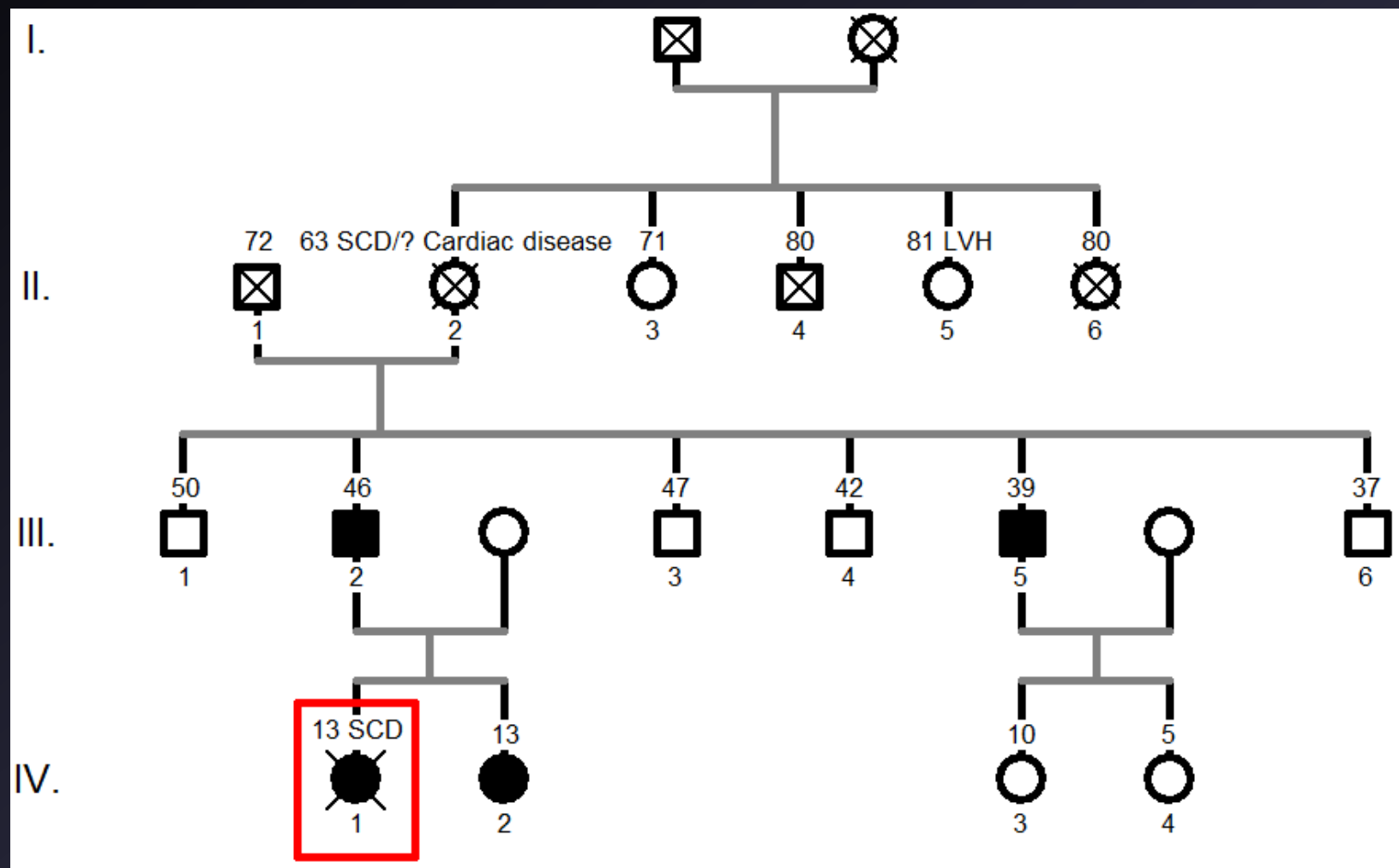
Family Pedigree



Index pt III 5

- 39-y
- Age at first diagnosis 34-y
- Angina (+)
- NYHA Class II
- No unexplained syncope
- ECG Small q waves
- Echo ASH, MWT 1.8 cm, no resting or provokable gradient
- 24-h Holter no episodes of NSVT
- Normal BP response to exercise
- MRI No late Gadolinium enhancement
- Genetic test for Anderson Fabry's negative

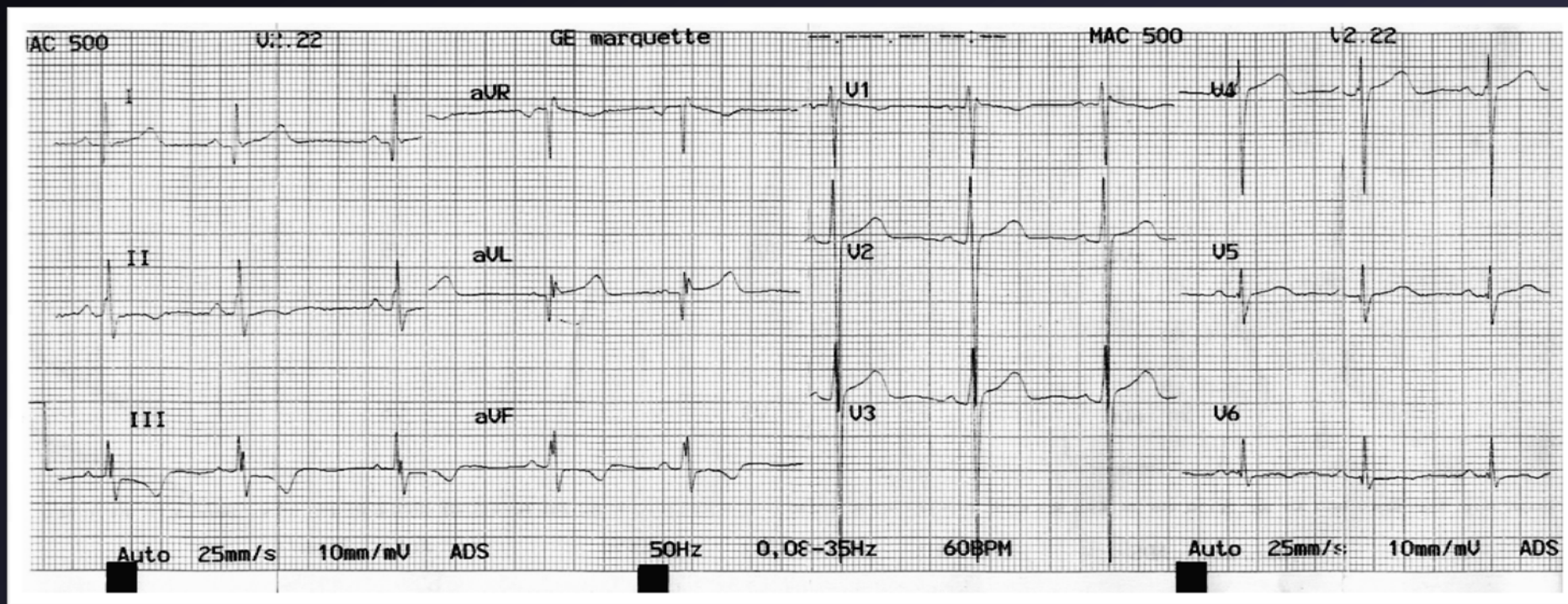
Family Pedigree



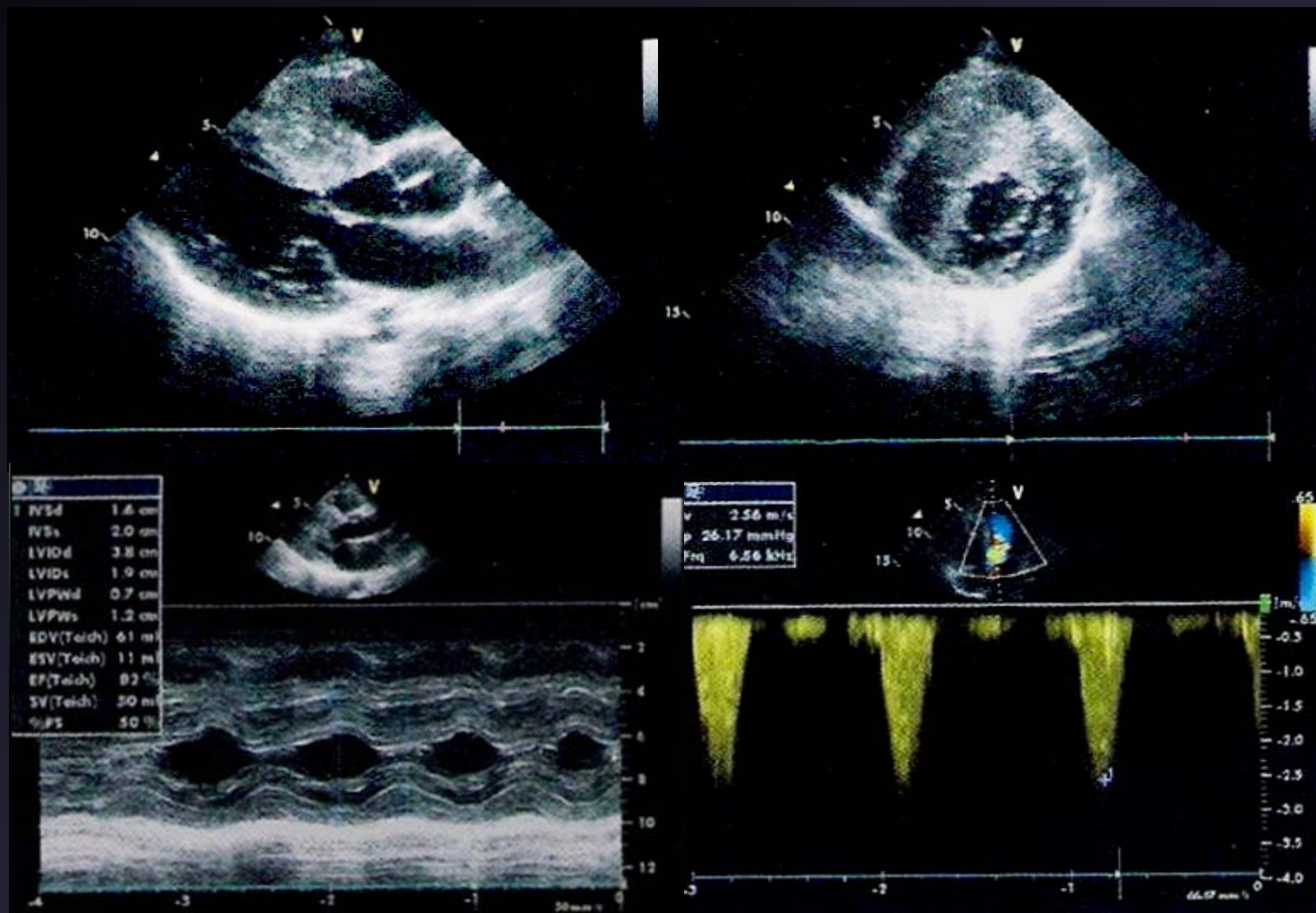
Index pt IV 1

- Sudden cardiac death at home while studying, aged 13
- Echo (2.5-y): ASH, mild LVH
- Echo (10-y): ASH, MWT \approx 2.0 cm, LVOT resting gradient 26 mmHg

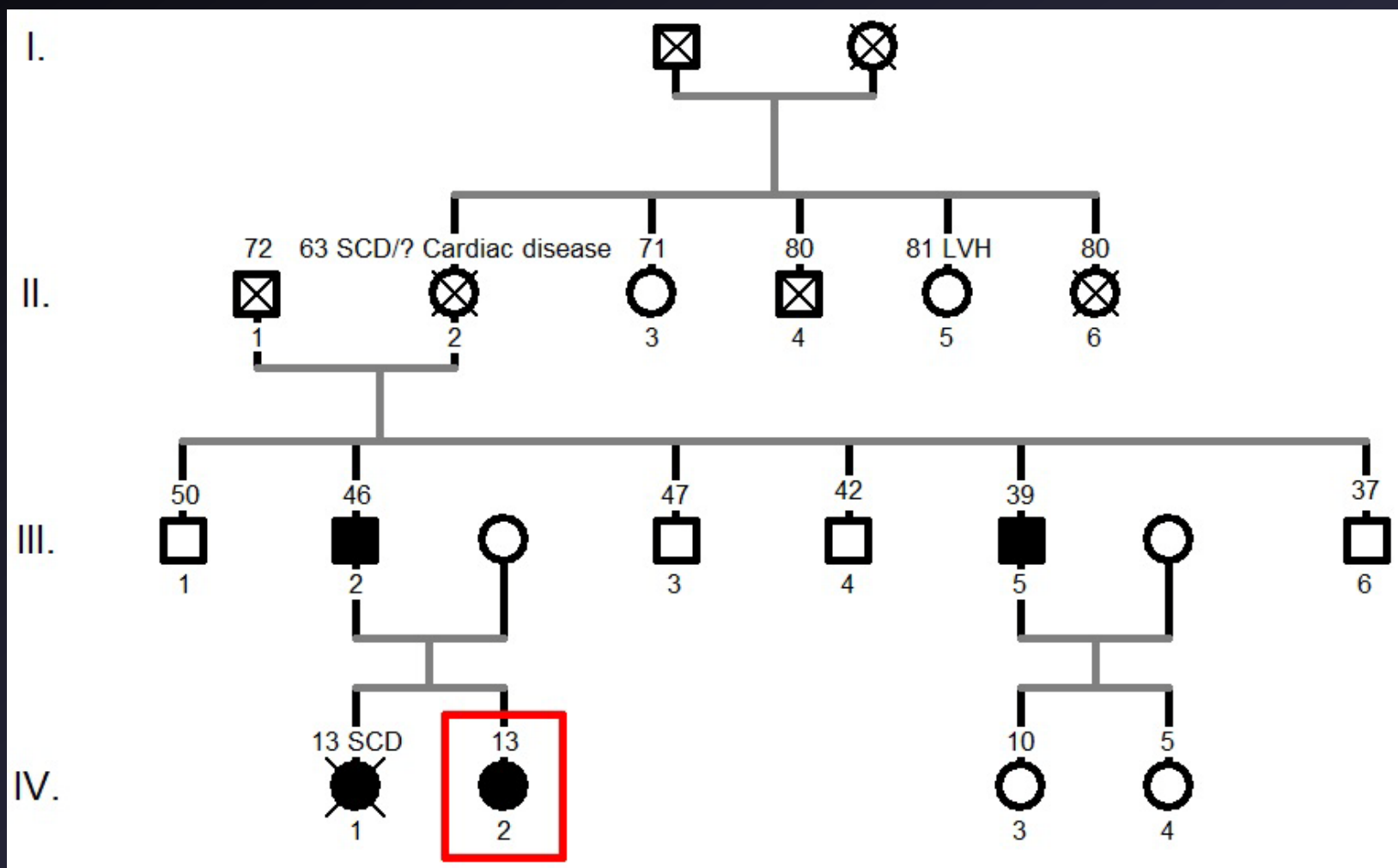
Index pt IV 1 ECG - 2008



Index pt IV 1 Echo - 2008



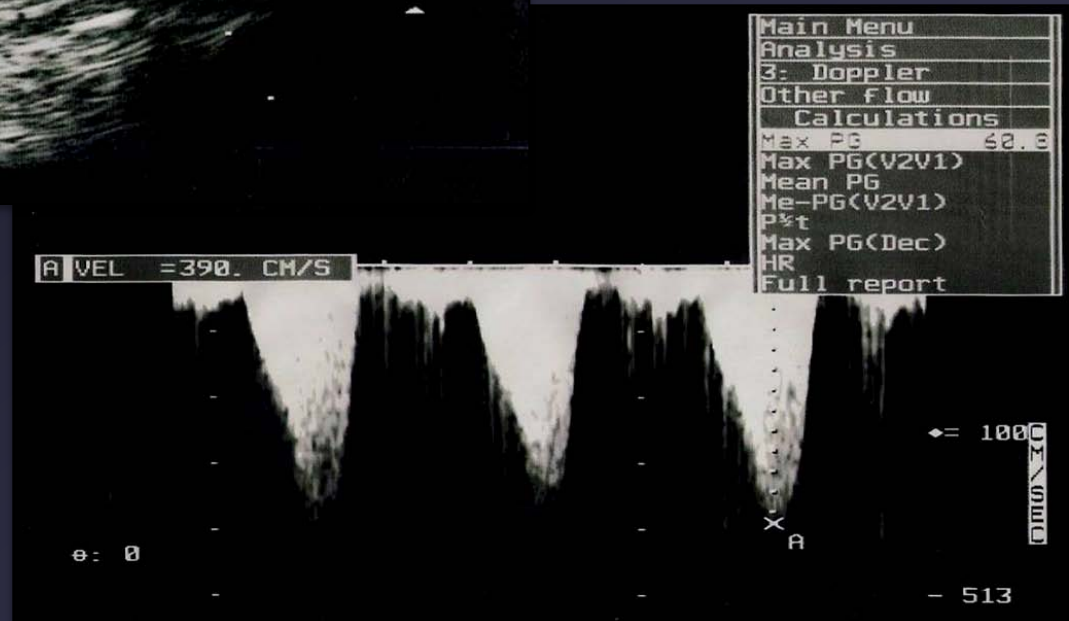
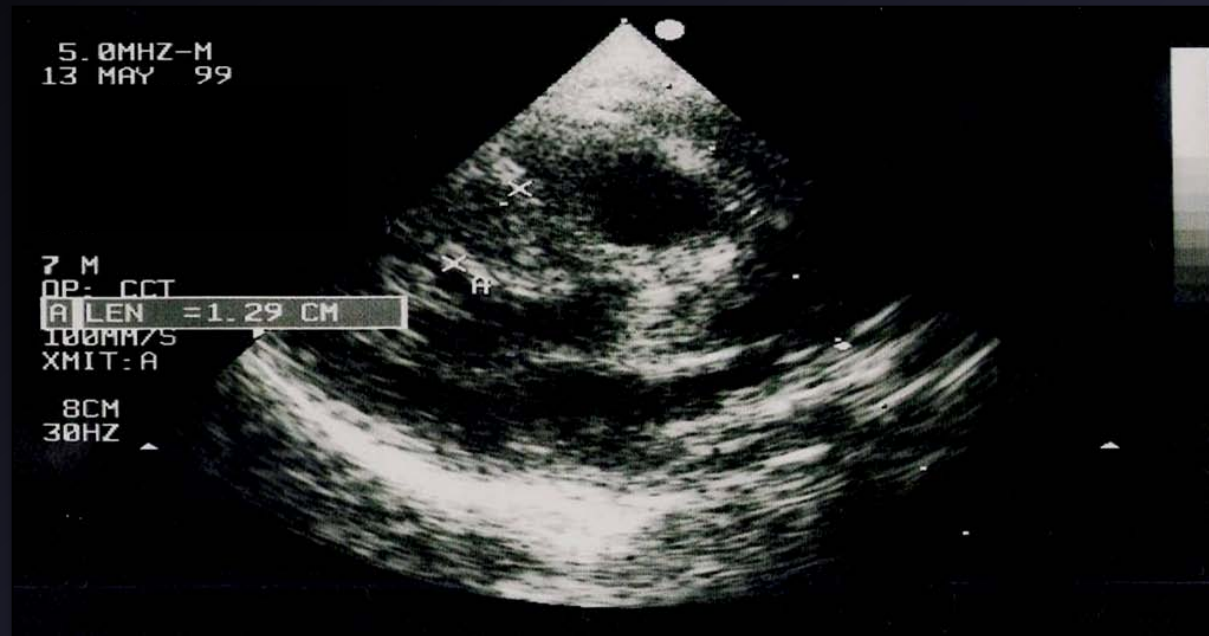
Family Pedigree



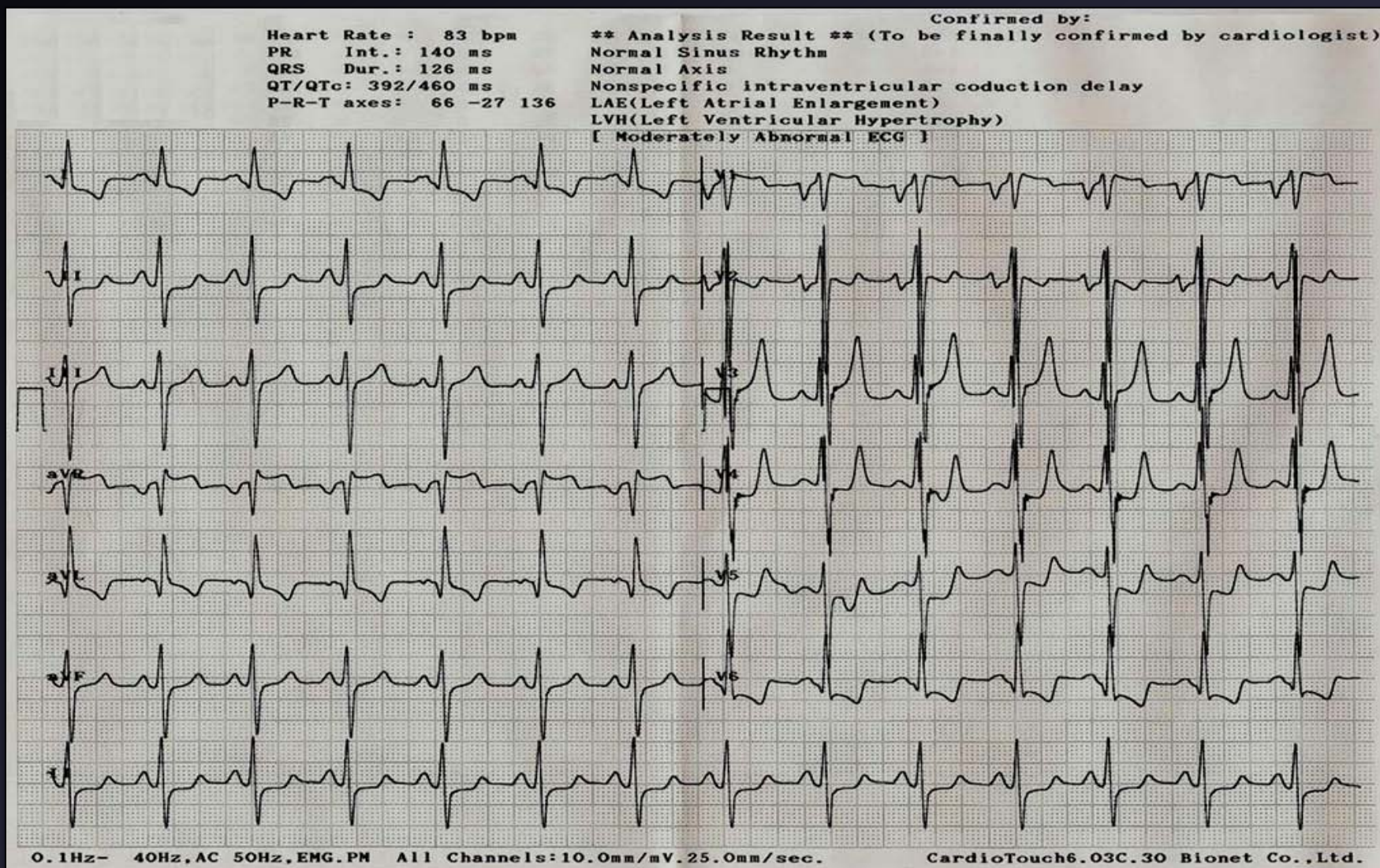
Index pt IV 2

- 12-y, Height 175 cm, BSA 1.8
- Age at first diagnosis 2 mo
- Adapted to low activity levels
- NYHA Class III, PND (+)
- Post-prandial exacerbation of dyspnea
- No syncope
- 24-h Holter 2 episodes of asymptomatic NSVT (3 & 5 beat run)
- No comorbidities (eg development abnormalities)

Index pt IV 2 Echo (2-mo)



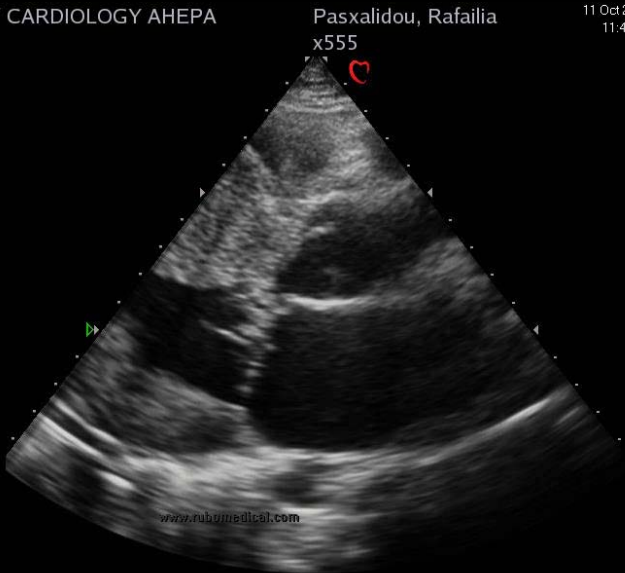
Index pt IV 2 ECG - 2010



Index pt IV 2 Echo - 2010

Unknown name
10/11/2010 A' CARDIOLOGY AHEPA
11:53:42

2-4PA 79 fps
Heart
2D BGain 18
15 cm Smooth 2
High H Reg 4
Enh -1
Gamma 4

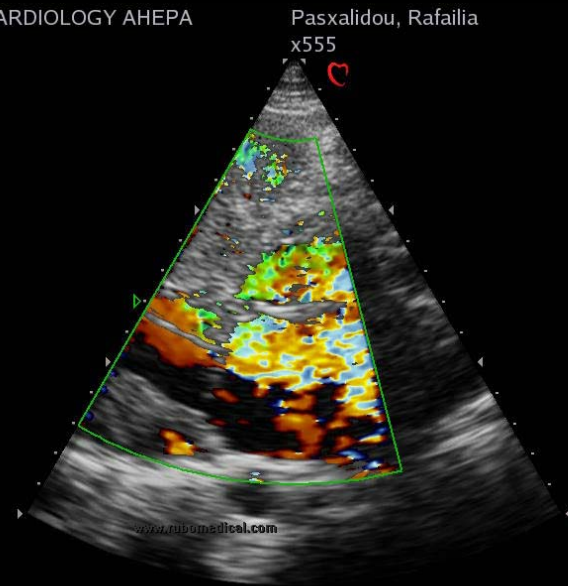


11 Oct 2010
11:49:22

10/11/2010 A' CARDIOLOGY AHEPA
11:54:04

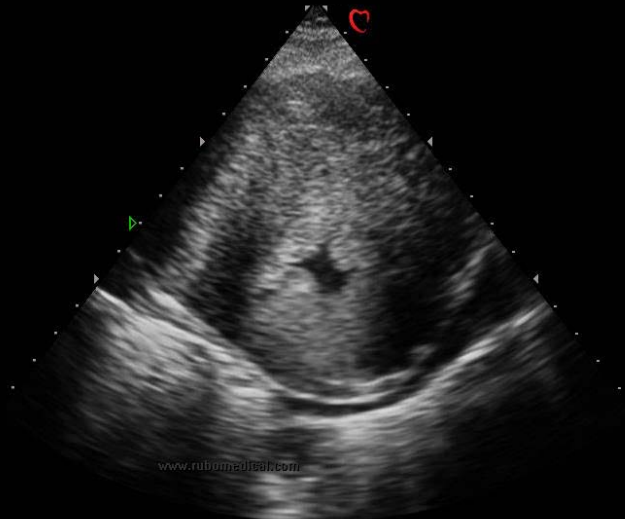
2-4PA 13 fps
Heart
2D BGain 19
15 cm
CFM CGain 15
2.6MHz Res Mid
Pers 0 En 0dB
ColMap1

60.2
cm/s
-60.2



Zoom (1.000x)

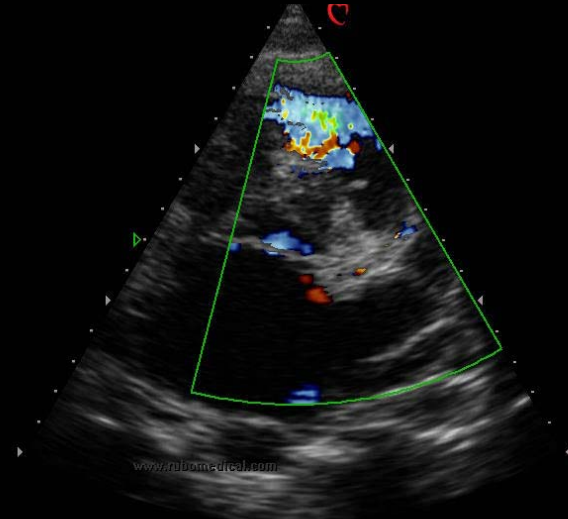
2-4PA 79 fps
Heart
2D BGain 18
15 cm Smooth 2
High H Reg 4
Enh -1
Gamma 4



1/600

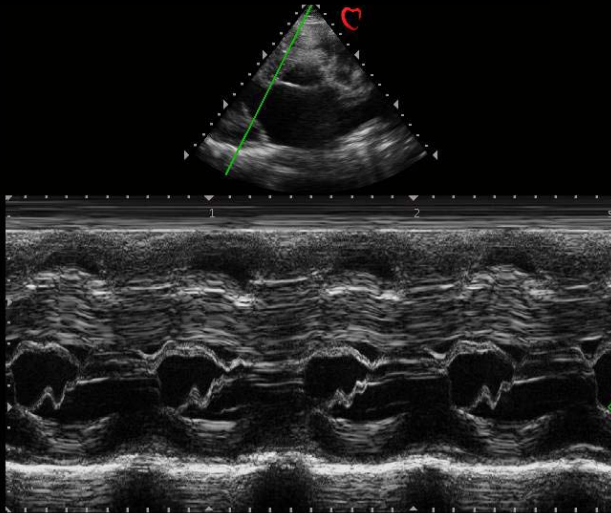
2-4PA 13 fps
Heart
2D BGain 19
15 cm
CFM CGain 15
2.6MHz Res Mid
Pers 0 En 0dB
ColMap1

60.2
cm/s
-60.2

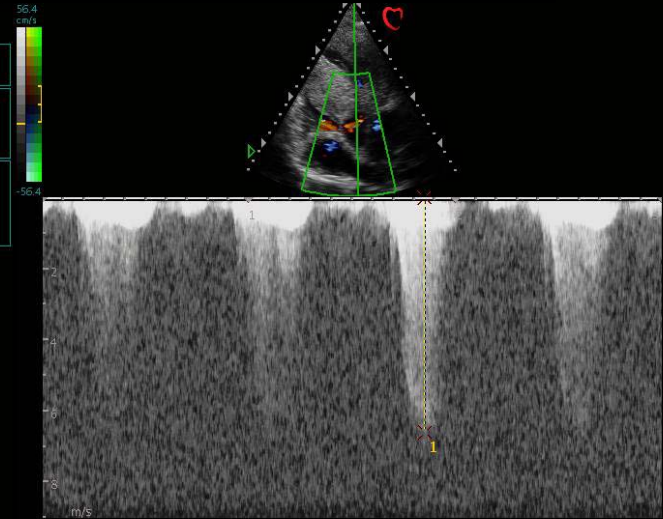


Index pt IV 2 Echo - 2010

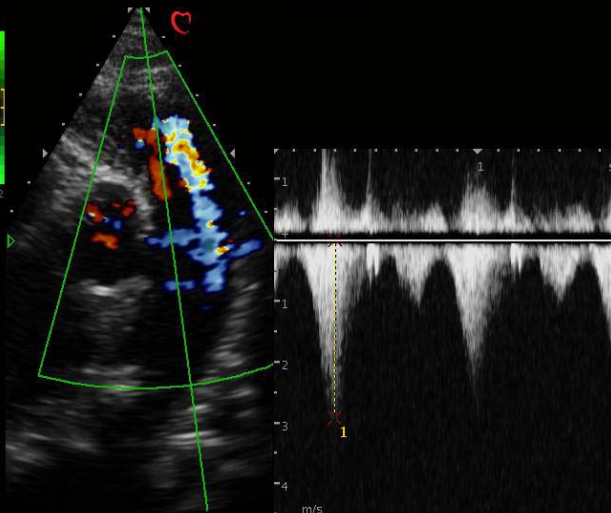
2-4PA 64 fps
Heart
2D BGain 18
15 cm Smooth 2
High H Rej 4
Enh -1
Gamma 4
M MGain 15
Gamma 4 Rej 3
Enh 3



2-4PA 14 fps
Heart
2D BGain 19
18 cm
CFM CGain 15
2.0MHz Res Mid
Pers 0 En 0dB
ColMap1
CW Gain 27dB
2MHz W 400Hz
Ang 0°
En 0dB
Gamma 4

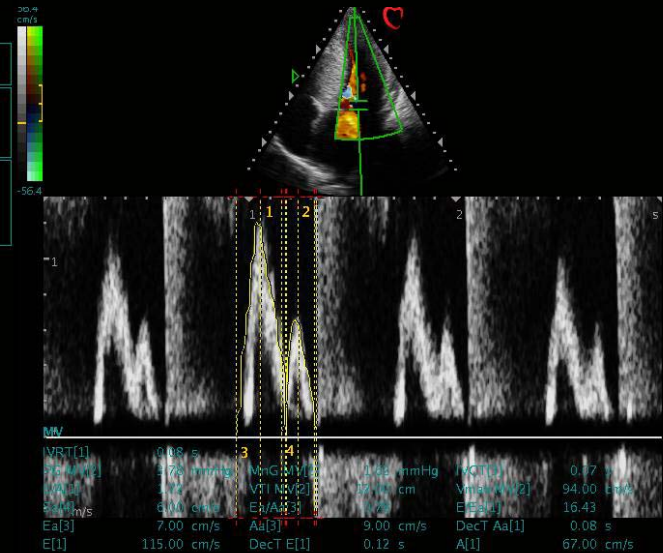


2-4PA 13 fps
Heart
2D BGain 19
15 cm
CFM CGain 15
2.6MHz Res Mid
Pers 0 En 0dB
ColMap1
CW Gain 18dB
2MHz W 400Hz
Ang 0°
En 0dB
Gamma 4



2-4PA 14 fps
Heart
2D BGain 19
18 cm
CFM CGain 15
2.0MHz Res Mid
Pers 0 En 0dB
ColMap1
PW Gain 15dB
2MHz W 400Hz
Gate 8mm
Ang 0°
En 0dB
Gamma 6

IT 0.12 s
2T 0.08 s
3VTI 17.4 cm
Vmax 120.7 cm/s
PG 5.82 mmHg
MnG 2.47 mmHg
T 0.24 s
4VTI 6.6 cm
Vmax 65.8 cm/s
PG 1.73 mmHg
MnG 0.78 mmHg
T 0.17 s





Treatment options

- Severe symptoms
 - Resting Gradient >100 mmHg
 - Severe MR
 - LA enlargement
-
- Medical treatment
 - Interventional treatment

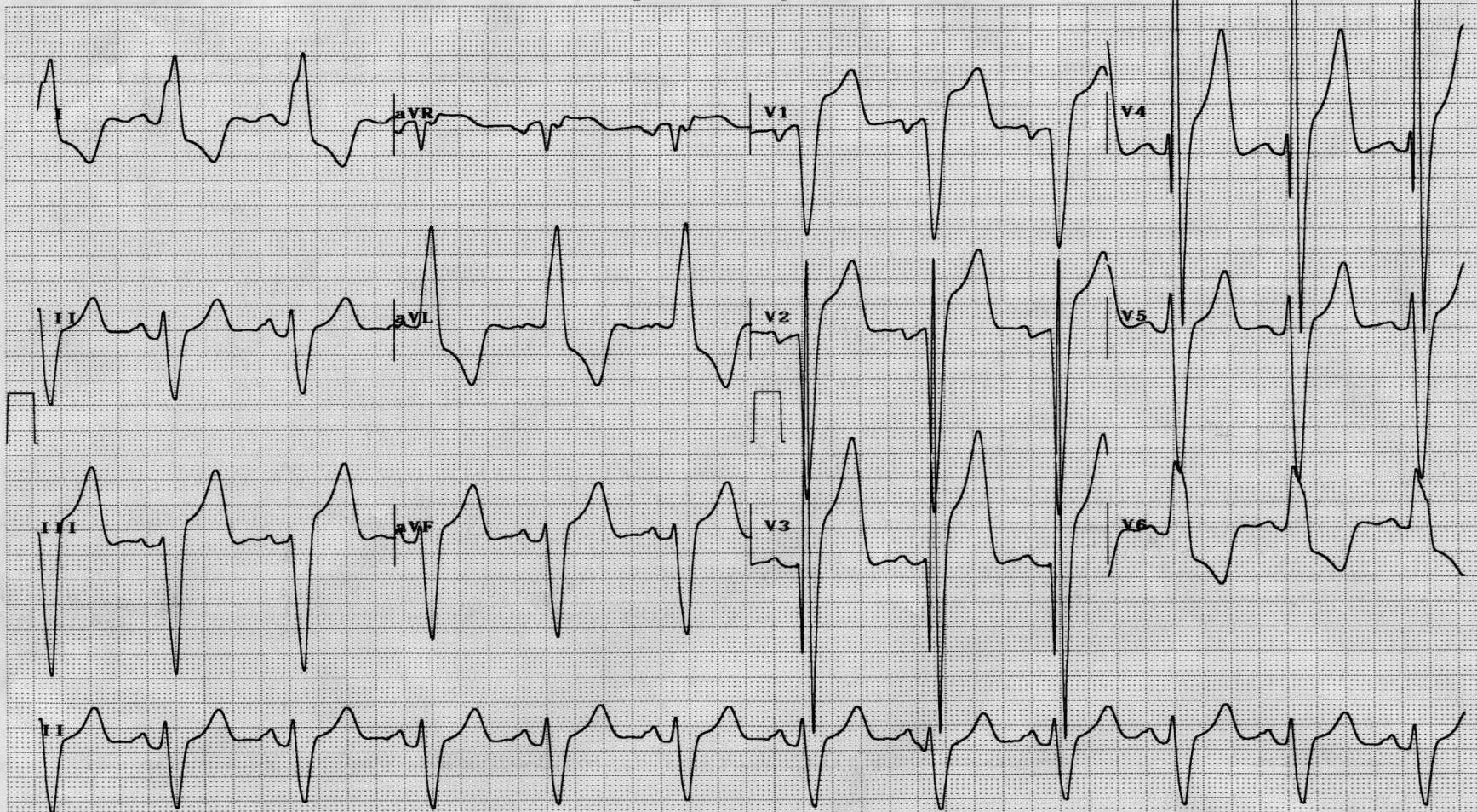


Risk stratification

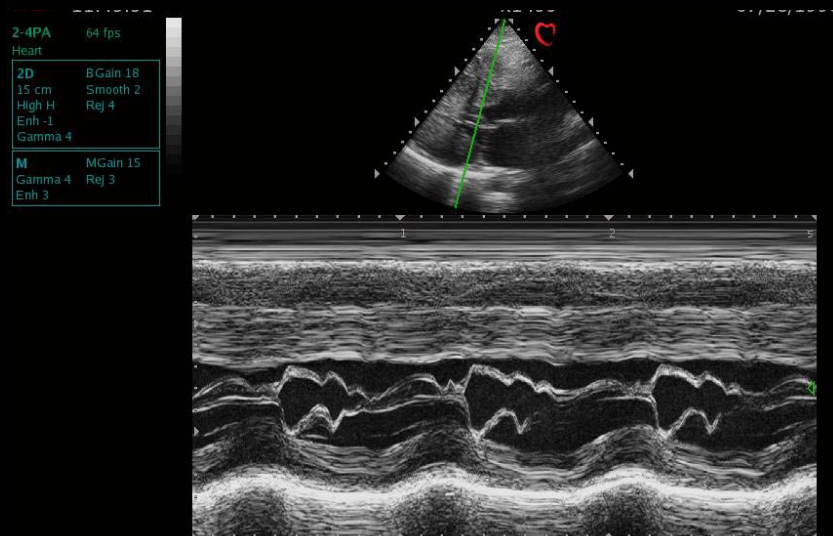
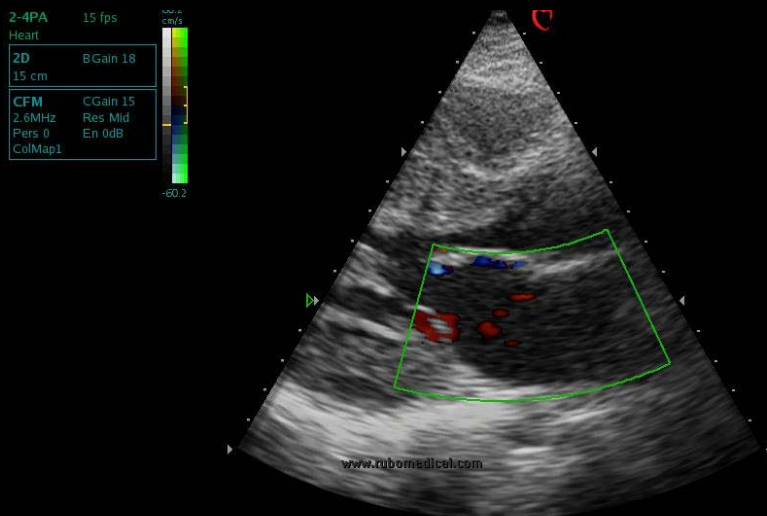
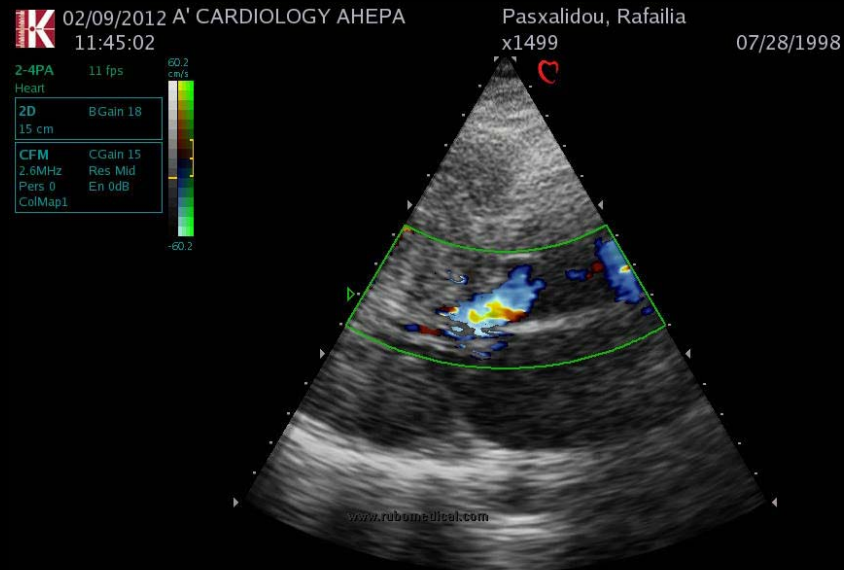
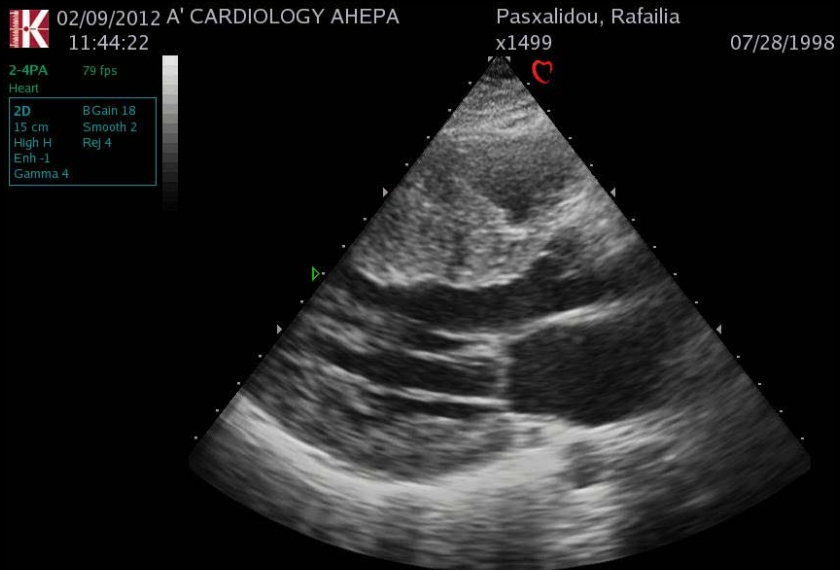
- Family history SCD
- NSVT
- Maximal wall thickness > 30 mm
- History of syncope
- ABPR
- Suggestion for ICD implantation (pt denied)
 - Amiodarone added until decision finalized

Post-operative ECG

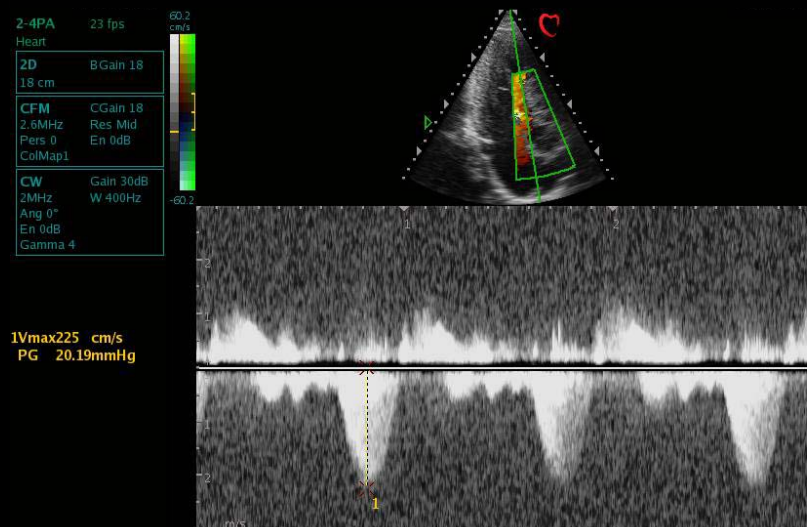
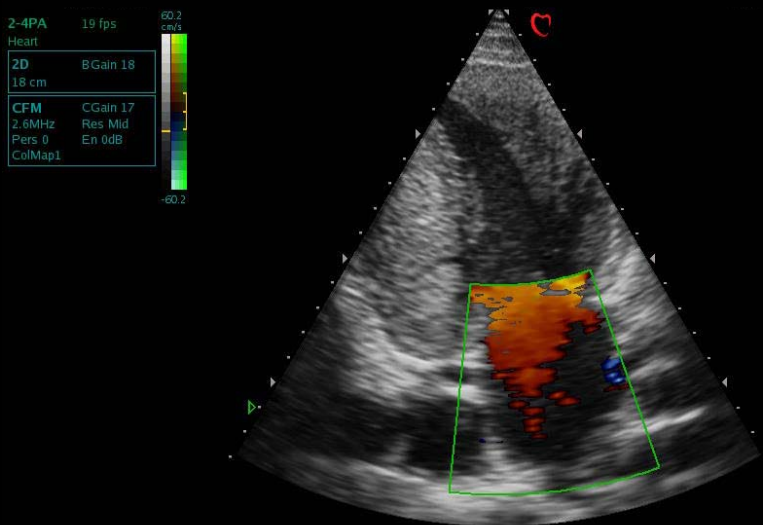
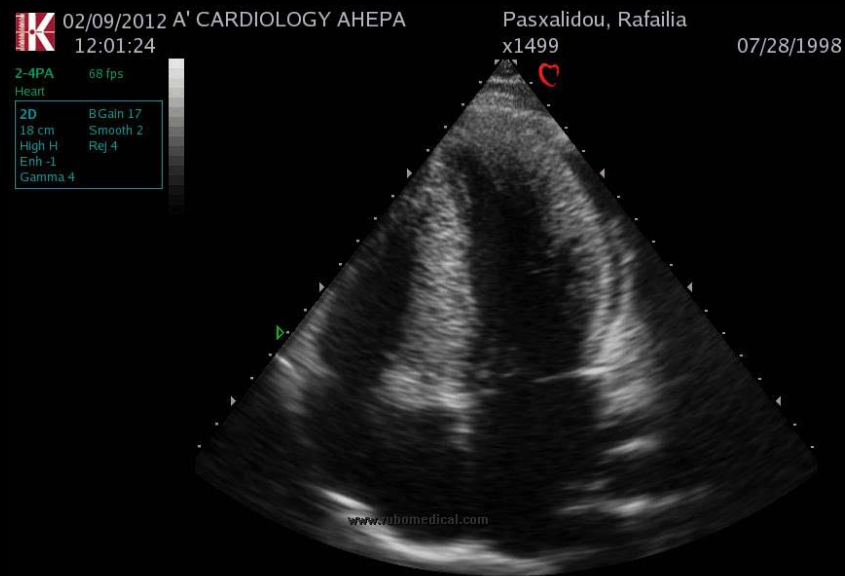
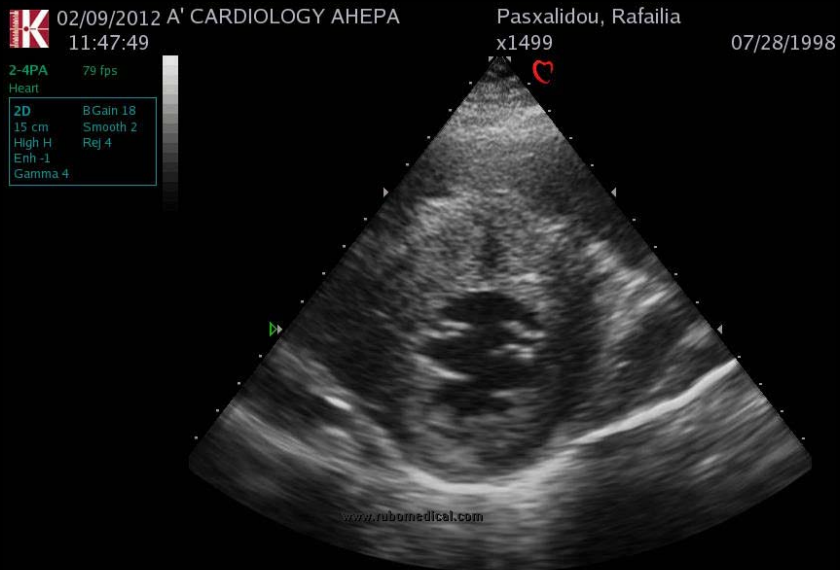
ID:	Heart Rate : 68 bpm	** Analysis Result ** (To be finally confirmed by cardiologist)
Name:	PR Int.: 182 ms	Normal Sinus Rhythm
Age: Years	QRS Dur.: 200 ms	Left Axis Deviation
Sex:	QT/QTc: 518/548 ms	LBBB(Left Bundle Branch Block)
H:cm / W:Kg	P-R-T axes: 59 -50 122	LAE(Left Atrial Enlargement)
		[Moderately Abnormal ECG]



Postoperative echo

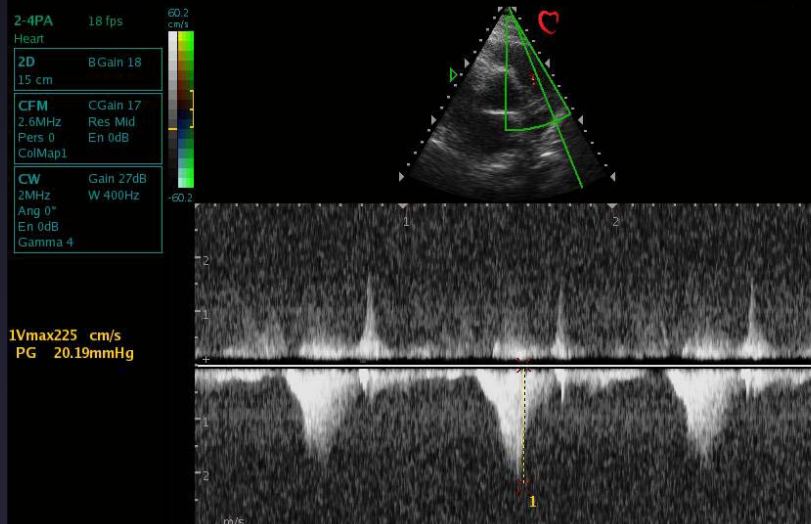
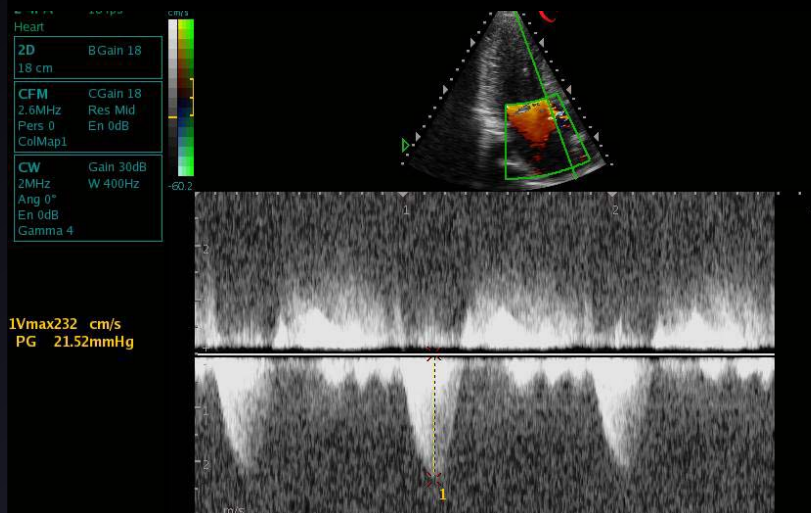


Postoperative echo

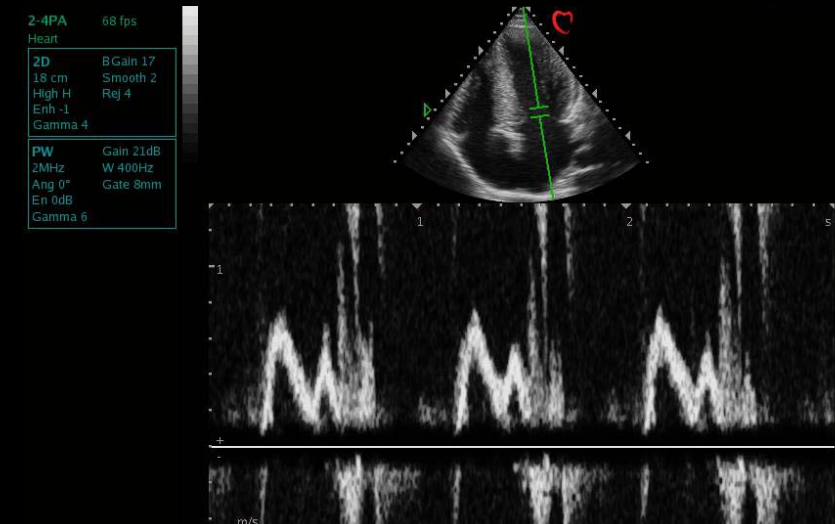
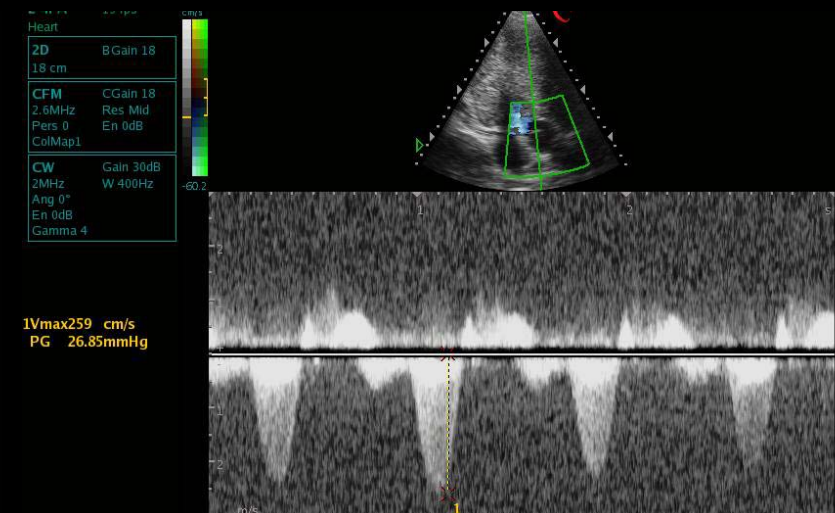


Postoperative echo

Valsalva



Upright position





Discussion II

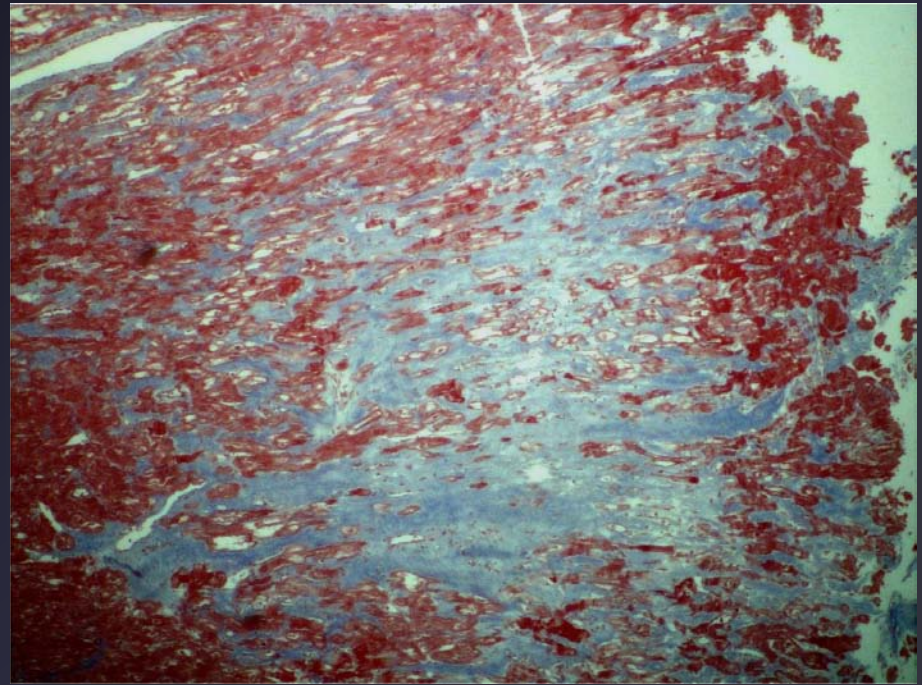
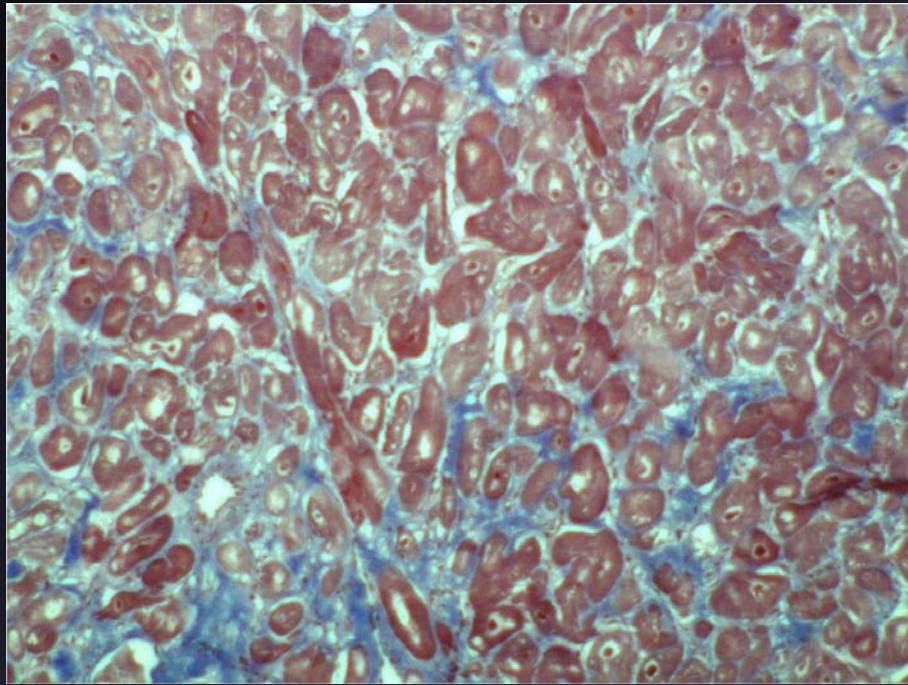
- Post-operative status (1 yr follow-up)
- NYHA I-II
- No post-prandial exacerbation of symptoms
- NSVT (6 beat episode during attempt to down-titrate Amiodarone)
- ? Long term effect of myectomy

Discussion III

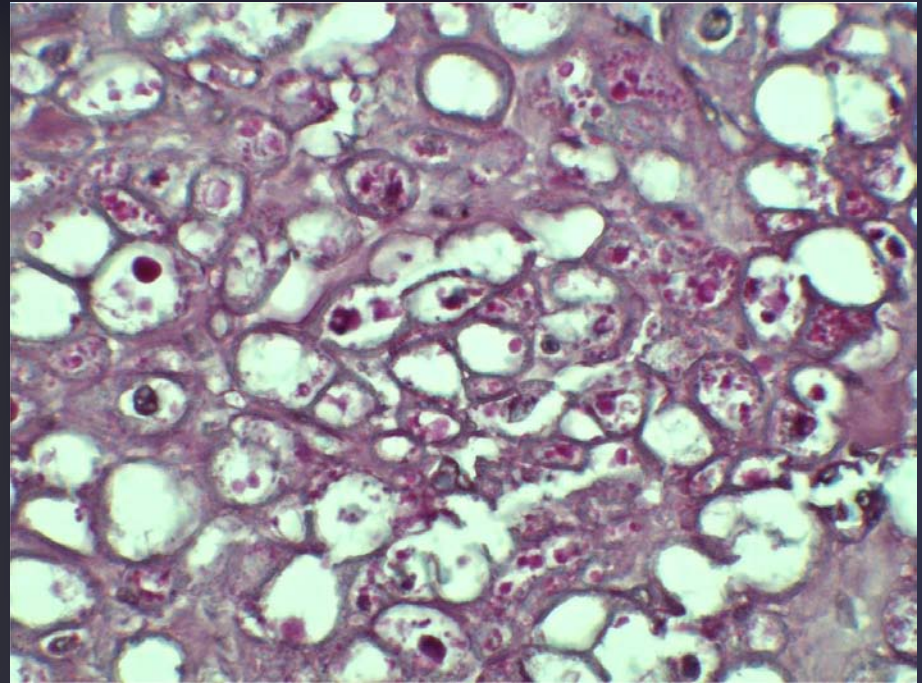
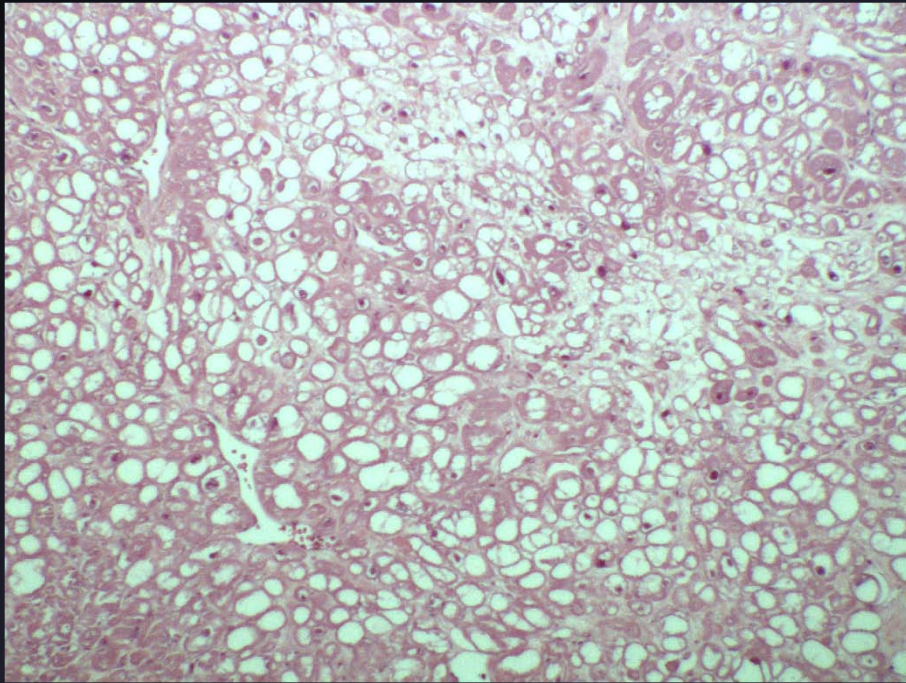
- Phenotypical variability between generations III and IV
 - Early development of LVH
 - More severe LVH
 - Arrhythmic burden
- Childhood sarcomeric HCM: $4.7/10^6/\text{year}^*$
- Compound/regulatory mutations ?
 - Mother screened, normal phenotype
- Other differential diagnosis ?

**Lipshultz S, et al. N Engl J Med 2003;348:1647*

Histology

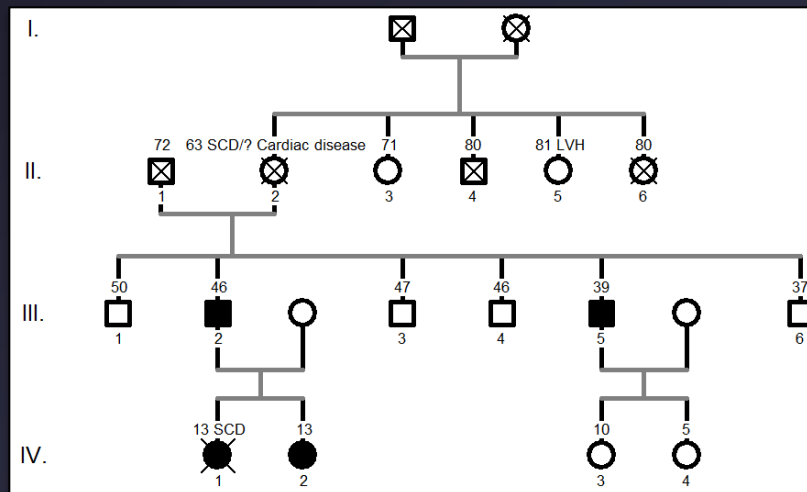


Histology



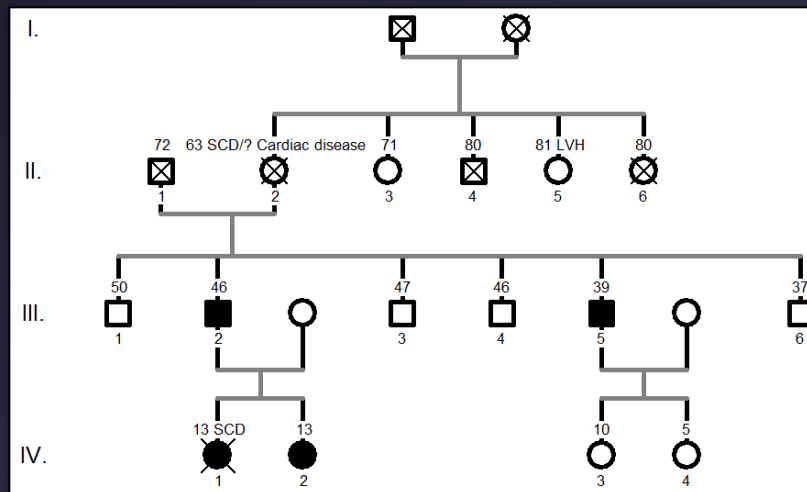
Cardiac glycogen deposition

- Differential diagnosis
 - Pompe's disease: autosomal recessive inheritance
 - Danon disease: X-linked inheritance
 - Cori's disease: autosomal recessive inheritance
 - PRKAG2 deficiency: autosomal dominant inheritance



Cardiac glycogen deposition

- Differential diagnosis
 - Pompe's disease: autosomal recessive inheritance
 - Danon disease: X-linked inheritance
 - Cori's disease: autosomal recessive inheritance
 - **PRKAG2 deficiency: autosomal dominant inheritance**



PRKAG2 deficiency

- Protein kinase, AMP-activated, gamma 2 non-catalytic subunit
- Regulation of energetic turnover
- Amylopectin deposition (PAS staining) and fibrosis
- Key features
 - Progressive LVH of early onset
 - Conduction disease (progressive)
 - Pre-excitation (familial WPW)
 - Striated muscle disease



Take home messages

- Early onset LVH should prompt for investigation and early management
- Risk stratification and symptomatic relief are equally important
- Intrafamilial phenotypic variation should be carefully assessed
- Phenocopies should be taken into account
- Family pedigree is an important modality