Case Presentation
A family with LVH

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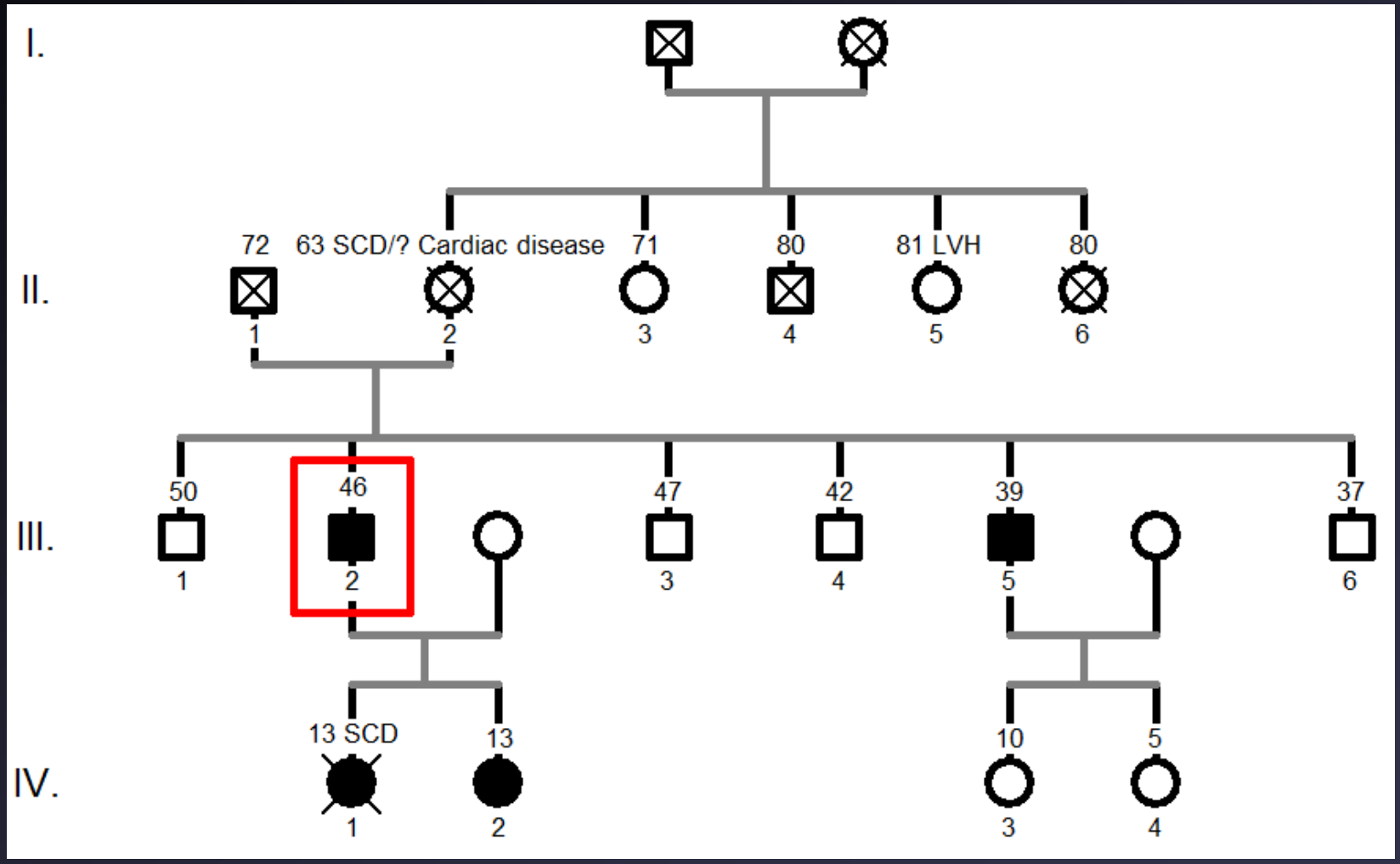
Α’ Καρδιολογική Κλινική ΑΧΕΠΑ

Αριστοτέλειο Πανεπιστήμιο Θεσ/νίκης

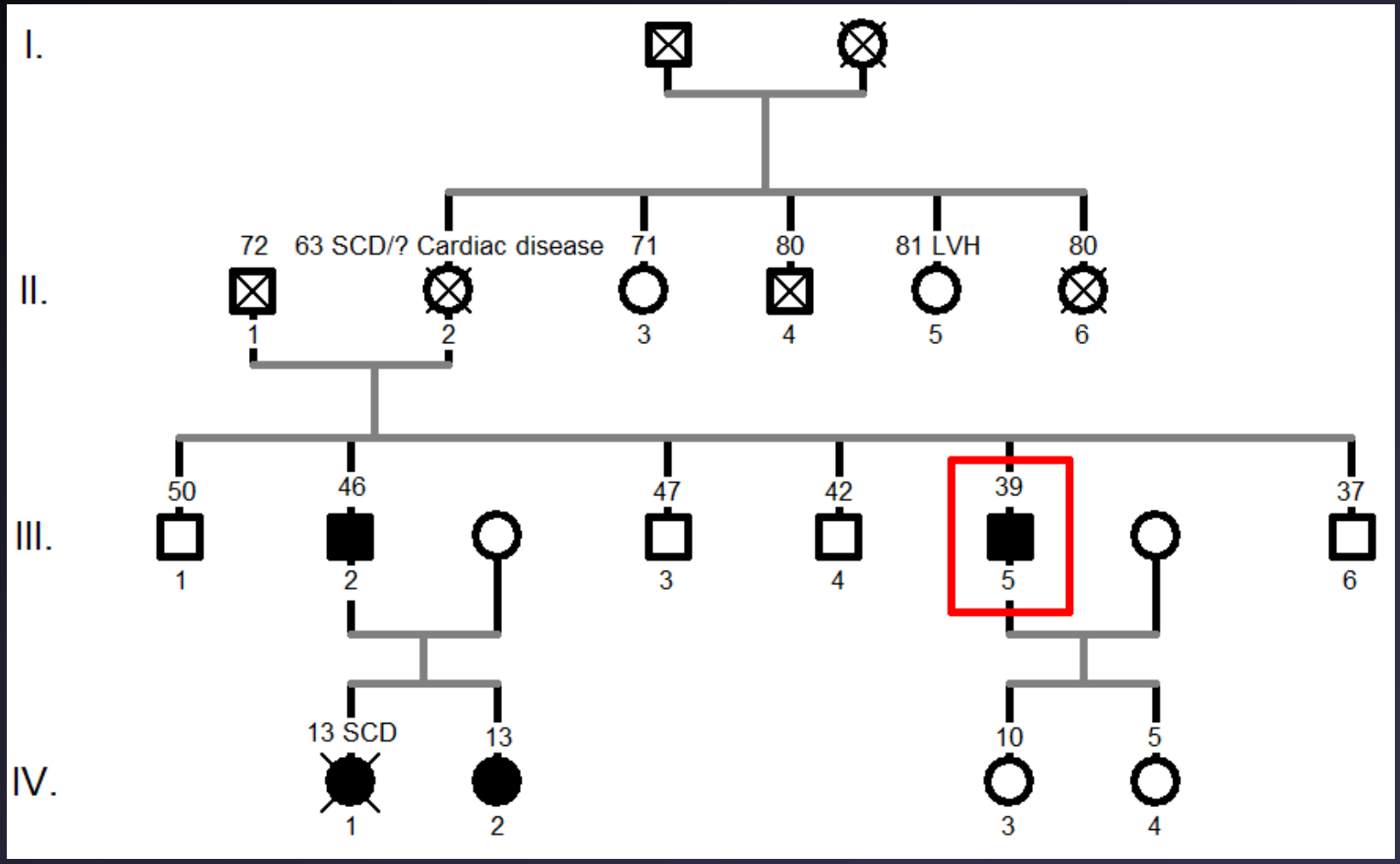
Family Pedigree



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 provocable gradient
- 24-h Holter no episodes of NSVT
- Normal BP response to exercise
- MRI 30% LGAD enhancement
- Genetic test for Anderson Fabry's negative

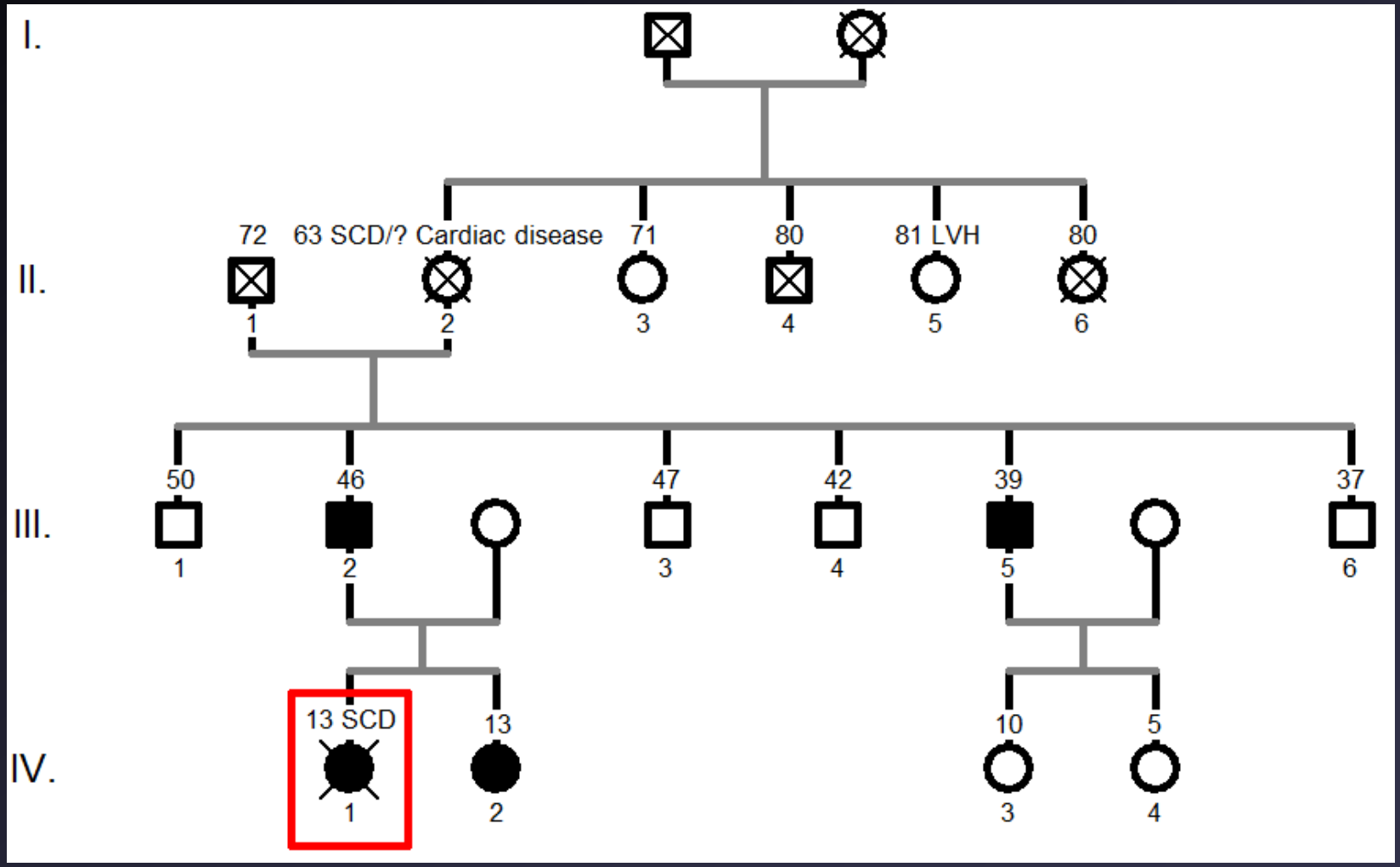
Family Pedigree



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 provocable 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

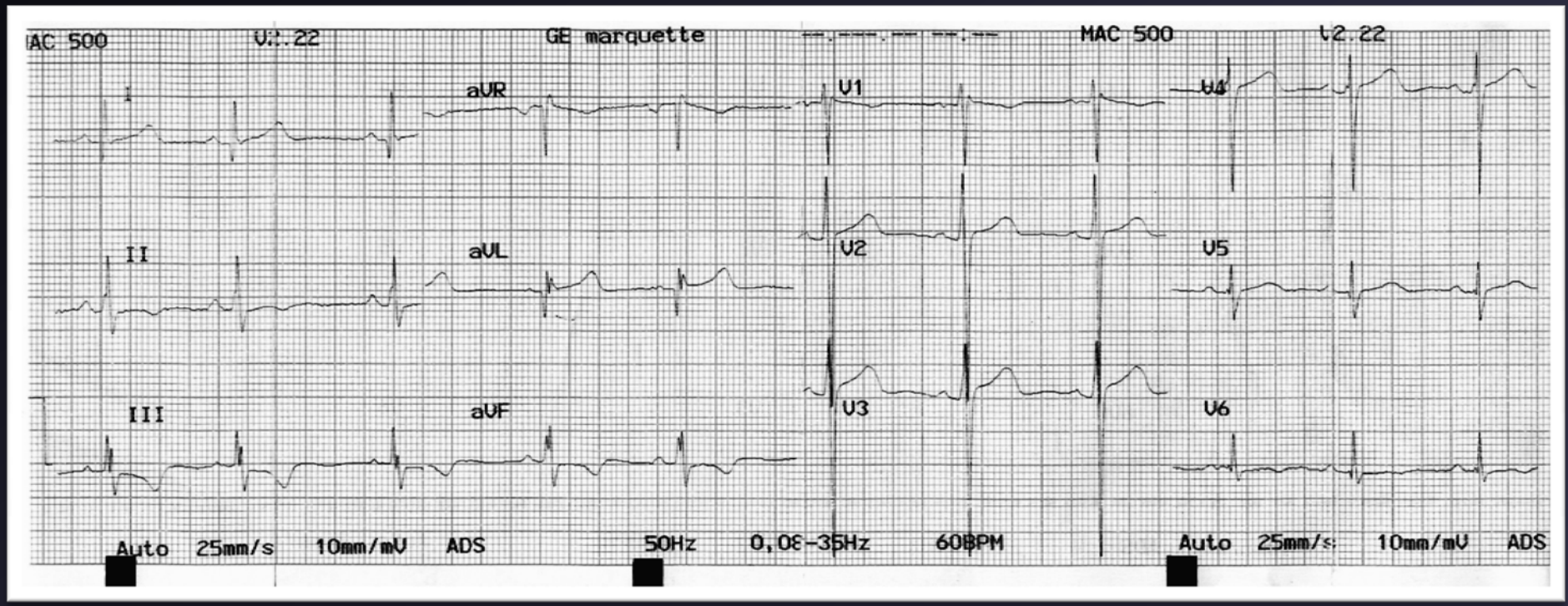
Family Pedigree



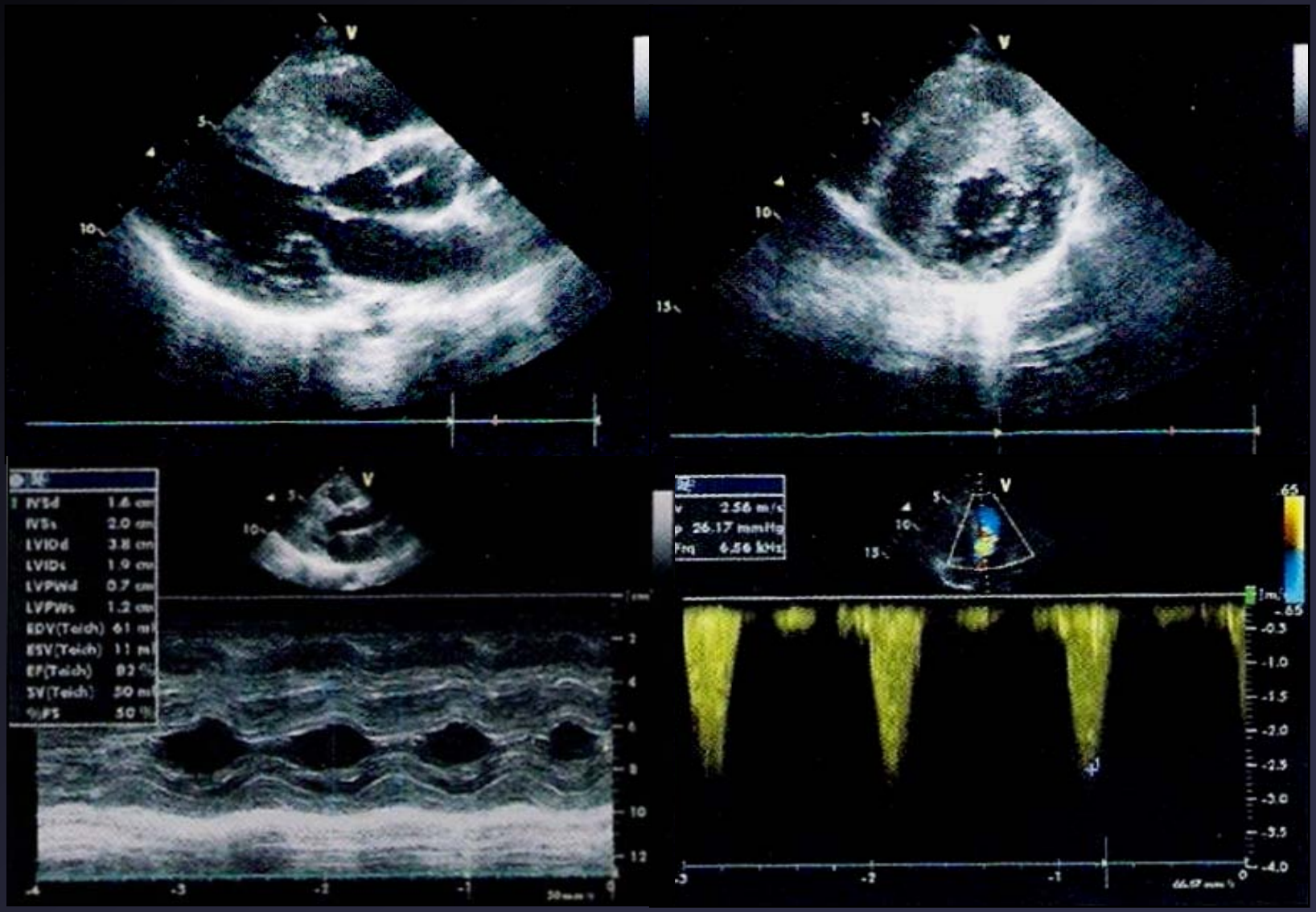
Index pt IV 1

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

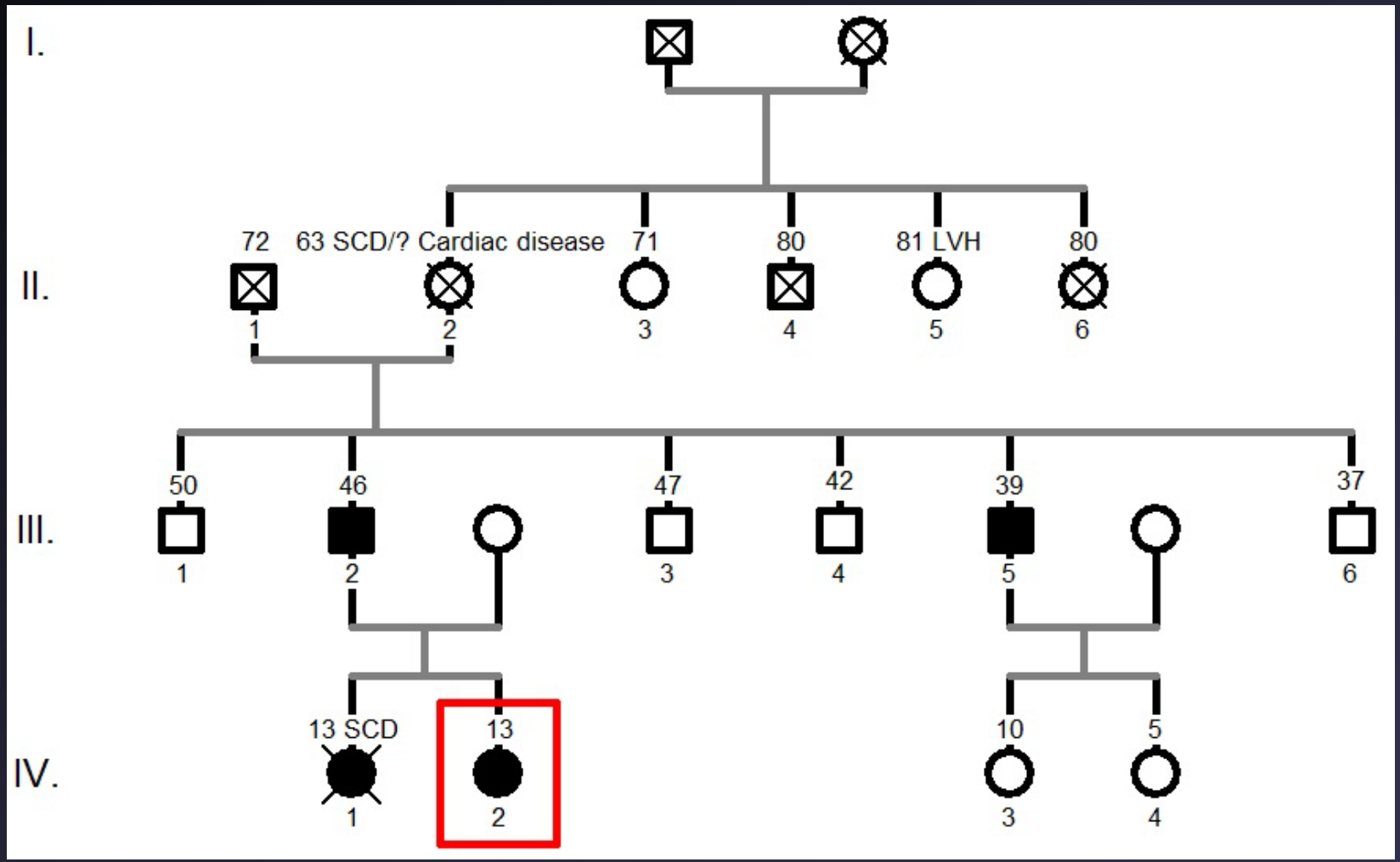
Index pt IV 1 ECG - 2008



Index pt IV 1 Echo - 2008



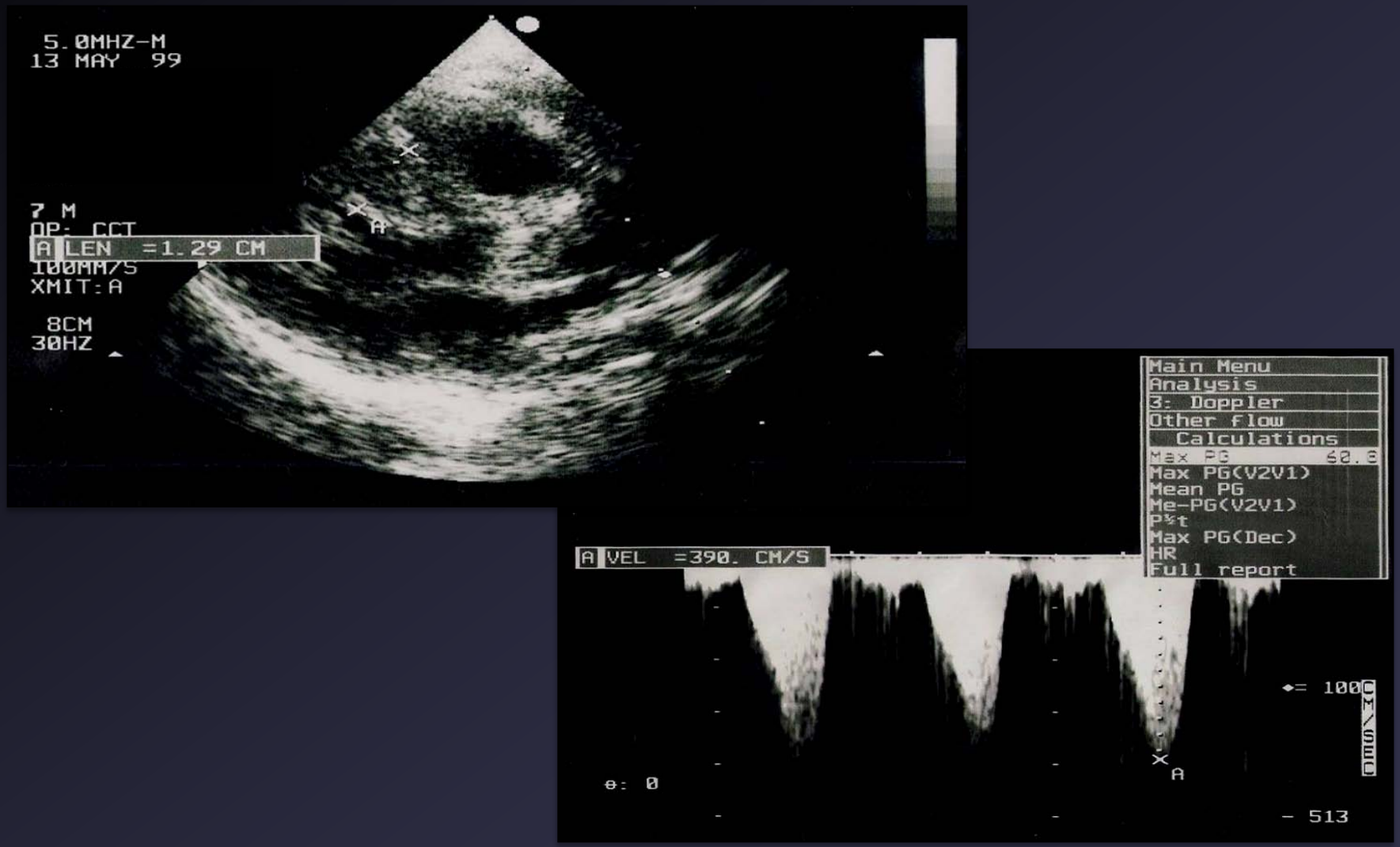
Family Pedigree



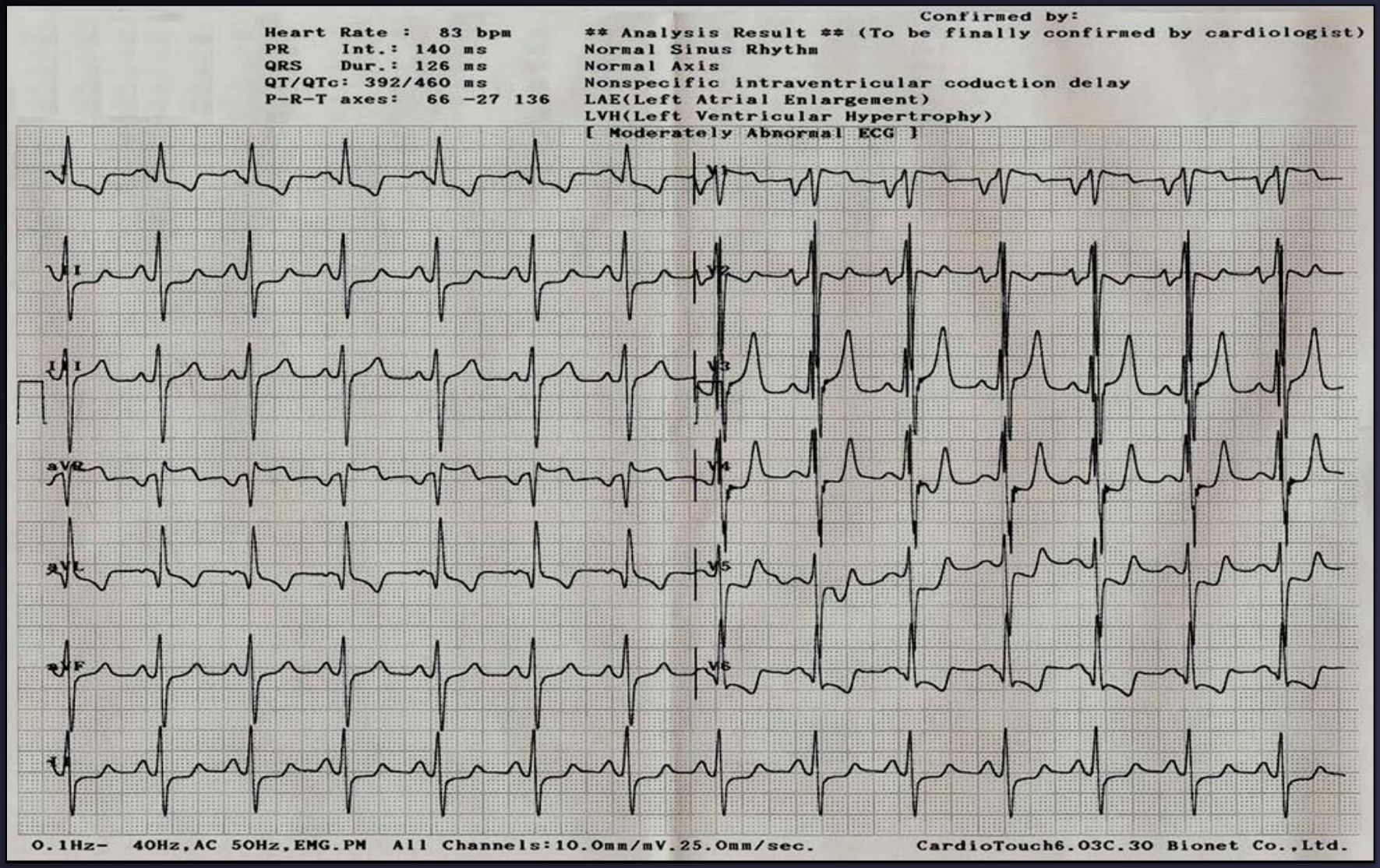
Index pt IV 2

- 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)

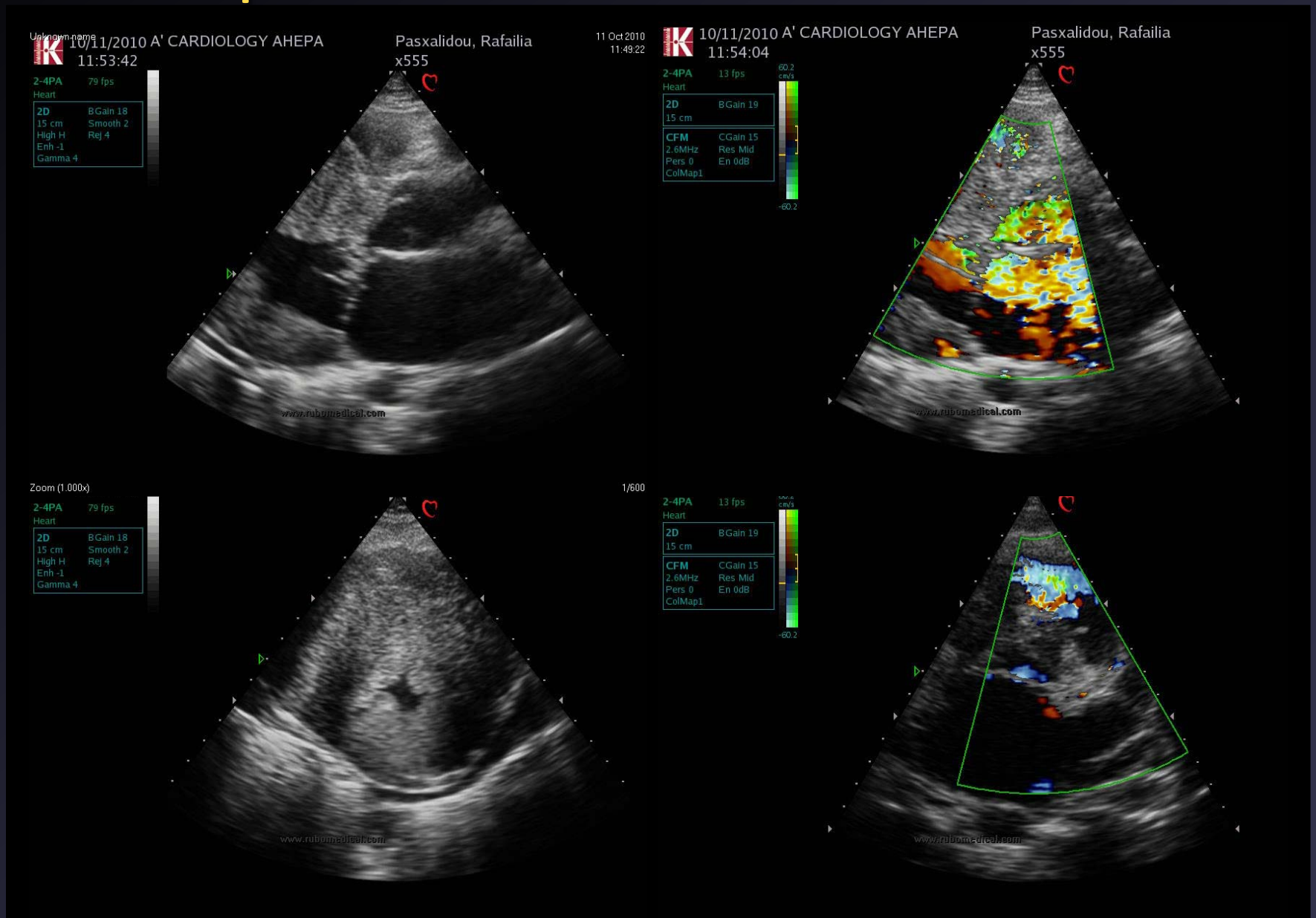
Index pt IV 2 Echo (2-mo)



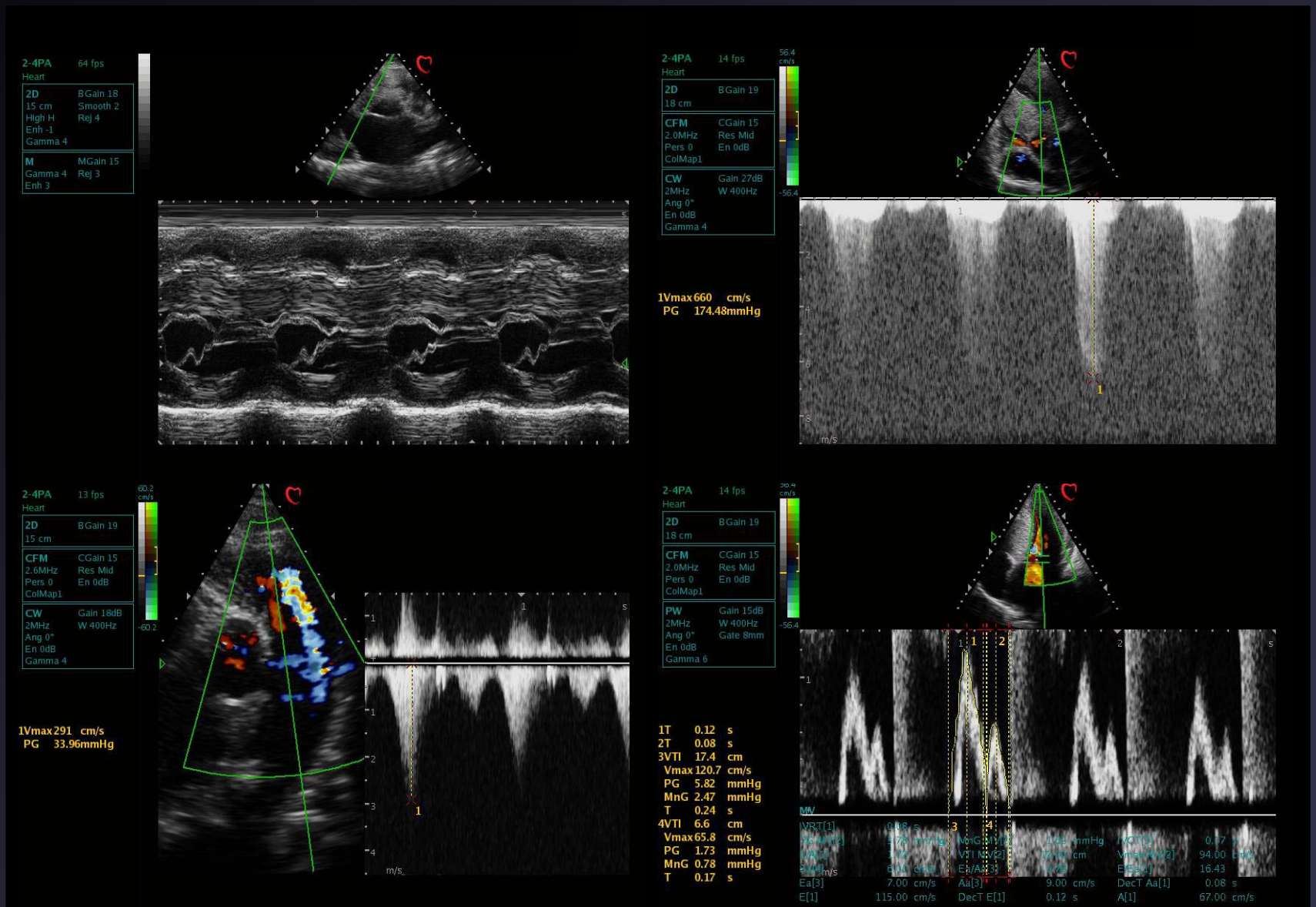
Index pt IV 2 ECG - 2010



Index pt IV 2 Echo - 2010



Index pt IV 2 Echo - 2010



Treatment options

- Severe symptoms
- Resting Gradient >100 mmHg
- Severe MR
- LA enlargement

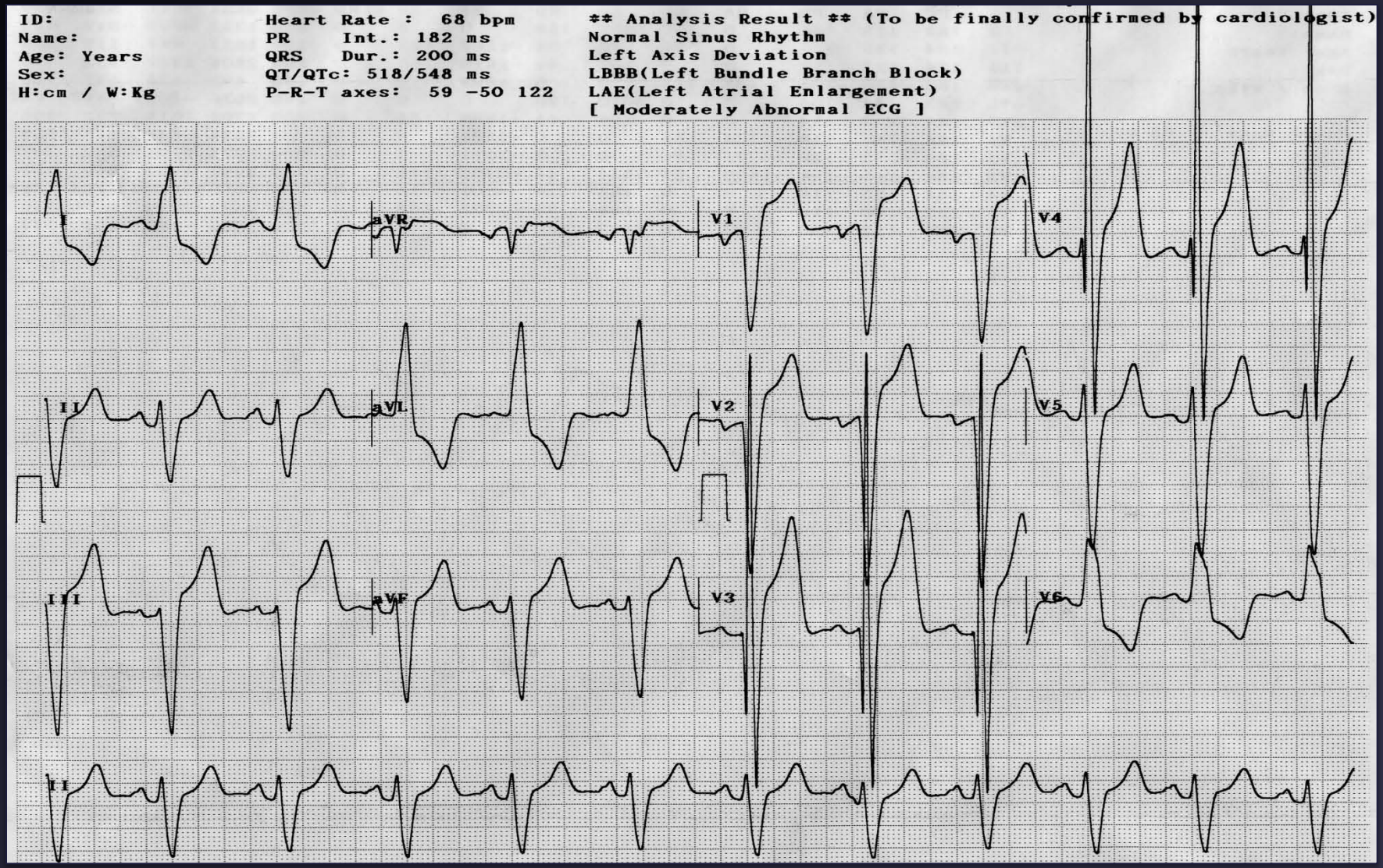
- Medical treatment
- Interventional treatment

Risk stratification

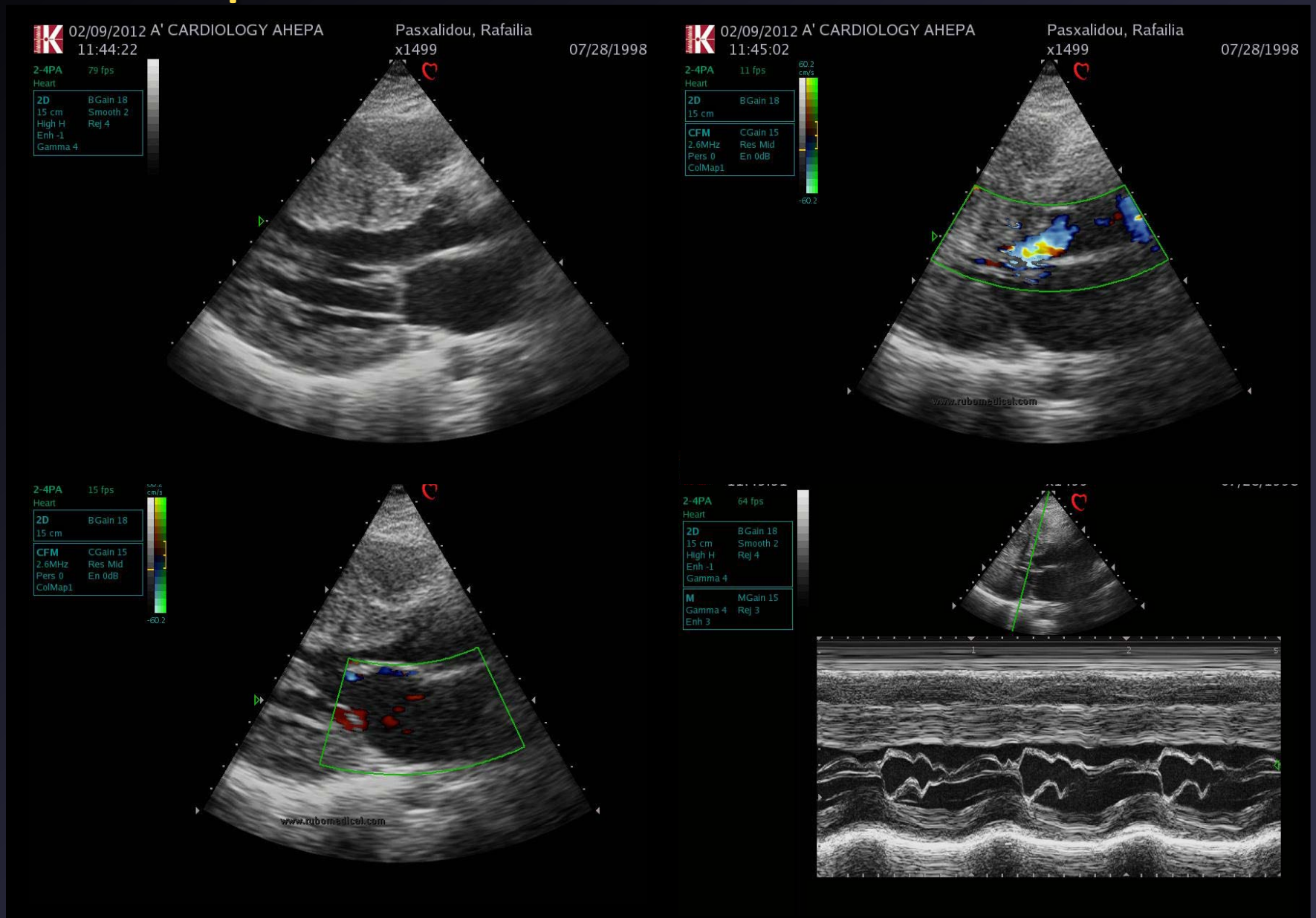
- Family history SCD
- NSVT
- Maximal wall thickness > 30 mm
- History of syncope
- ABPR

- Suggestion for ICD implantation (pt denied)
  - Amiodarone added until decision finalized

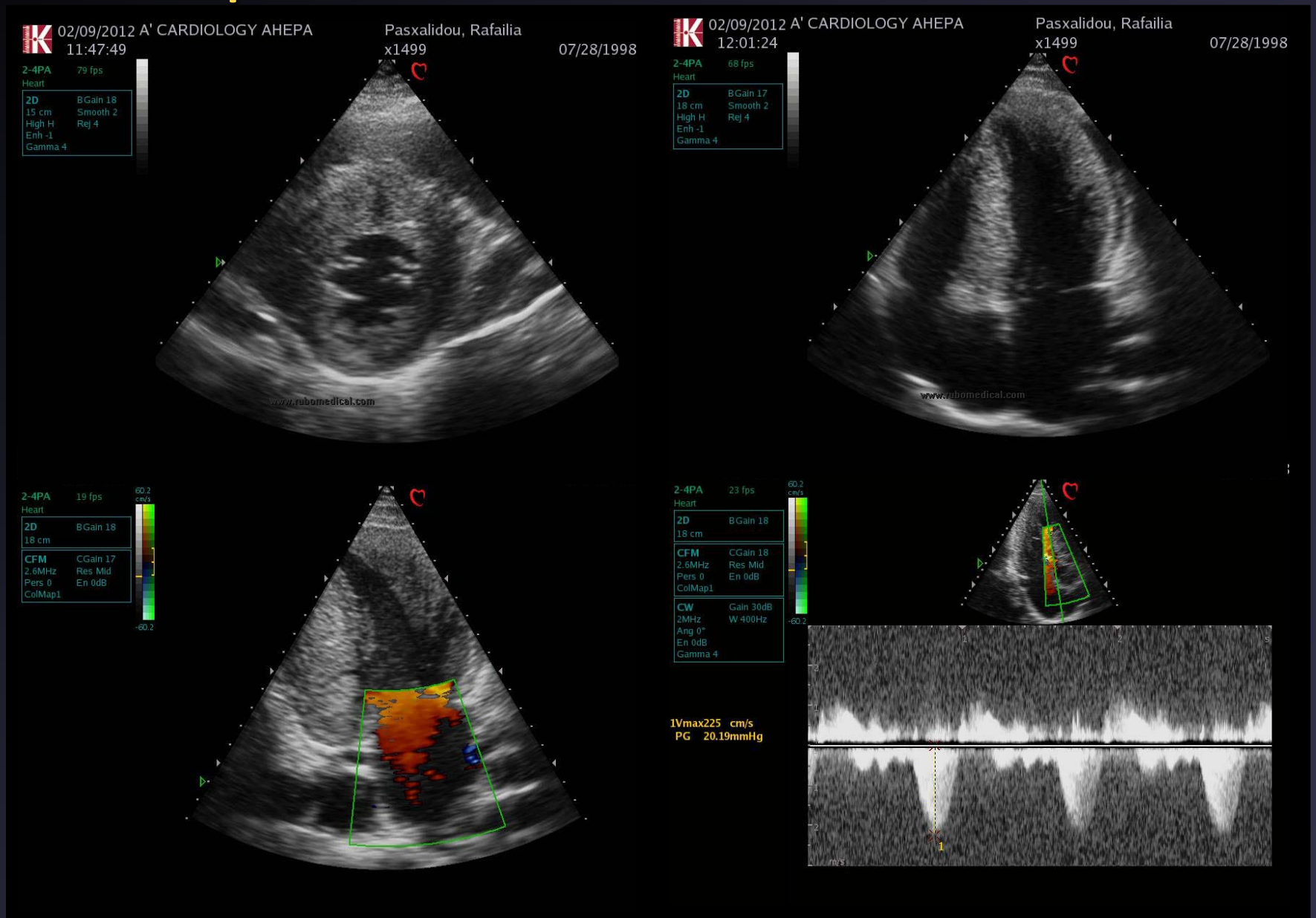
Post-operative ECG



Postoperative echo

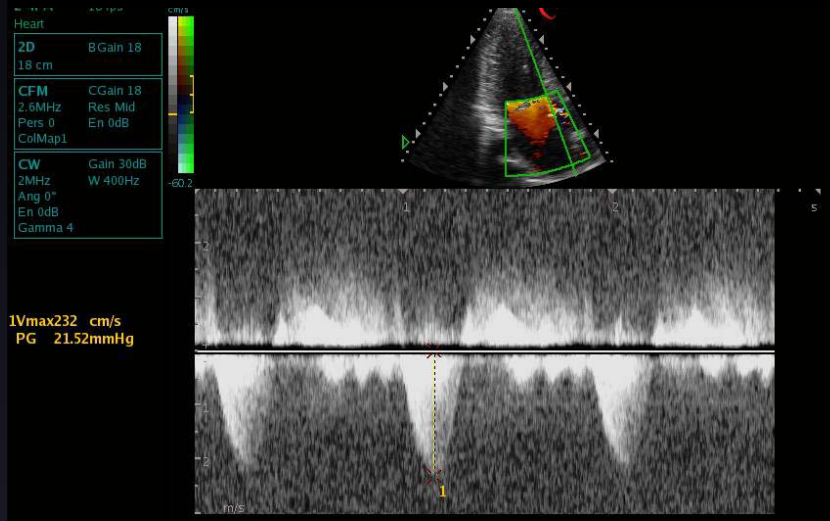


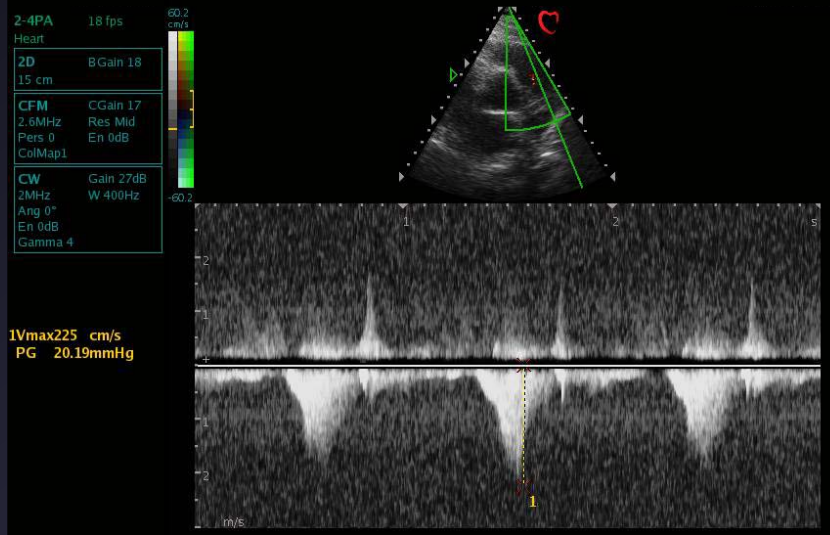
Postoperative echo



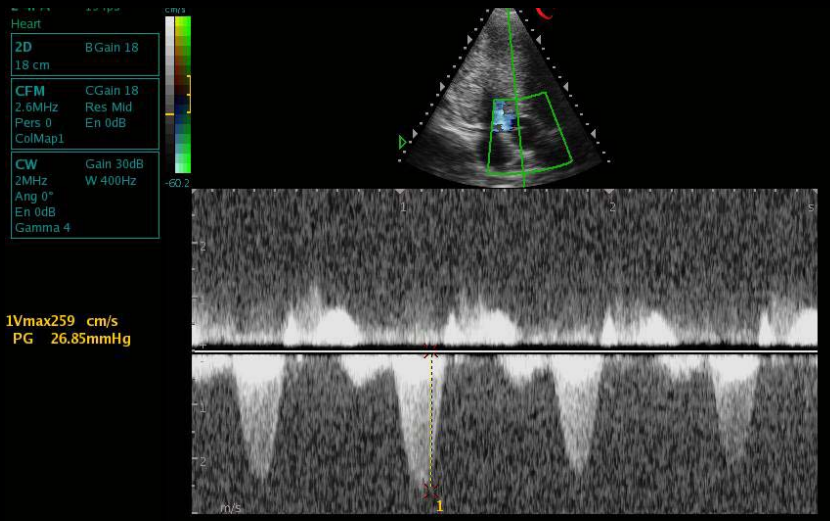
Postoperative echo

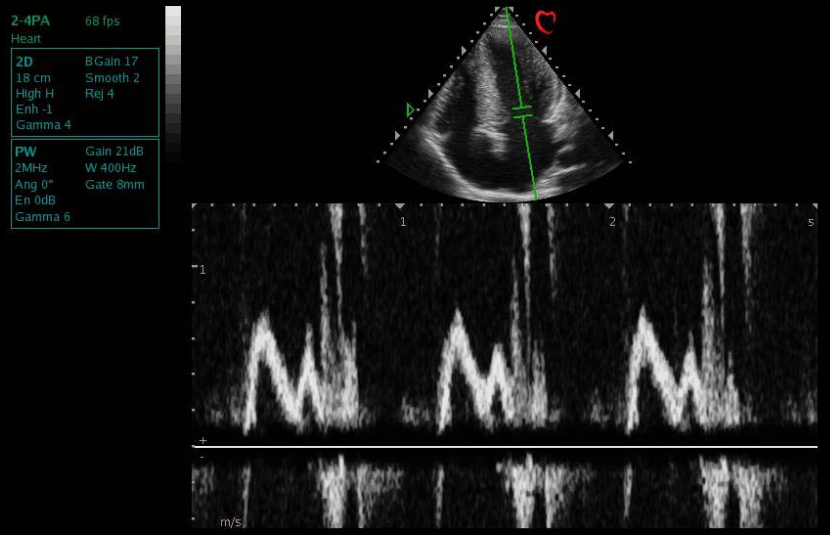
Valsalva





Upright position





Discussion II

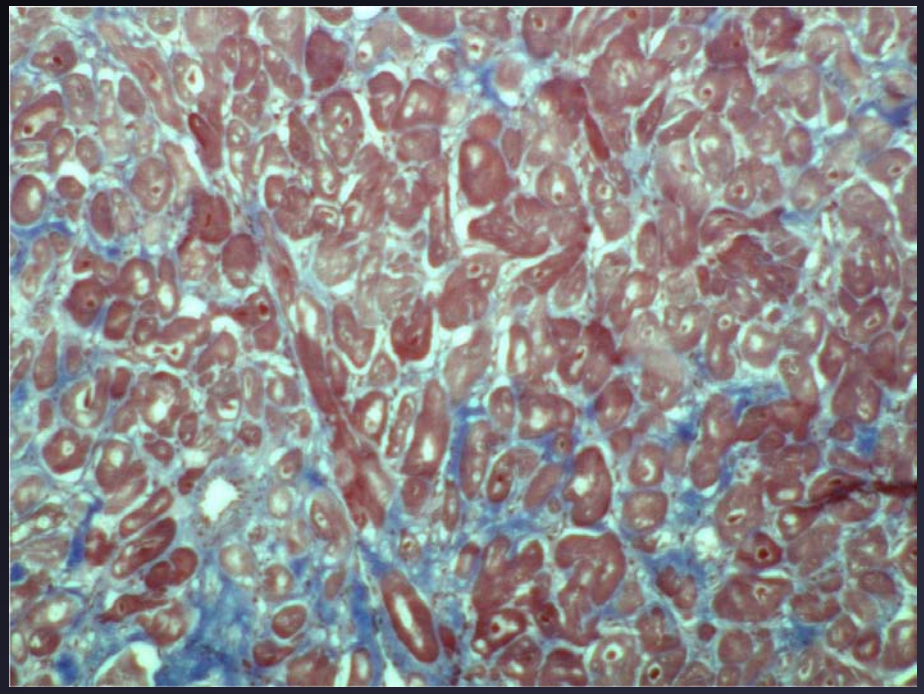
- Post-operative status (1 yr follow-up)
- NYHA I-II
- No post-prandial exacerbation of symptoms
- NSVT (6 beat episode during attempt to down-titrate Amiodarone)
- ? Long term effect of myectomy

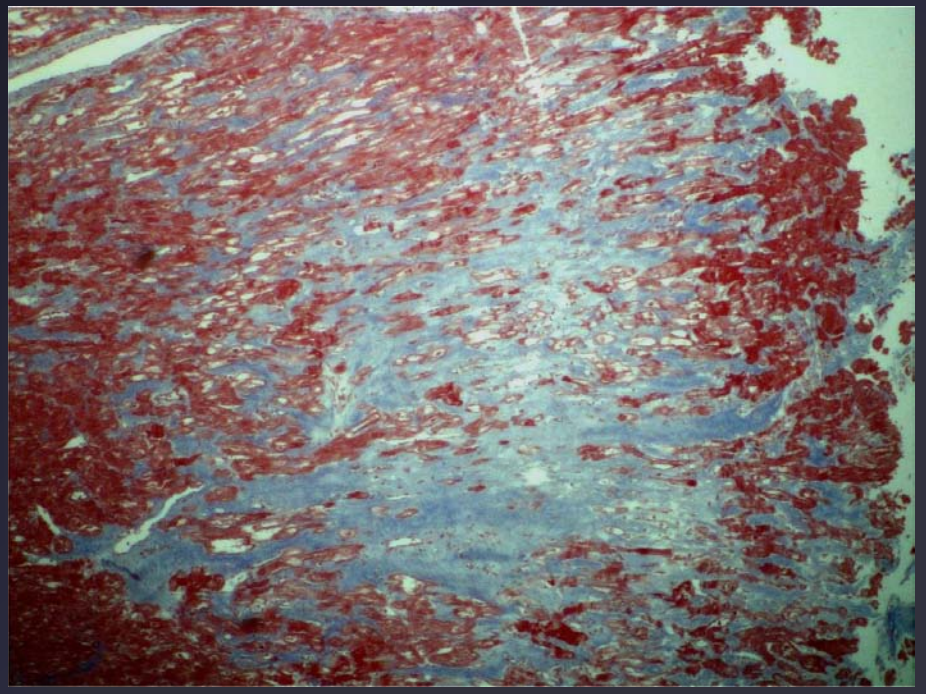
Discussion III

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

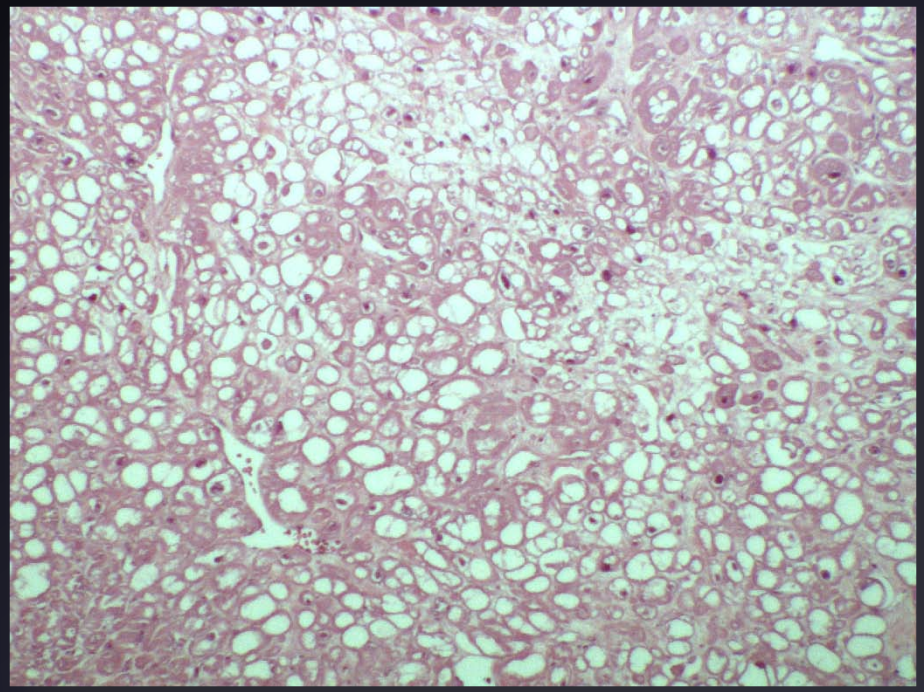
**Lipshultz S, et al. N Engl J Med 2003;348:1647*

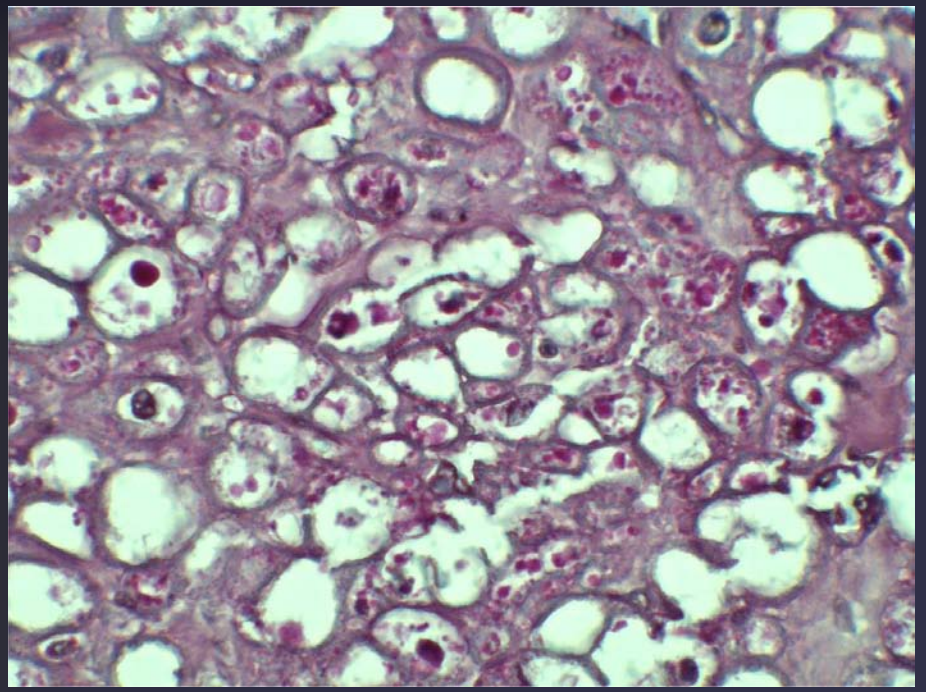
Histology





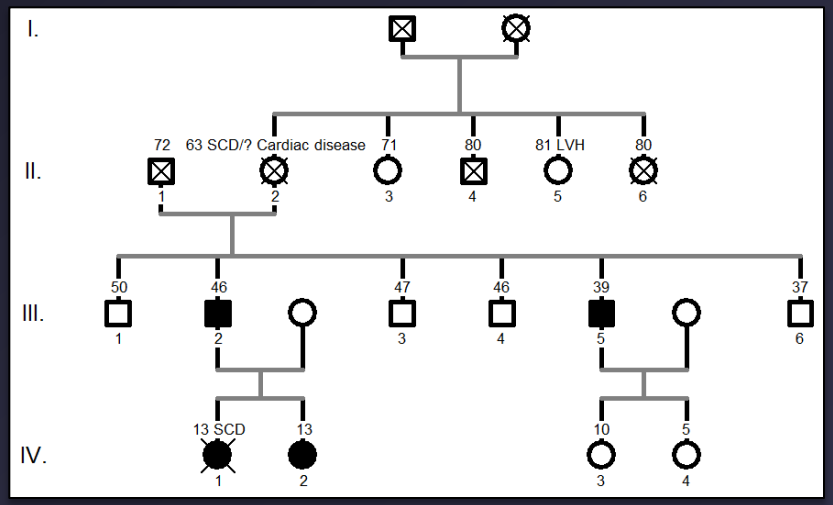
Histology





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



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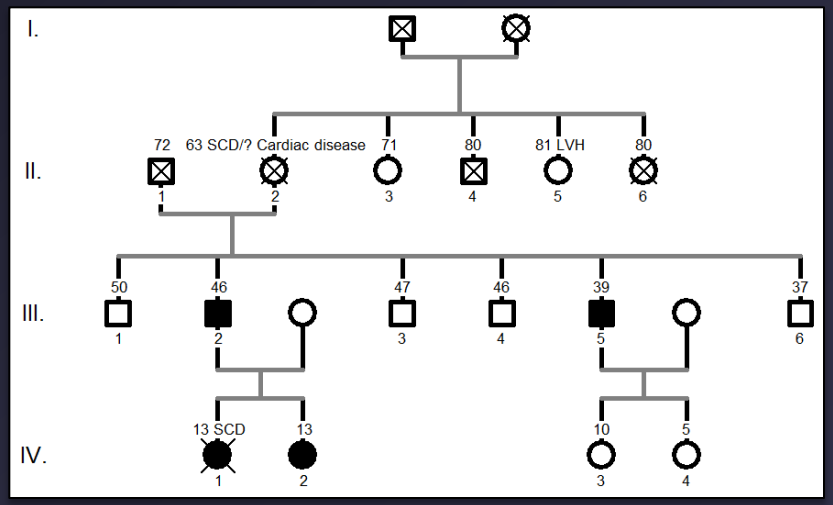

PRKAG2 deficiency

- 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

Murphy RT et al. J Am Coll Cardiol. 2005 45(6):922-30.

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