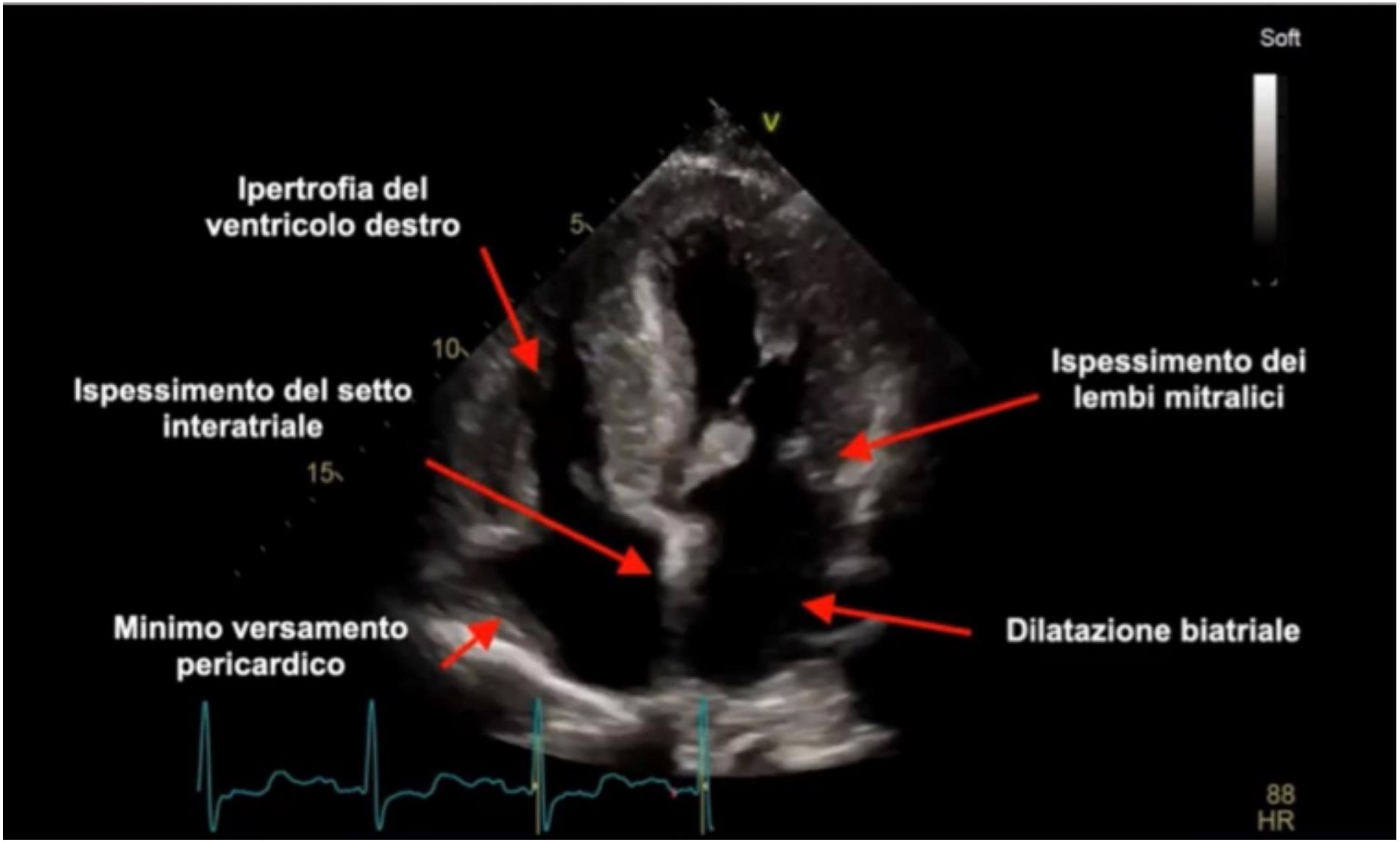

EXIT 12
9
Framingham
Southboro
½ MILE


Soft
V
5
10
15
Ipertrofia del ventricolo destro
Ispessimento del setto interatriale
Minimo versamento pericardico
Ispessimento dei lembi mitralici
Dilatazione biatriale
88
HR

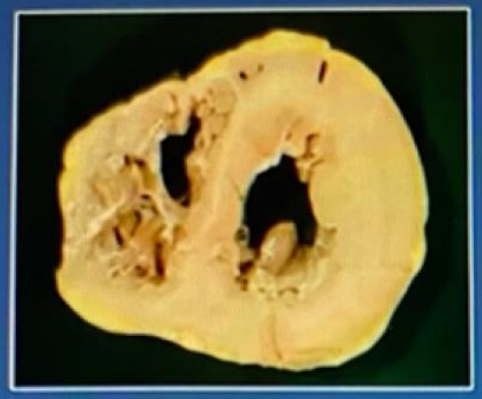
PAZIENTE CON (PSEUDO) IPERTROFIA

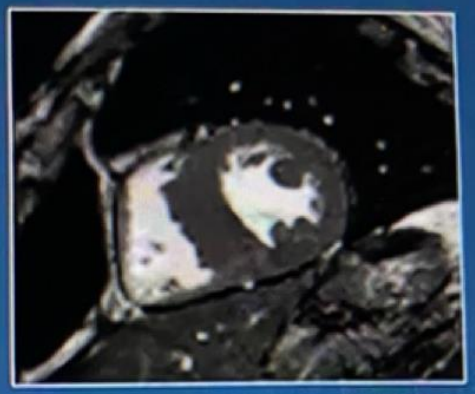
Segni suggestivi di amiloidosi cardiaca:

ispessimento della parete libera del ventricolo destro, del setto interatriale e delle strutture valvolari

presenza di versamento pericardico (modica entità)

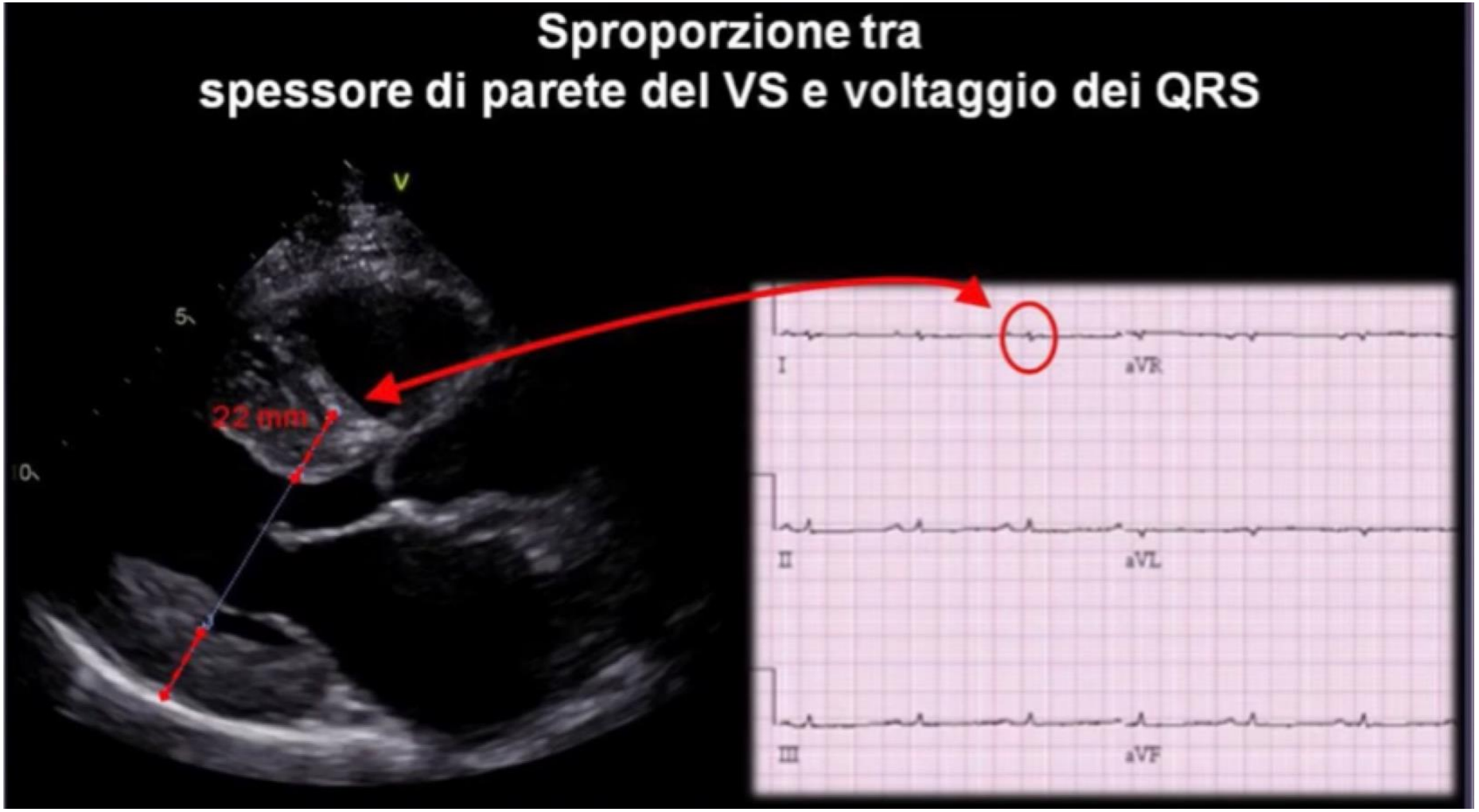
incongruenza tra incremento della massa ventricolare sinistra e voltaggi del QRS.

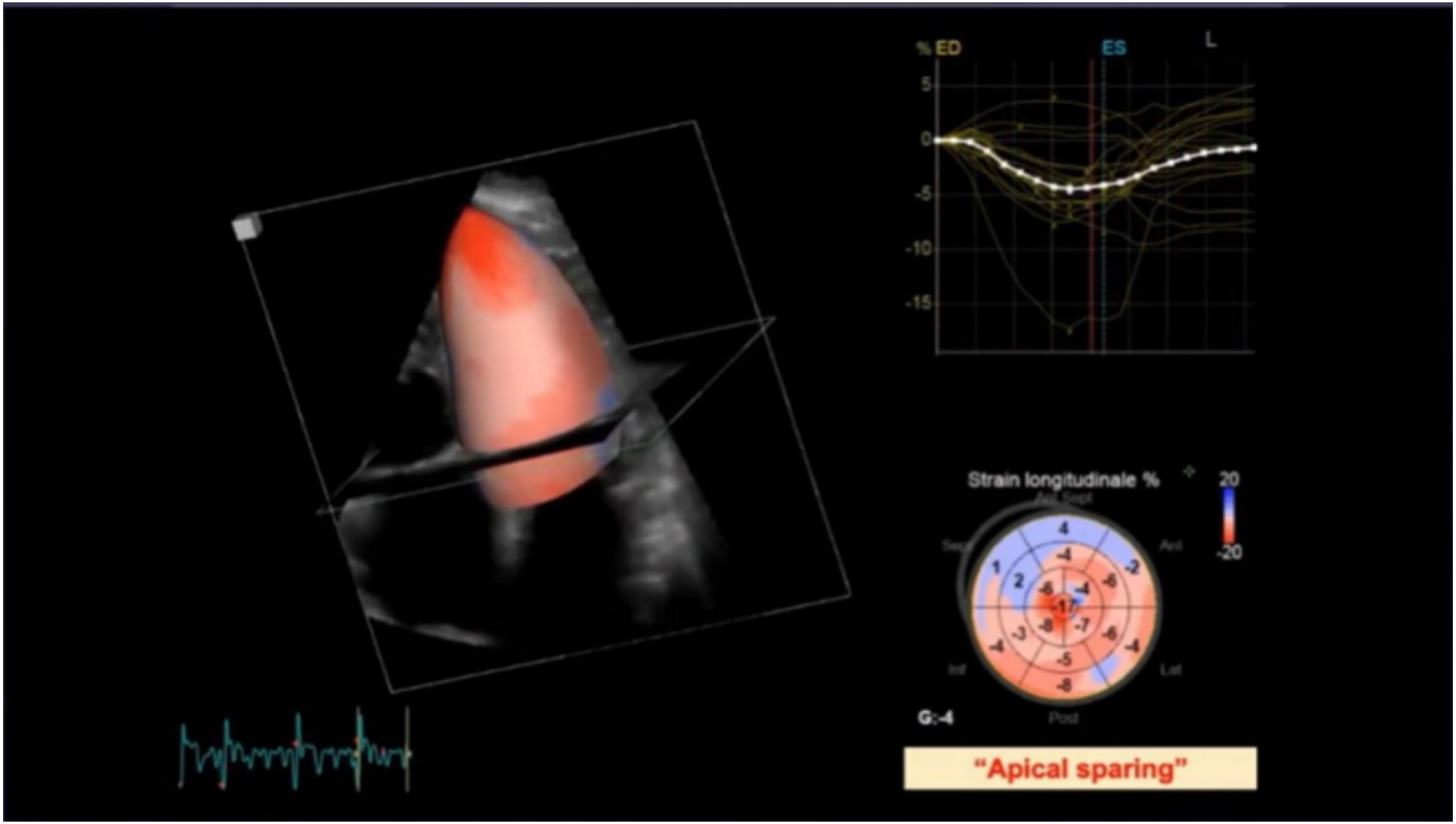




- Cardiomiopatia ipertrofica (HCM)
- **Malattia di Anderson-Fabry**
- **Glicogenosi** (Malattia di Pompe, Malattia di Danon, Sindrome PRKAG2)
- **Sindrome di Noonan**
- **Sindrome di Leopard**
- Sindrome di Beckwith-Wiedemann
- Sindrome di Swyer
- Malattie mitocondriali
- Amiloidosi cardiaca
- Fibrosi endomiocardica
- Sindrome di Loeffler

Sproporzione tra spessore di parete del VS e voltaggio dei QRS

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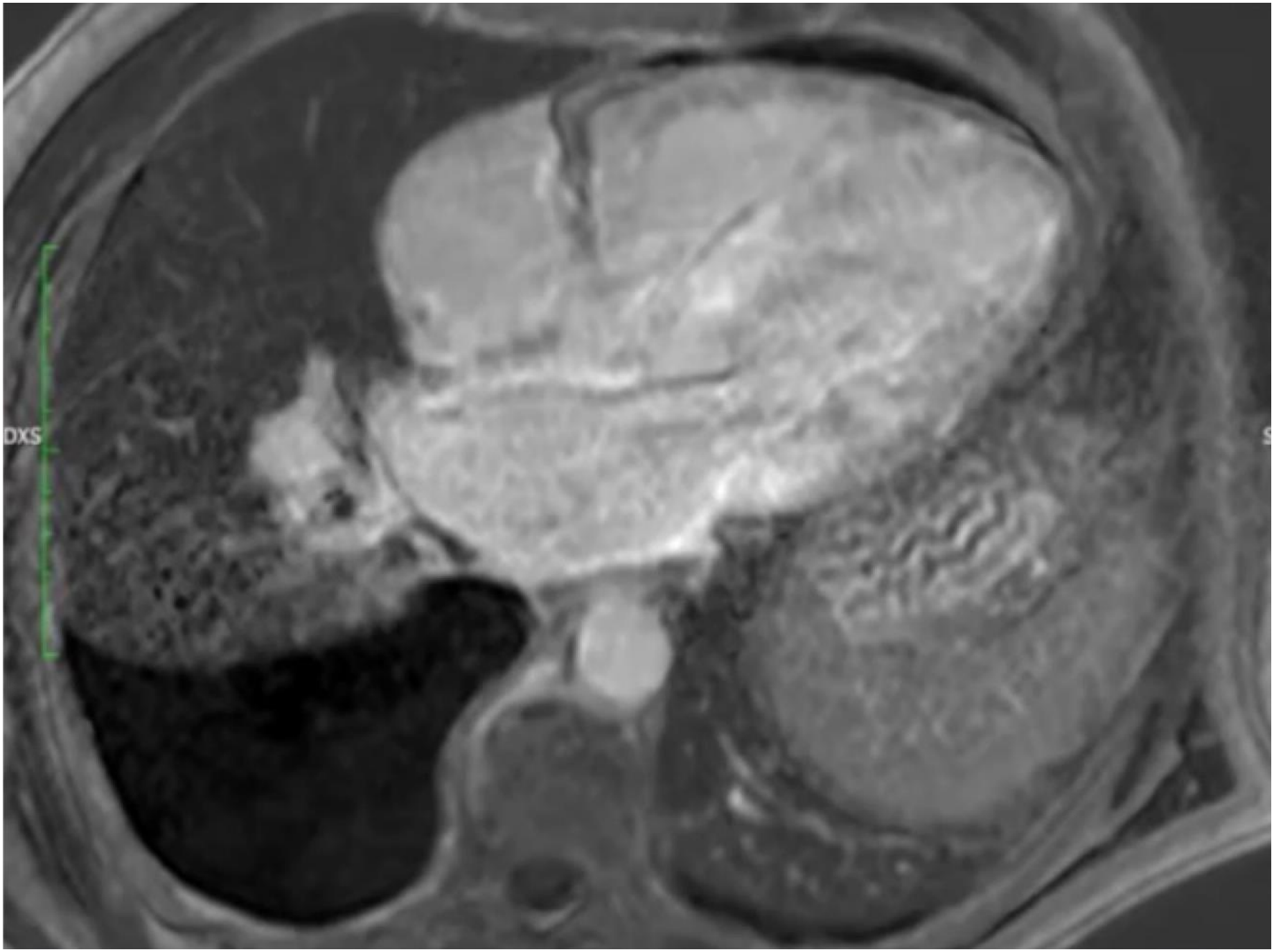
G:-4
"Apical sparing"

Amiloidosi cardiaca	Caratteristiche cliniche peculiari
AL	• Soggetti meno anziani rispetto ad ATTRwt • Storia di discrasia plasmacellulare
ATTR wild type	• Età avanzata • Storia di tunnel carpale bilaterale, di stenosi del canale midollare o di rottura del capo lungo del bicipite brachiale • Anamnesi di cardiopatia ipertensiva
ATTR familiare	• Esordio più precoce rispetto all'equivalente wild type • Linea di trasmissione autosomica dominante • Interessamento neurologico frequente

AL: legata alle catene leggere delle immunoglobuline
ATTR: da transtiretina

Risonanza magnetica cardiaca nella ATTR-CM:

- evidenzia le modificazioni morfologiche
- caratterizza i tessuti (late gadolinium enhancement; T1 mapping)


DXS

nell'amiloidosi se l'LGE non è visibile la sopravvivenza a due anni è del 92% se è solo subendocardica è dell'80% se è transmurale è del 40%

12.mov

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Why the new interest

- Recognized as an important etiology for heart failure
- Underdiagnosed (its been there - we rarely looked)
- Can have poor prognosis
- Diagnostic modalities improved
- New FDA approved treatment with Tafamidis (transthyretin stabilizer)
- Two TTR silencing drugs “knock down” Patisiran and Inotersen (neuropathic)

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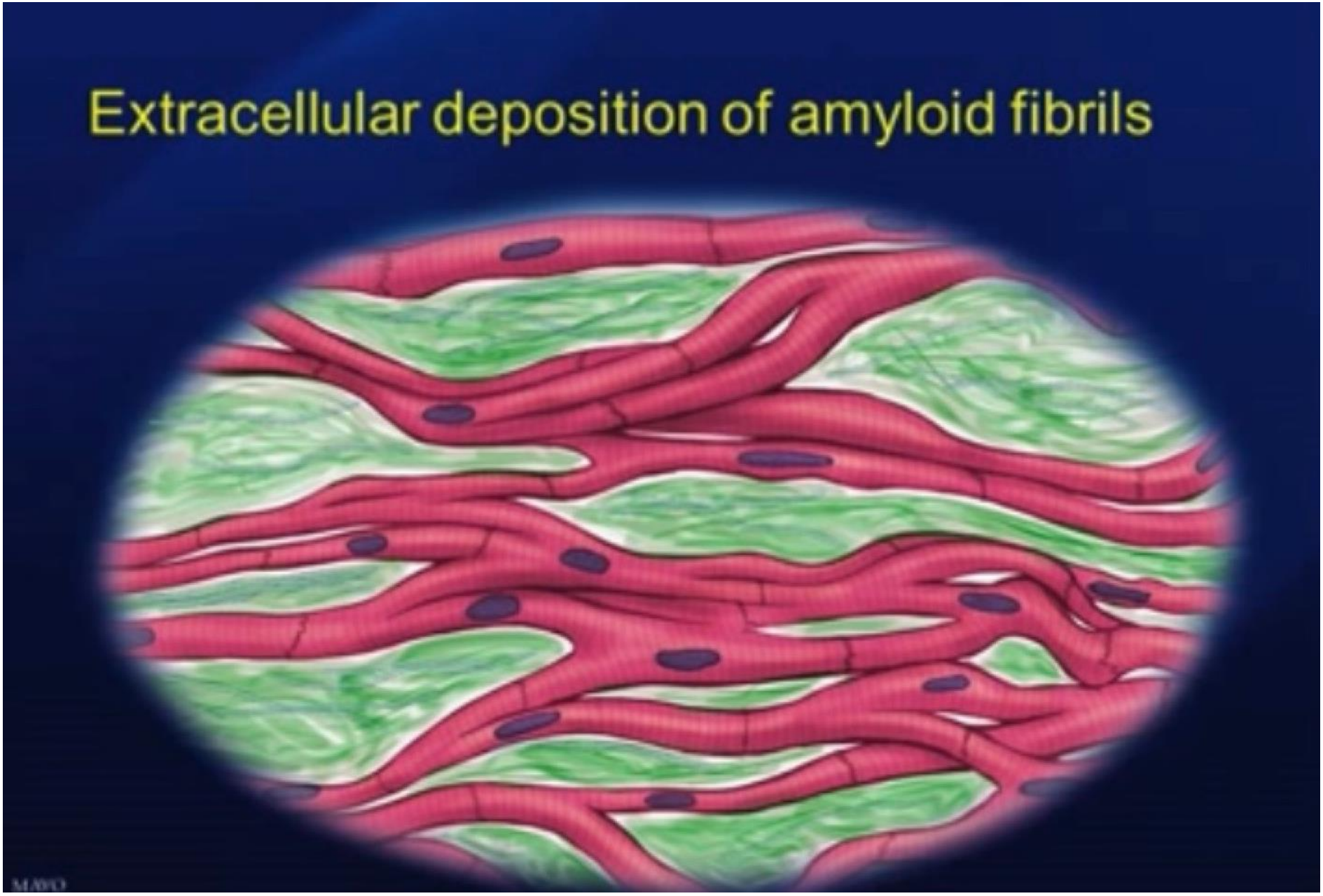
What is Amyloid

- A disorder of misfolded protein
- Misfolded protein deposit in organs and tissues

Extracellular deposition of amyloid fibrils



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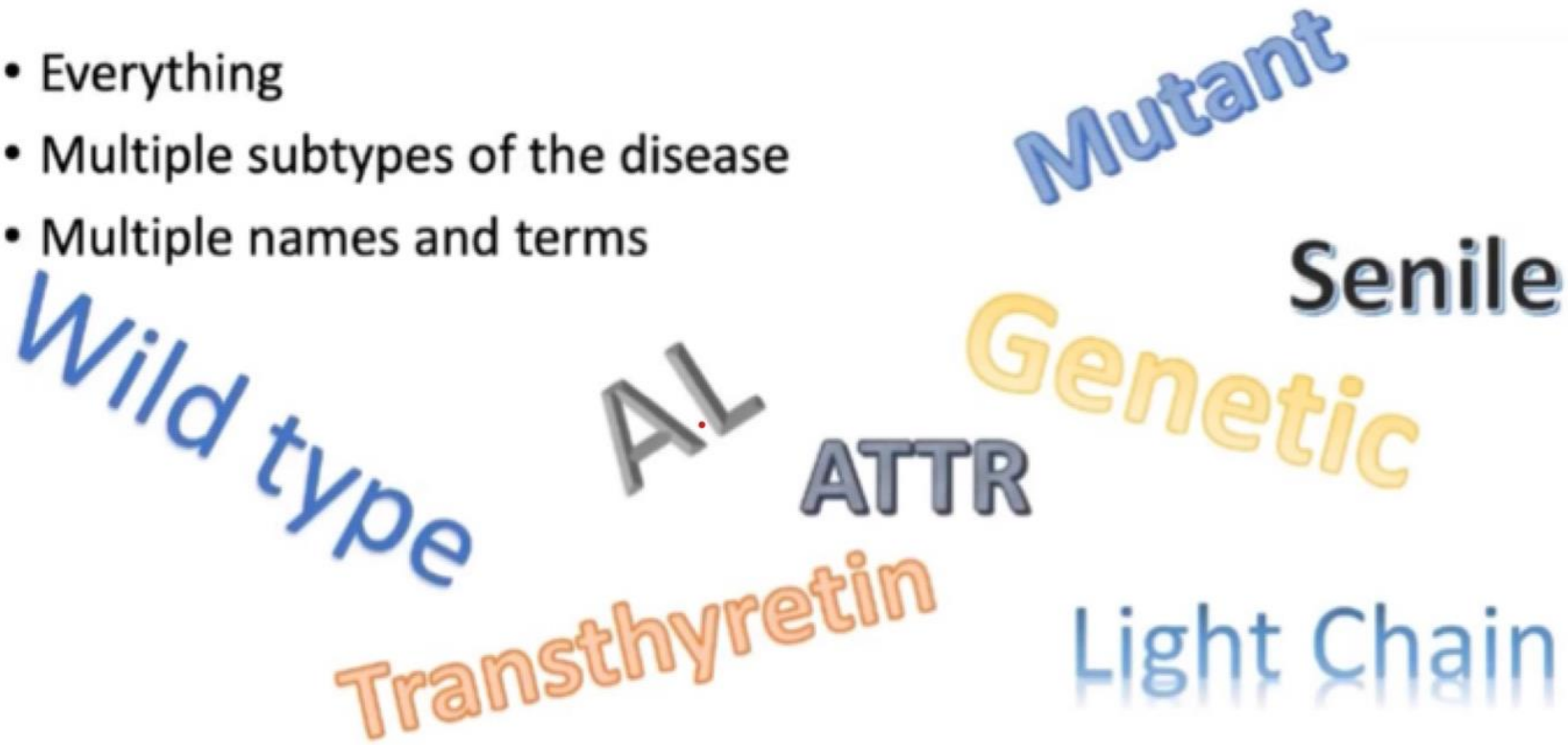
What is confusing about this disease

- Everything
- Multiple subtypes of the disease
- Multiple names and terms



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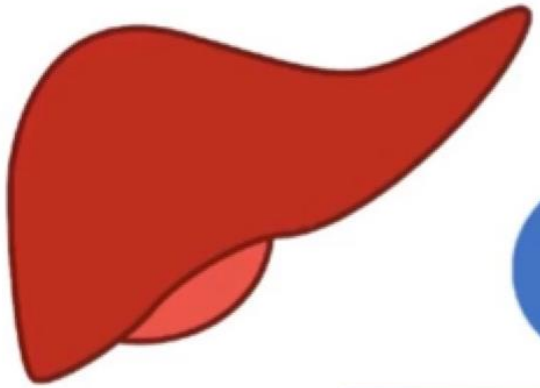
Amyloid



Cardiac Amyloid Types

AL (primary)	Monoclonal light chains	Plasma cell disorder (bone marrow)
Familial (ATTR)	Transthyretin (TTR) Unstable, mutant	DNA mutation (liver)
Senile (SSA)	Wild type TTR	Liver

Amyloid Type
Cardiac Involvement

- AL – cardiac biopsy + in all
  - Variable clinical significance
- ATTR (familial)
  - Varies with mutation
  - Spectrum: neuropathy to cardiomyopathy
- SSA (senile)
  - Isolated cardiac + carpal tunnel

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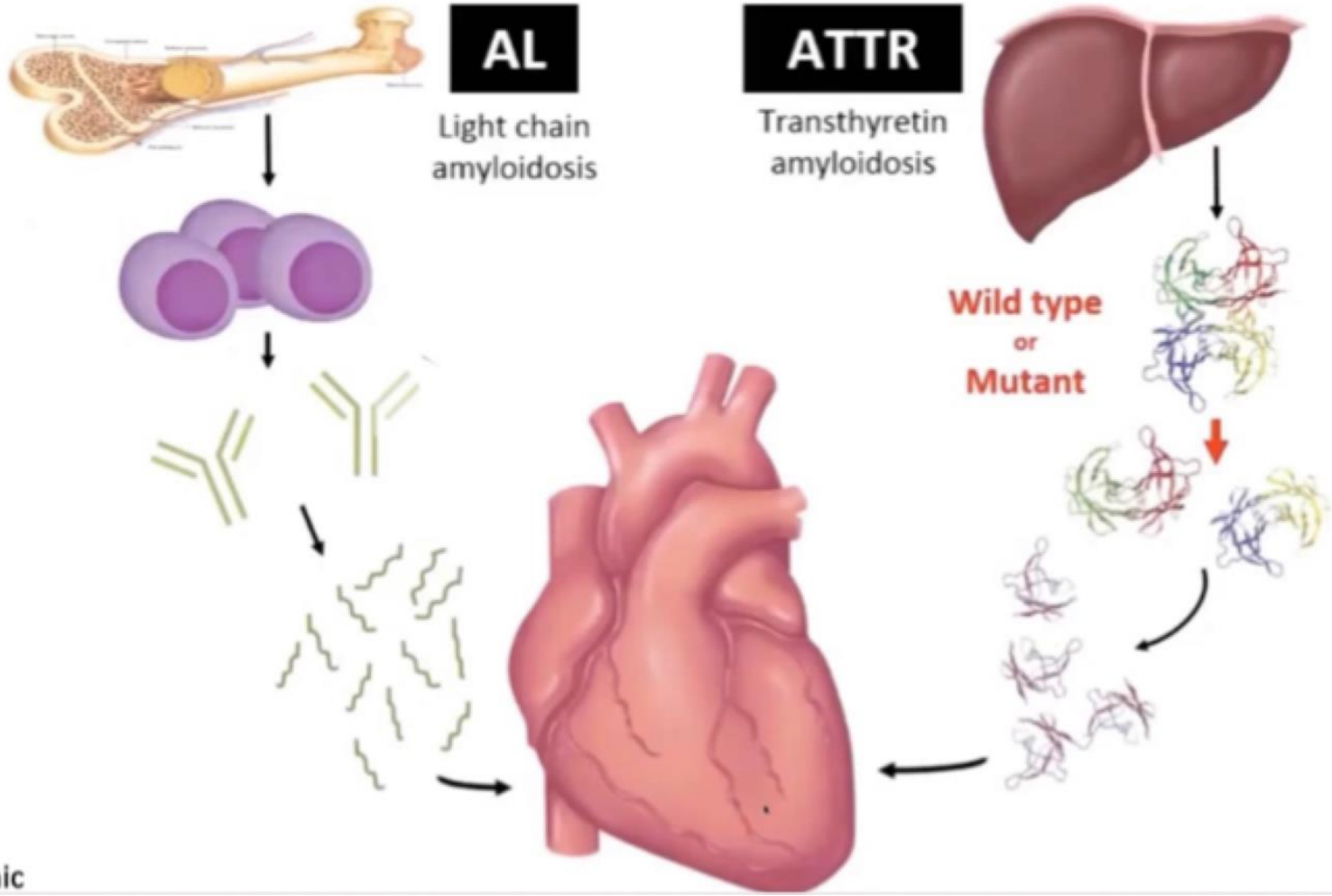


Cleveland clinic

Cardiac Amyloid, 2 major types
Liver Origin: ATTR Transthyretin
Many other types of amyloid

Senile/Wild Type Transthyretin

- Age related
- Transthyretin (Transport Thyroid Retinol

Mutant/genetic

- Autosomal dominant
- Val 122 ile most common (African American)
- 120 mutations
- Synthetized in the liver
- Age > 50

Red Flags for all types of amyloid systemic disease

Sensory-motor neuropathy[3,5]

- Pain, tingling
- Altered sensation
- Bilateral carpal tunnel syndrome
- Weakness
- Difficulty walking

Autonomic neuropathy[3,5]

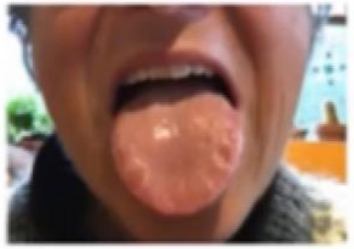
- Orthostatic hypotension
- Diarrhea, constipation, nausea and vomiting
- Unintentional weight loss

Cardiac manifestations[6]

- Conduction abnormalities
- Arrhythmias
- Heart failure

Bilateral carpal tunnel surgery past 10 yrs
Spinal stenosis

Macroglossia



Other symptoms of the disease

Ocular manifestations[5]

- Vitreous opacification
- Glaucoma
- Abnormal conjunctival vessels
- Papillary abnormalities

Nephropathy[5]

- Proteinuria
- Renal failure

CNS manifestations[5]

- Progressive dementia
- Headache
- Ataxia
- Seizures
- Spastic paresis
- Stroke-like episodes

Additional signs[5]

- Rapid symptom progression
- Family history of the disease or hATTR amyloidosis symptoms
- Failure to respond to immunomodulatory treatment
- Intolerance of commonly used cardiovascular medications

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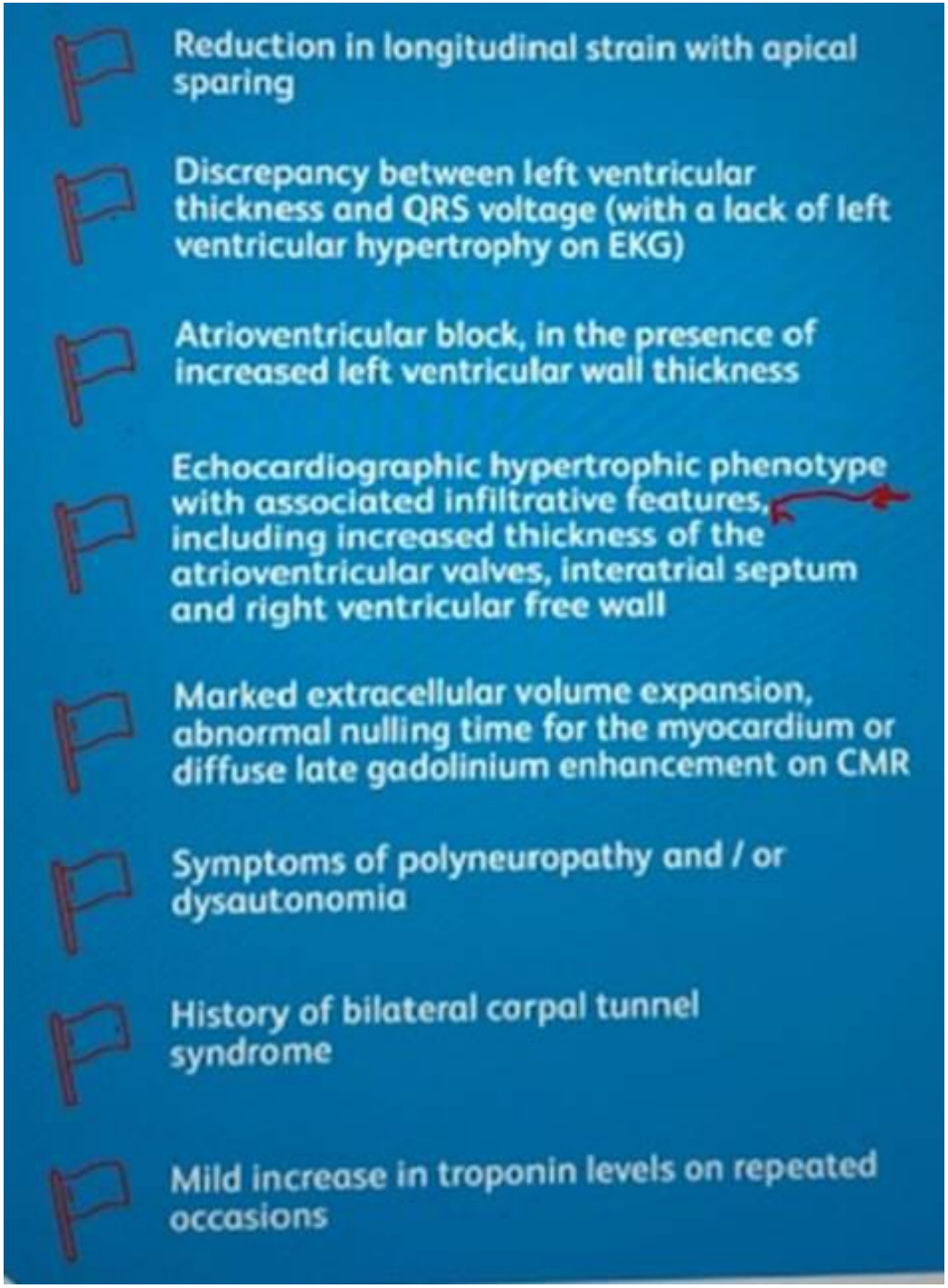
Red Flags - Cardiac

- Heart failure (preserved EF) HFpEF
- Unexplained increased wall thickness on echo >12 mm
- Low voltage on EKG (56%)
- Aortic Stenosis, 16% of TAVR evaluations, thickened of valves
- New normalization of BP
- Atrial fibrillation
- Intolerance to HF meds


Reduction in longitudinal strain with apical sparing
Discrepancy between left ventricular thickness and QRS voltage (with a lack of left ventricular hypertrophy on EKG)
Atrioventricular block, in the presence of increased left ventricular wall thickness
Echocardiographic hypertrophic phenotype with associated infiltrative features, including increased thickness of the atrioventricular valves, interatrial septum and right ventricular free wall
Marked extracellular volume expansion, abnormal nulling time for the myocardium or diffuse late gadolinium enhancement on CMR
Symptoms of polyneuropathy and / or dysautonomia
History of bilateral corpal tunnel syndrome
Mild increase in troponin levels on repeated occasions

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Need to be looking at LVH need to relook >1.2 cm

- Hypertension
- Amyloid
- Hypertrophic cardiomyopathy
- Aortic stenosis
- Athletic
- Fabry

- Pts are complicated they can have more then one of the above

ECG in Cardiac Amyloid

ECG	AL (n=127)	TTR-Senile (177)	TTR-Fam (82)
Low voltage	45%	10%	4%
Pseudo-infarct	47	24	14
AF	10	34	10
LVH	16	3	10

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Need to differentiate types of amyloid Clinical differences

AL

- Sensorimotor – Peripheral Neuropathy
- Autonomic Neuropathy - Orthostatic Hypotension
- Renal involvement – Nephrotic Syndrome

ATTR

- White Male > 60 HFpEF
- African American > 60 HFpEF with out HTN
- New DX of Hypertrophic Cardiomyopathy
- New Dx low flow AS

Cardiac Amyloidosis

Presentation

Vague, common symptoms

- Dyspnea, fatigue, chest pain
- AF, syncope, stroke, conduction disease
- Overt heart failure

Delayed Diagnosis

A major factor in poor prognosis

Cardiac Amyloidosis
Diagnosis

- Tissue diagnosis – mandatory
- Fat aspirate
- Bone marrow

Prove: Amyloid organ involvement
Determine type: AL or transthyretin

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Diagnosis made by multimodalities

- Clinical suspicion (please follow the guideline)
  - LVH
  - HFpEF
- Nuclear PYP
- ECHO
- MRI
- Blood/Urine
- BX