

Cardiac Amyloidosis

Why is Early Diagnosis Important

September 24, 2026

Mazen Hanna, MD
Co-Director, Amyloidosis Center
Section of Heart Failure & Cardiac Transplant
Cleveland Clinic



Cleveland Clinic

Financial Disclosures

Have served on Advisory Boards

Pfizer, Alynlam, Ionis, BridgeBio, Alexion, Novo Nordisk, ATTRALUS

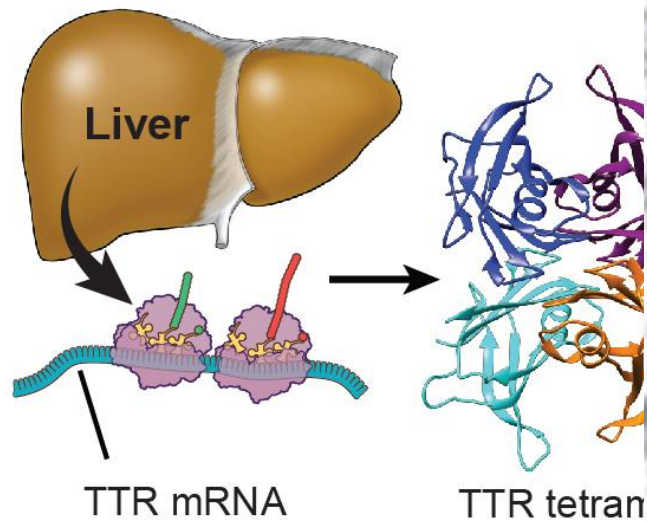
Three aspects to ATTR Cardiac Amyloidosis

1. Suspecting and Making the Right Diagnosis

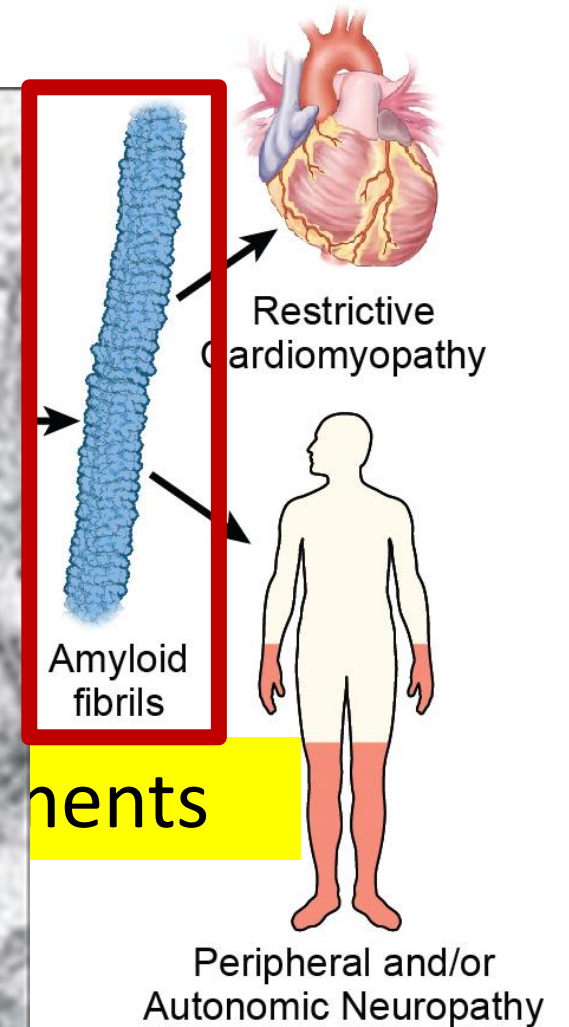
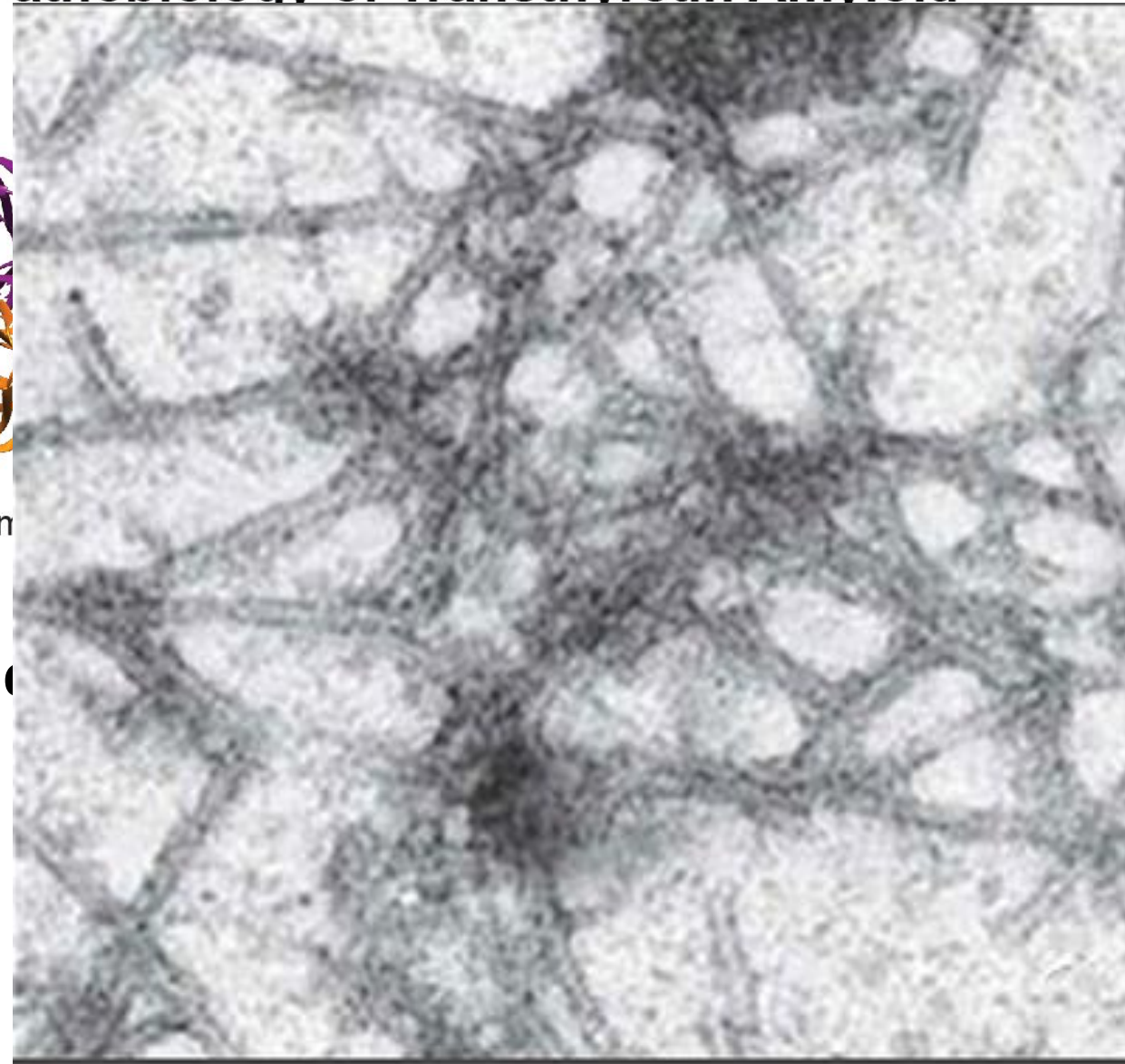
2. Treating the Cardiac Consequences

3. Treating the Disease with FDA approved drugs

Pathobiology of Transthyretin Amyloid



Tetramer



Manifestations

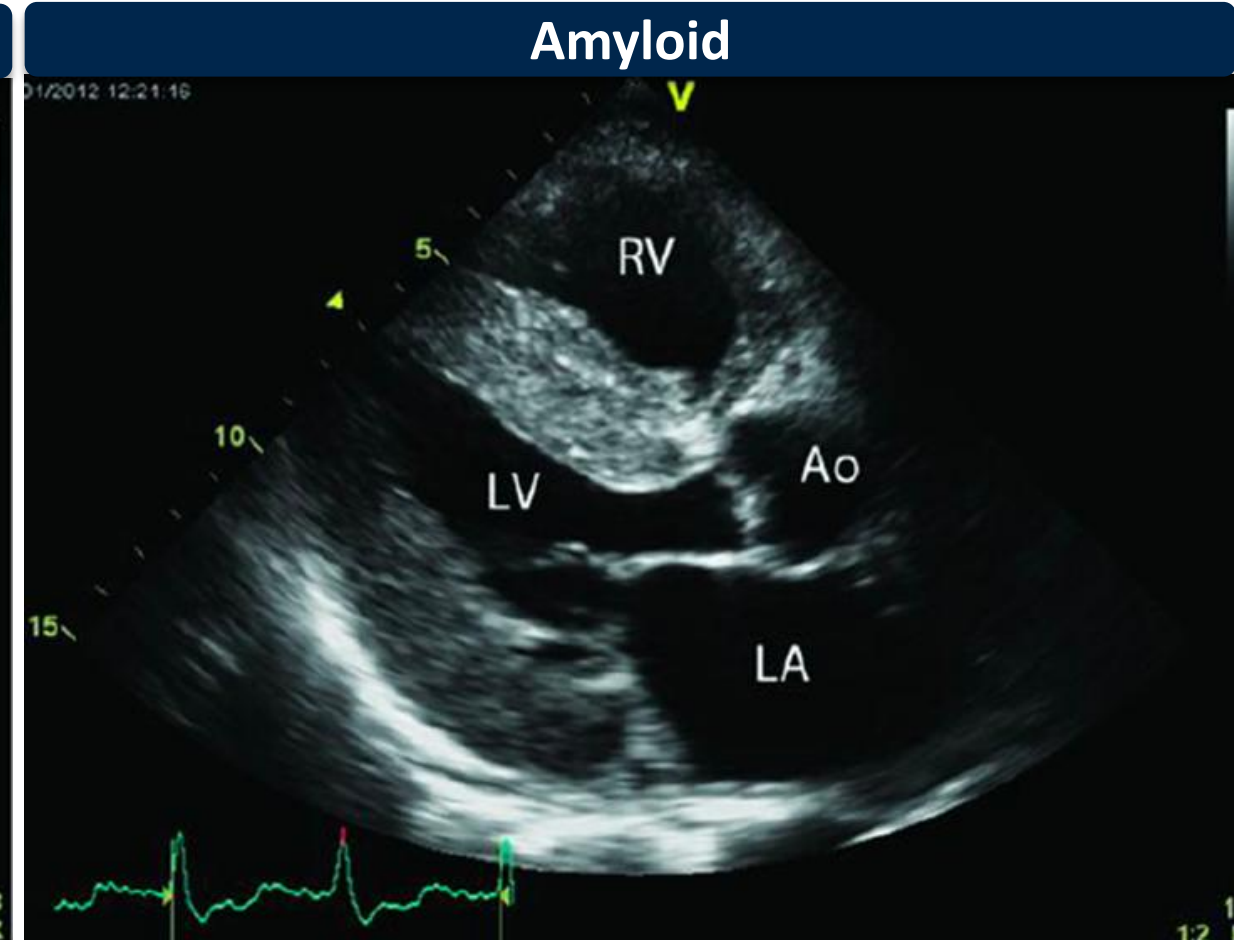
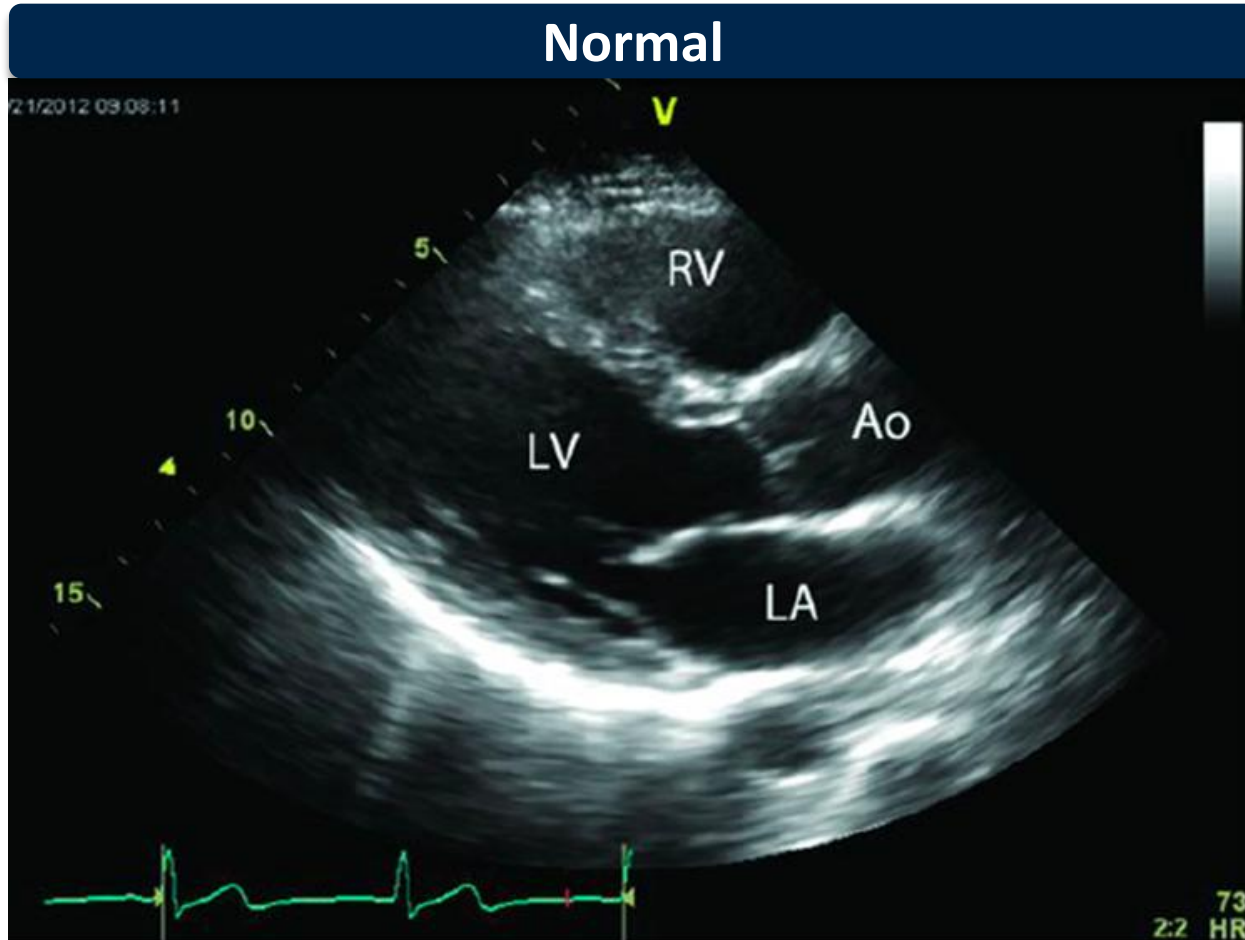
© Cleveland Clinic 2019

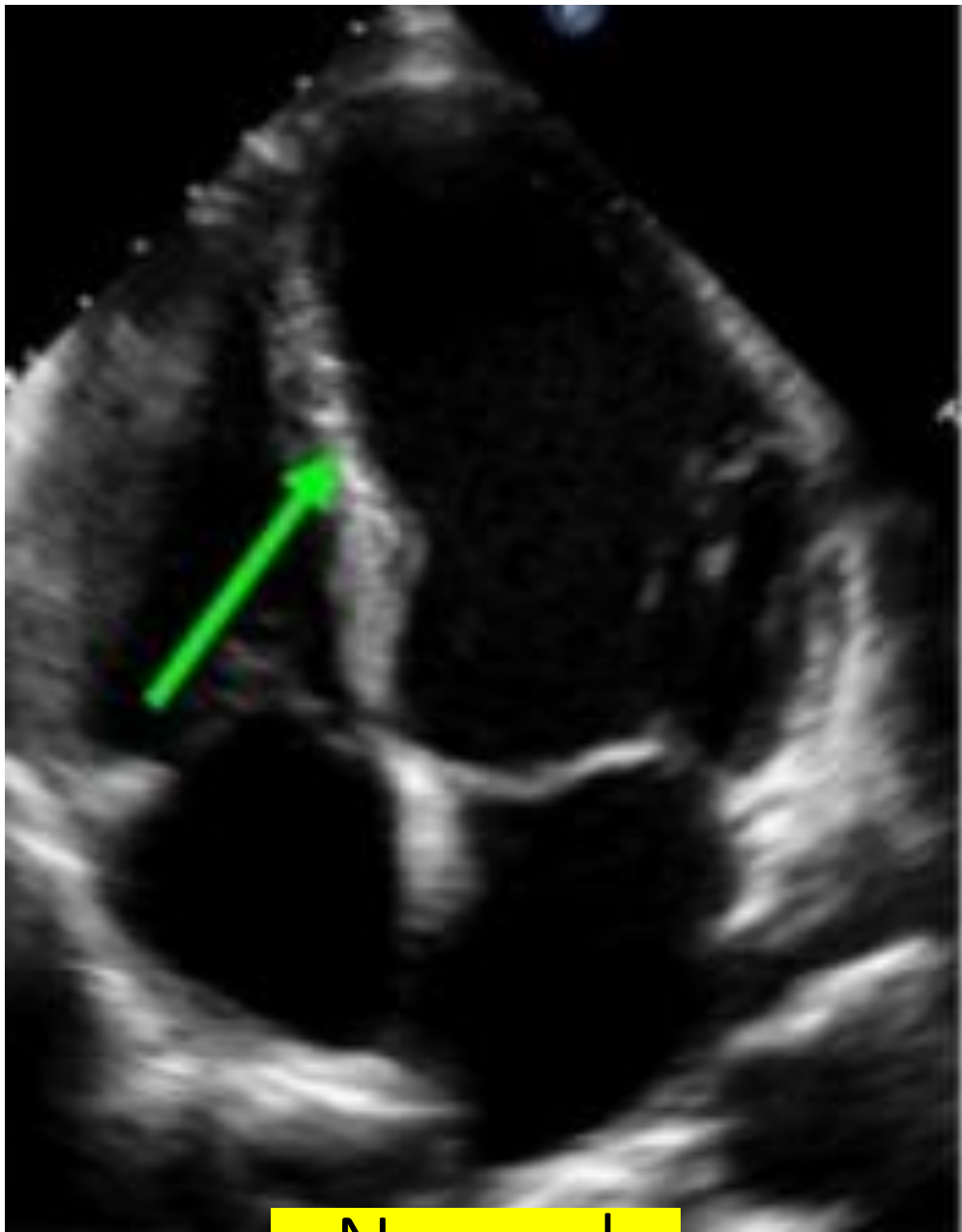
Ruberg et al. JACC 2019

Echocardiogram:

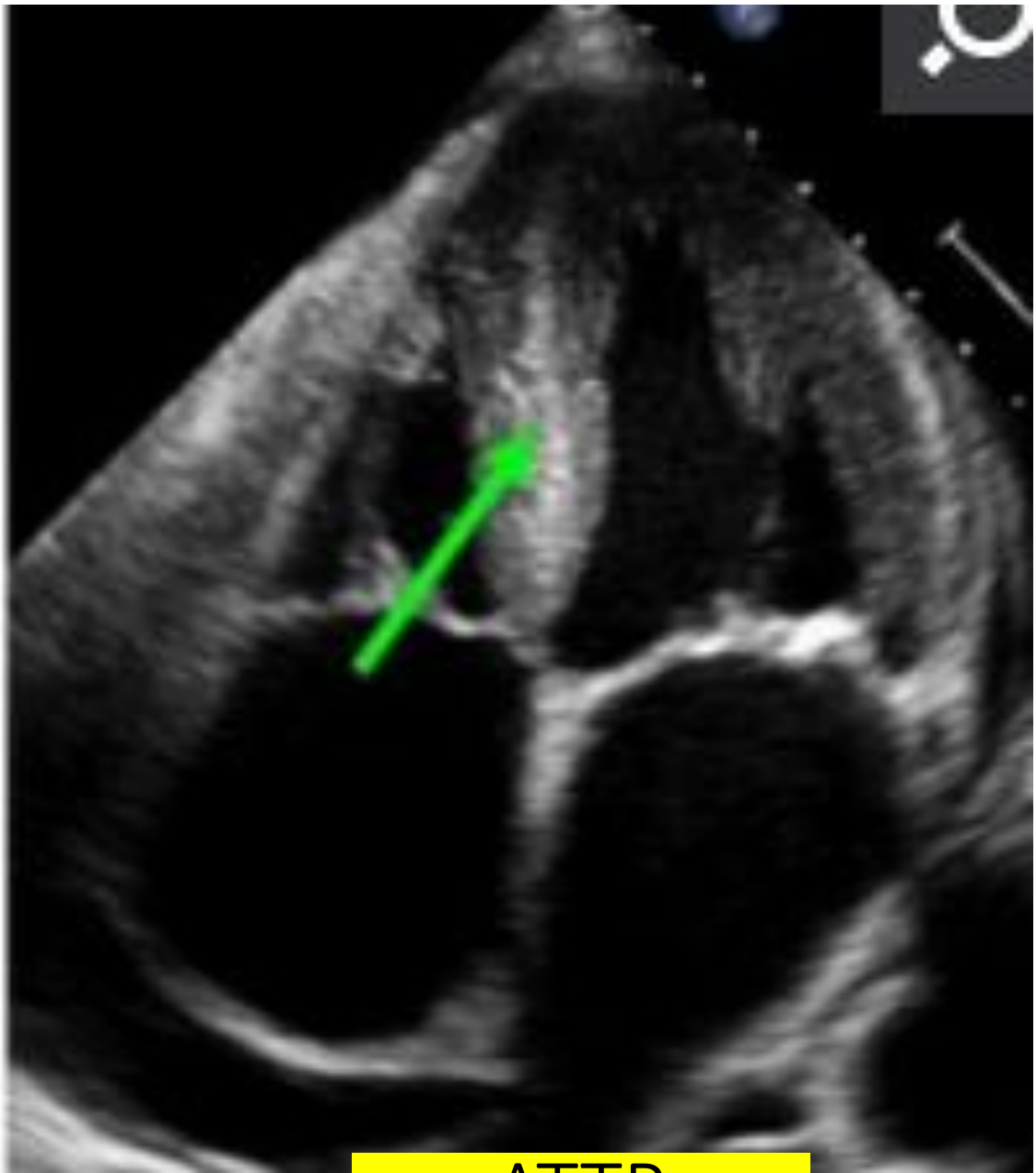
Amyloid Deposits throughout the heart

Increased wall thickness and stiffness

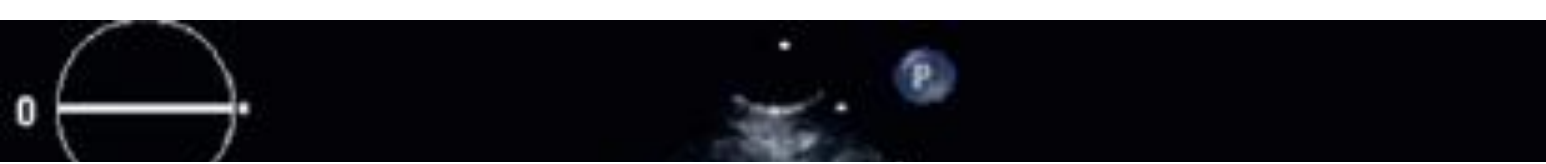




Normal

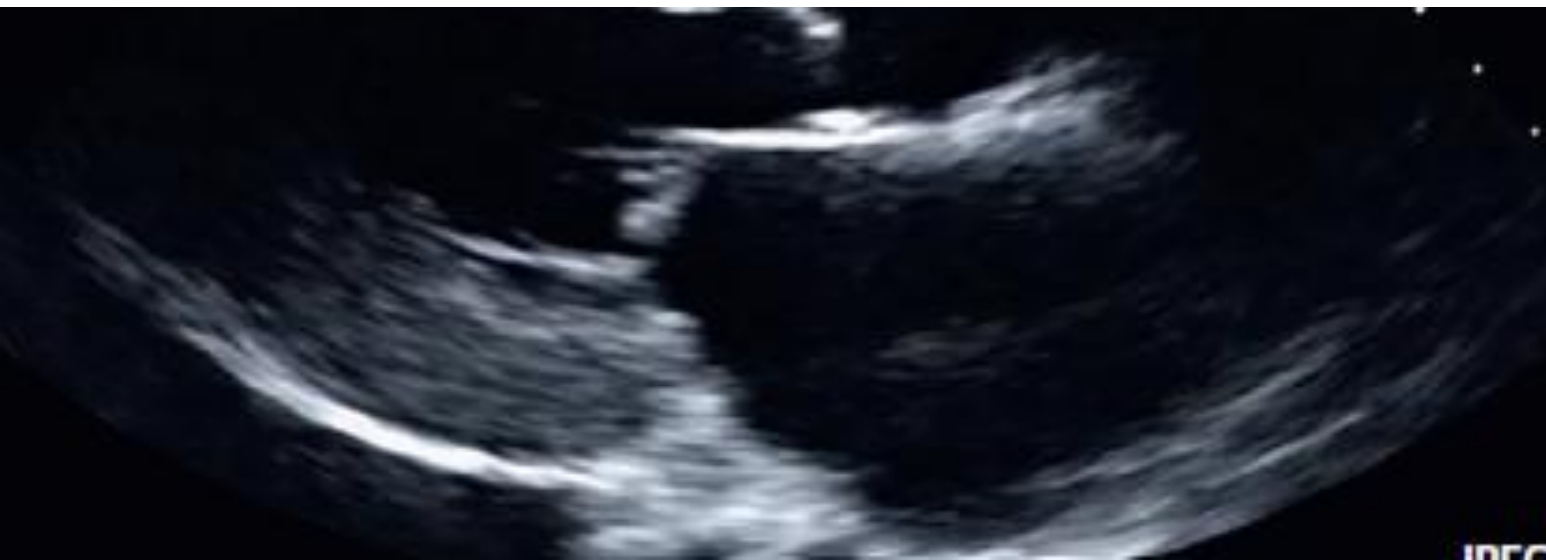


ATTR



Average Wall thickness at diagnosis
~ 1.7 cm

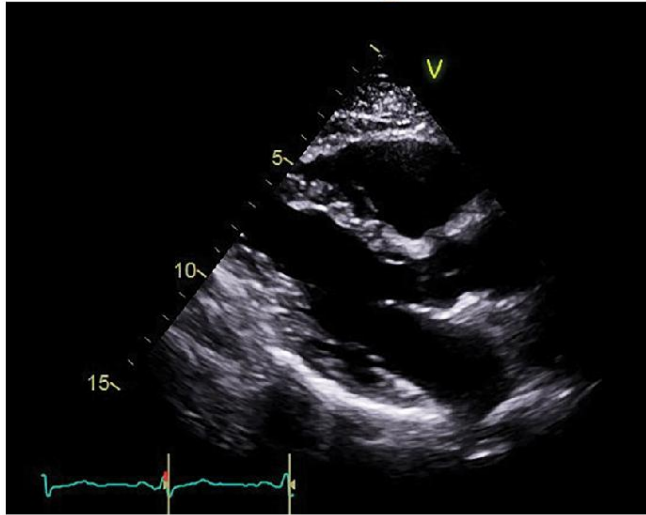
Average NT pro BNP at diagnosis
~ 1800 pg/ml



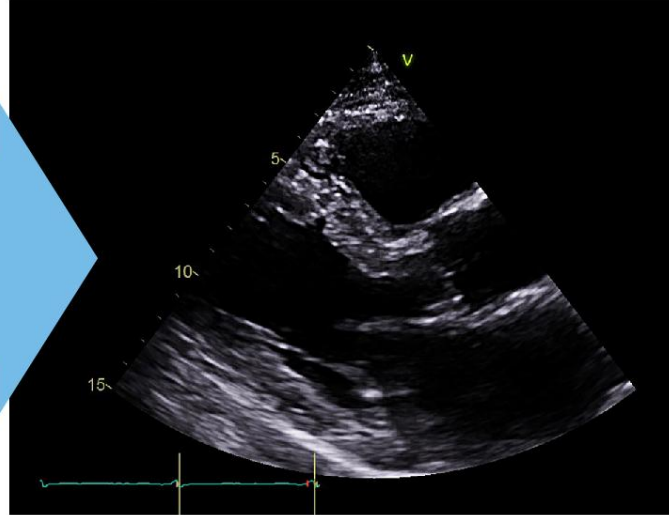
Septum > 1.2 cm
Post wall > 1.2 cm

EF > 50% (HFpEF)
EF 40-50%
EF < 40%

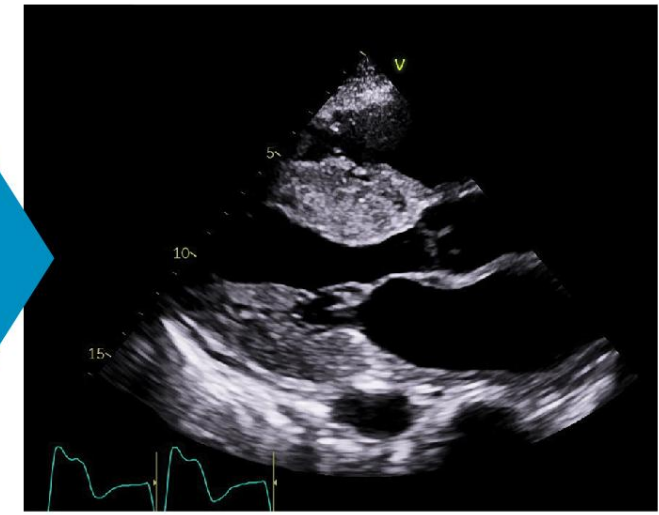
Early



Intermediate



Late



Ideal Therapeutic Window

NAC Stage I

Stage II

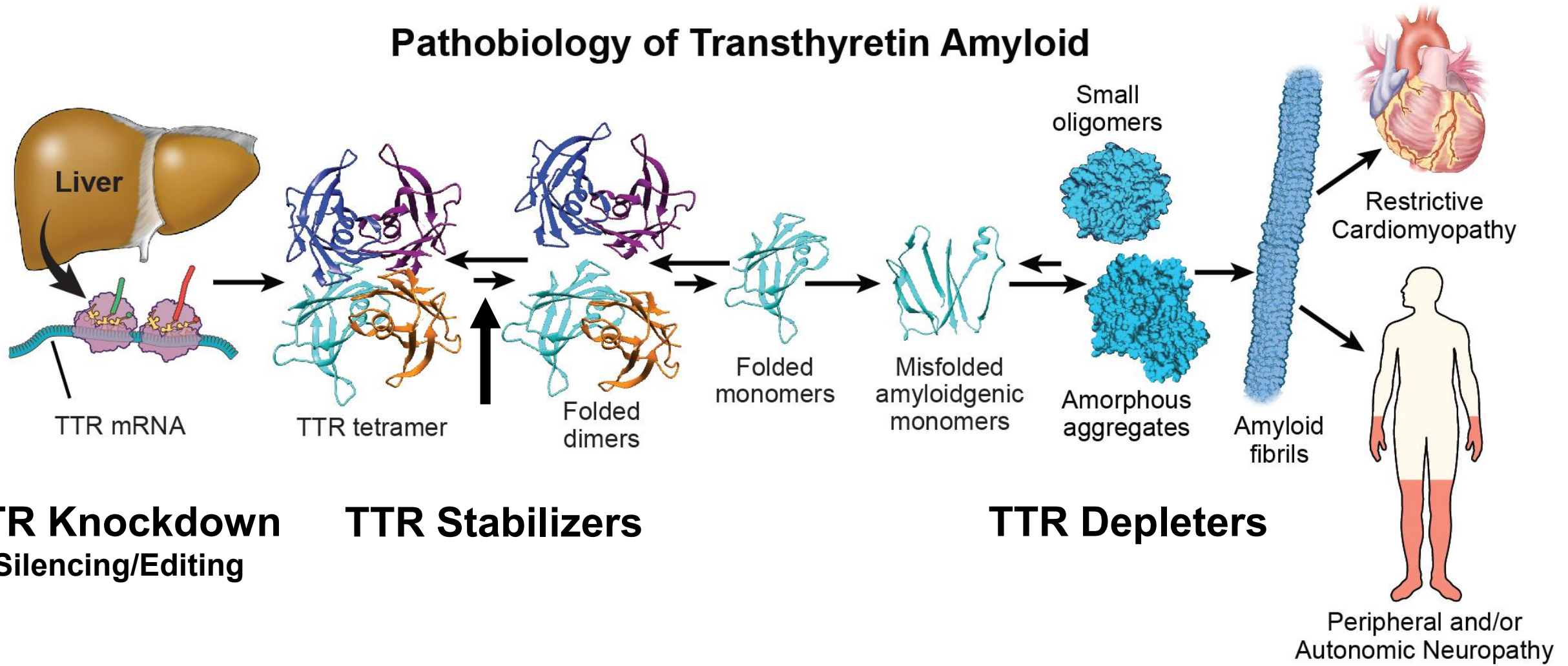
Stage III

Patient Symptoms • Quality of Life Assessments

Multimodality Diagnostic Tools (MRI, Echo, Nuclear, EKG)

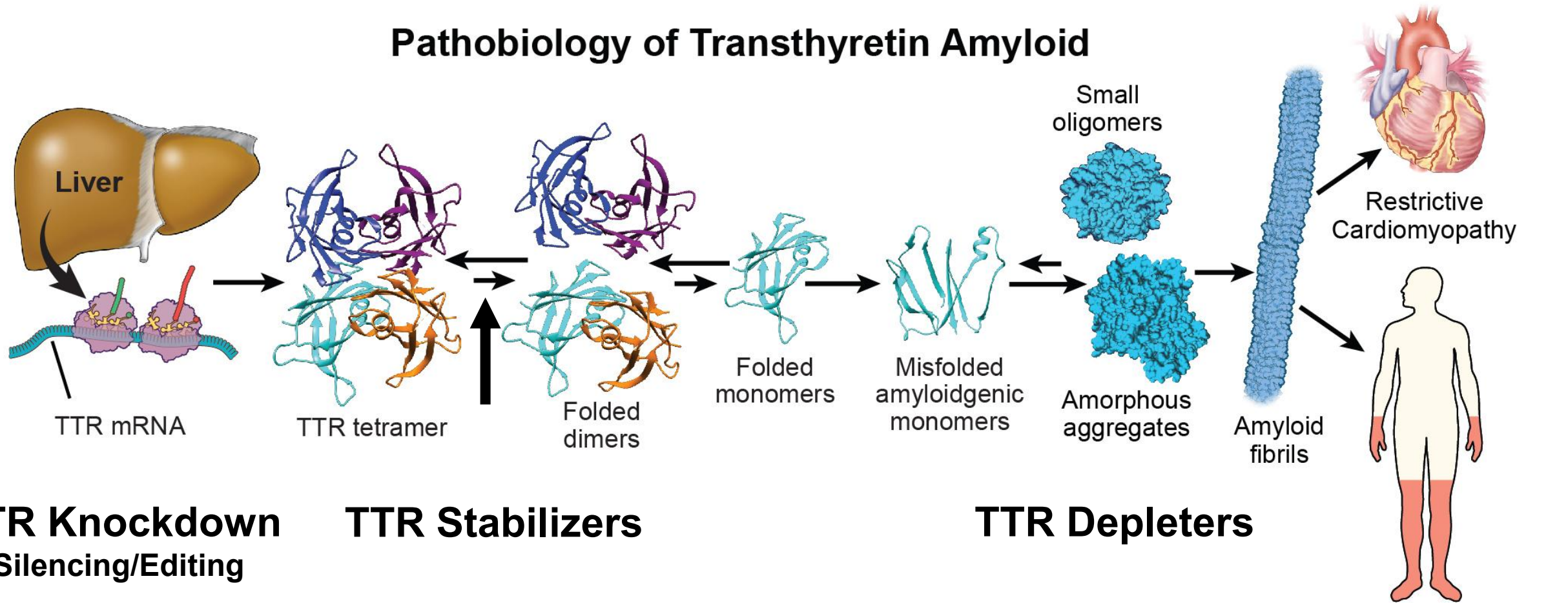
NTproBNP • Troponin T • TTR levels • Novel Biomarkers

Pathobiology of Transthyretin Amyloid



©Cleveland Clinic 2019

Pathobiology of Transthyretin Amyloid



TTR Knockdown Silencing/Editing

Patisiran (siRNA)
Vutrisiran (siRNA)
Eplontersen (ASO)
Nex Z (CRISPR)
Nucresiran (siRNA)

TTR Stabilizers

Tafamidis
Acoramidis

TTR Depleters

ALXN2220 (NI006)
Coramitug (NN6019)
AT-02

Peripheral and/or
Autonomic Neuropathy

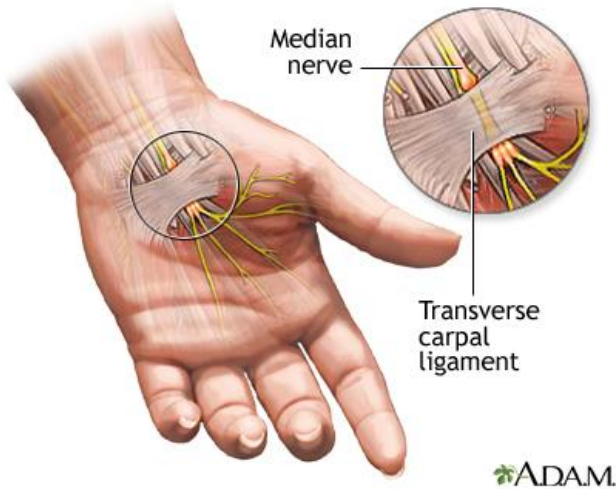
©Cleveland Clinic 2019

Why is Early Diagnosis Important?

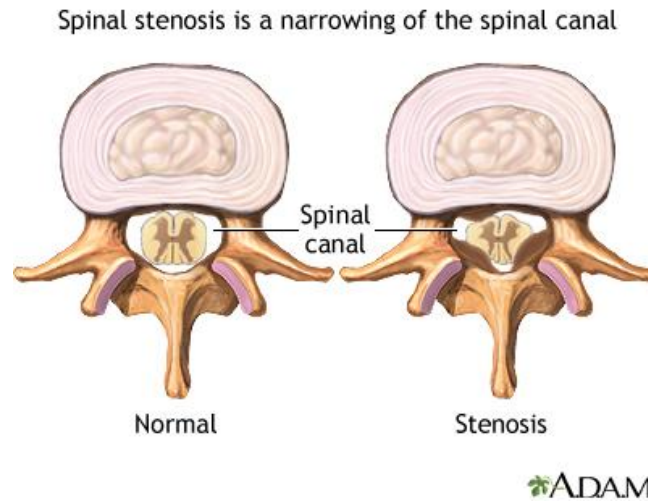
- We know from clinical trials (and experience) is that the earlier we diagnosis ATTR cardiac amyloidosis and the earlier we start medical treatment
- **1. The medications are more effective**
- **2. The better the outcome for the patient**
 - Less hospitalizations
 - Better quality of life
 - Better prognosis

ATTR Amyloidosis associated with multiple orthopaedic pathologies

Carpal Tunnel Syndrome



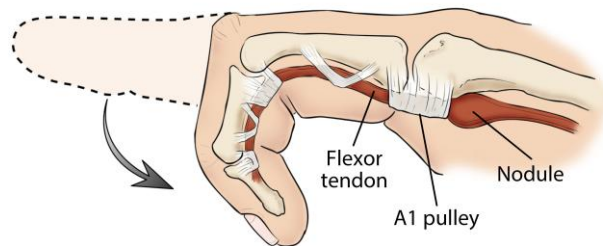
Spinal Stenosis



Bicep Tendon Rupture



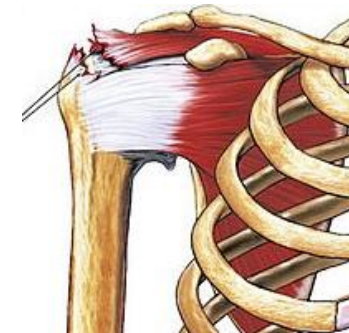
Trigger Finger

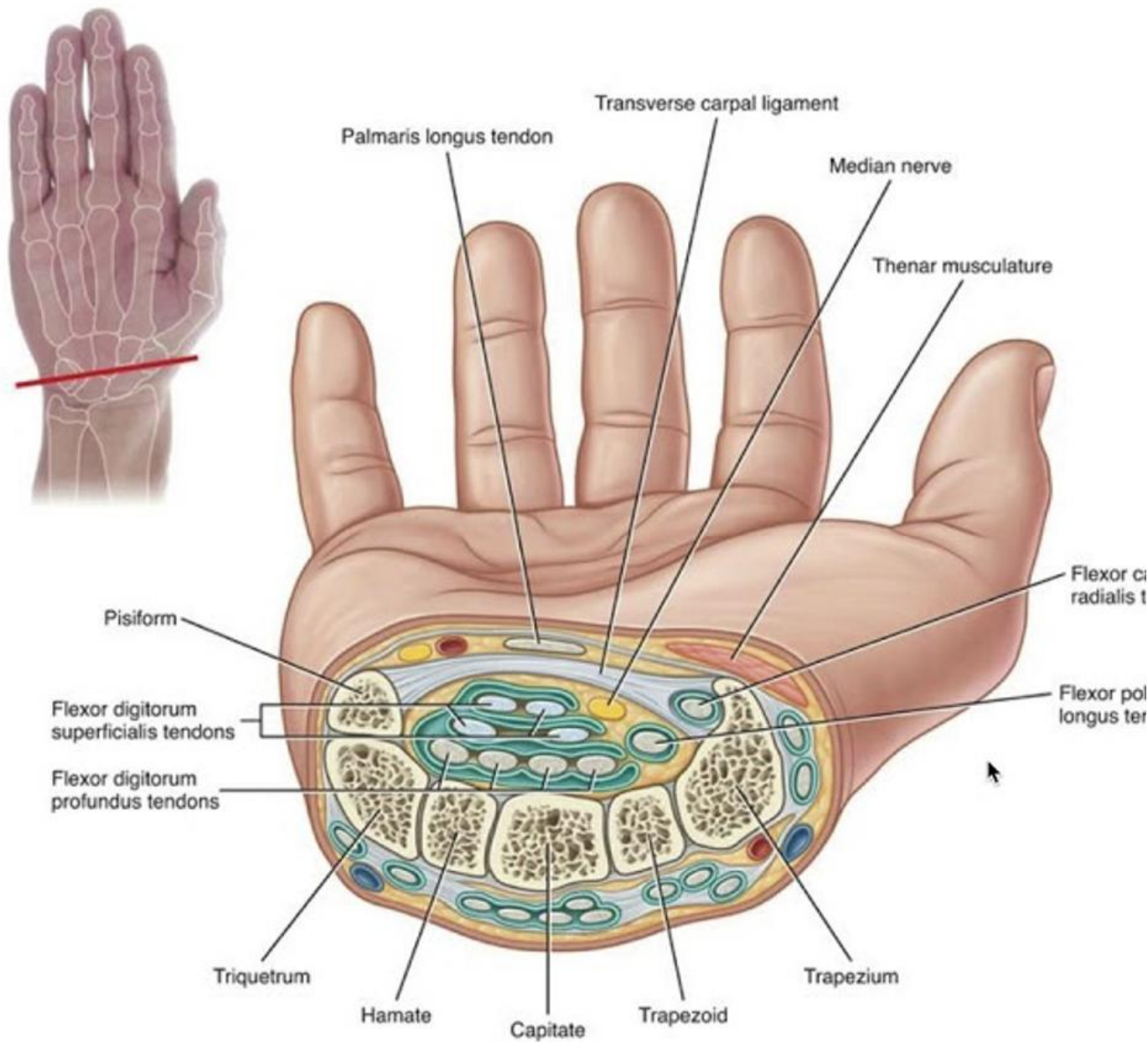


Lower Ext Joint Replacement (Hip and knee)



Shoulder pathology

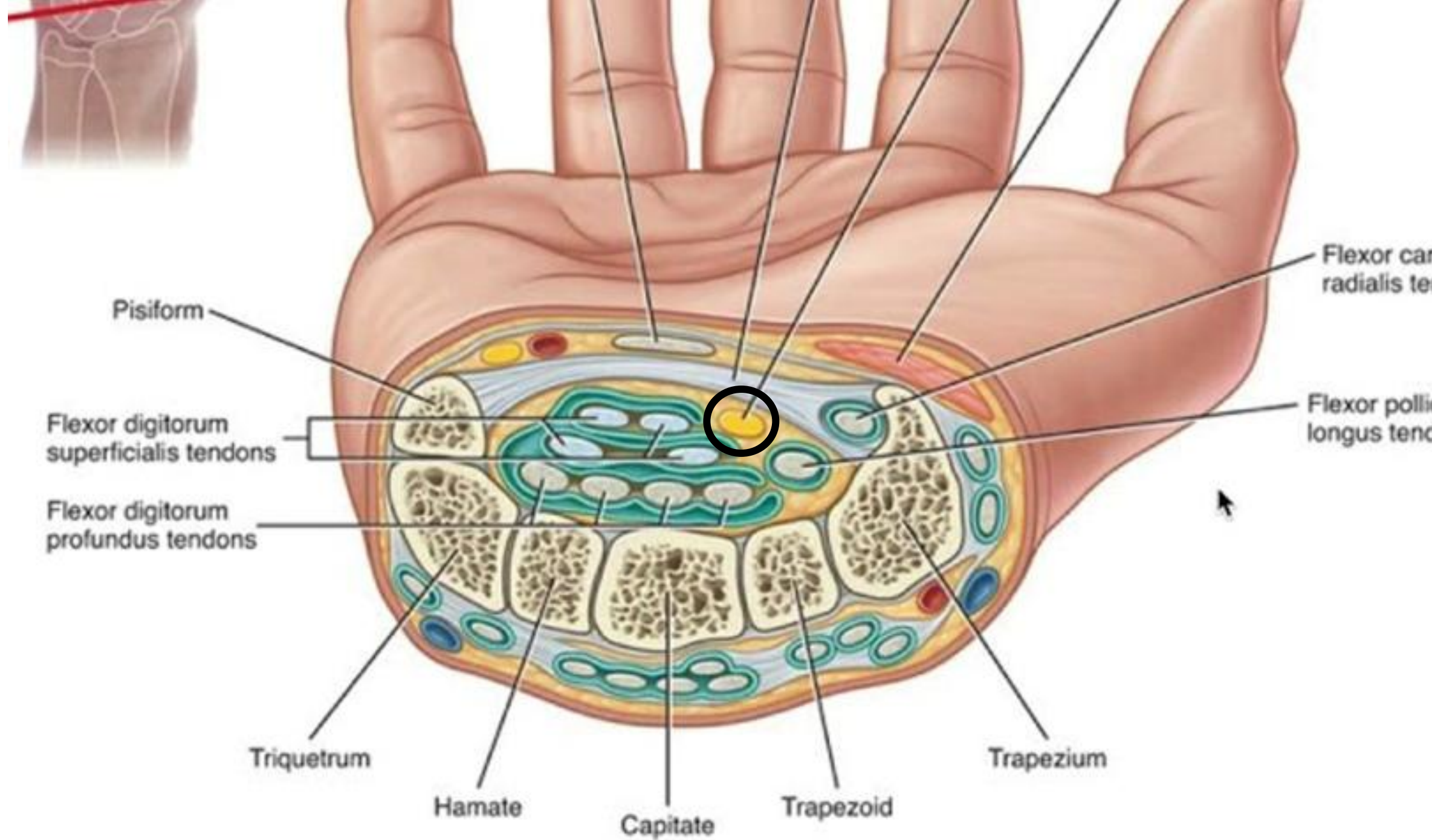




Amyloid Found

- Tenosynovium
- Transverse carpal ligament¹
- Synovium
- Flexor Tendon Sheath
- Fascia
- Vessel Walls (cap, venules, art)^{2,3}

1. Fernández Fuertes J et al., *Med Clin (Barc)* 2017.
2. Stein K et al. *Virchows Arch A Pathol Anat Histopathol.* 1987;412(1)
3. Bastian FO. *Am J Clin Pathol.* 1974;61(5)



TWO characteristics from **Tier 1**

OR

ONE characteristic from **Tier 1** *PLUS* any **ONE** from **Tier 2**



Tenosynovial and/or TCL tissue biopsy with
Congo red (or Thioflavin-S) staining

****Amyloid Typing****
(mass spectrometry)

Amyloid (+)

Referral to
amyloid expert

• Family history of AL or ATTR amyloidosis

BASELINE CARDIAC TESTING

ECG

Echo w/ strain imaging

NT pro BNP, Trop T

+ TTR amyloid

PYP scan
Prealbumin



Serial Testing

Untyped Amyloid

PYP scan
Prealbumin
FLC, IFE serum/urine
Urine Prot/Cr ratio+



Serial Testing

AL Amyloid

+/- cMRI
FLC, IFE serum/urine
Urine Prot/Cr ratio+



Serial Testing

ATTR Cardiac Amyloidosis

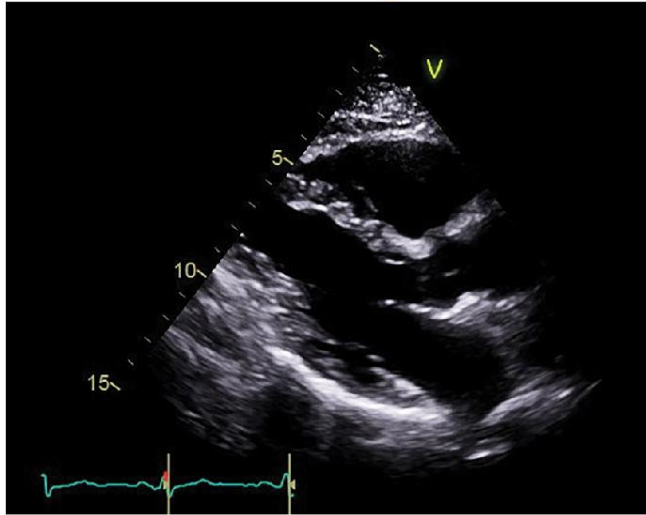
2006

We have nothing to treat this!!
What is the point?

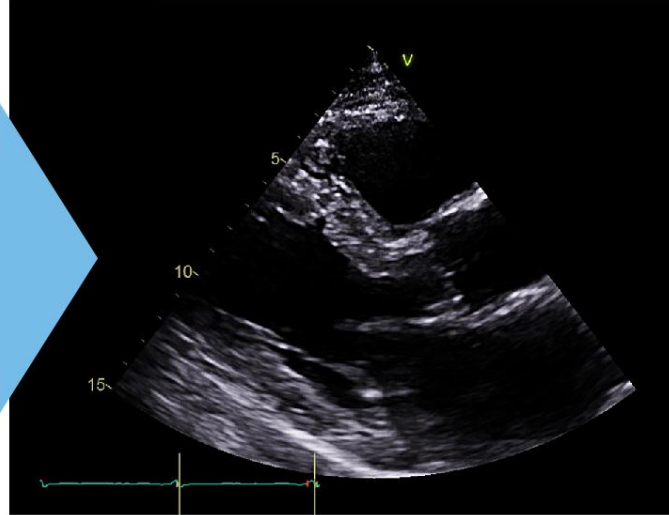
2026

We have 3 approved Treatments!
Please Enroll in Clinical Trials!

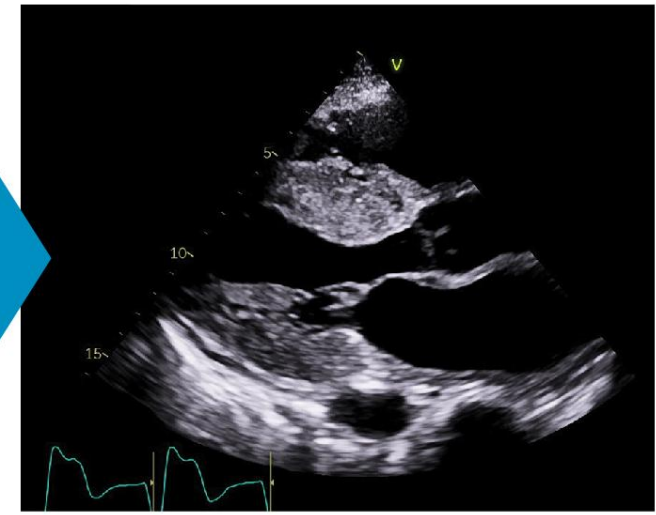
Early



Intermediate



Late



Ideal Therapeutic Window

NAC Stage I

Stage II

Stage III

Patient Symptoms • Quality of Life Assessments

Multimodality Diagnostic Tools (MRI, Echo, Nuclear, EKG)

NTproBNP • Troponin T • TTR levels • Novel Biomarkers

Thank you for your attention

