



Amyloidosis

FEBRUARY 14, 2016

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**Love-Making Reveals
a Broken Heart:**
*A 46-Year-Old Man with
Recurrent Hemoptysis
During Sexual Intercourse*

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Case presentation

- 46-year-old man w/history of type 2 diabetes
- Chief complaint:
 - » Recurrent hemoptysis during sexual intercourse
 - » Chest pain
 - » Shortness of breath
- Physical exam: normal
- ECG in office:
 - » Normal sinus rhythm, normal voltage
 - » Left anterior fascicular block
- CXR: normal

Pulmonary work-up: negative

- Pulmonary function testing
- Chest CT
- Bronchoscopy with BAL
- Transbronchial biopsy

Stress echocardiography

- Findings at rest:
 - » Normal LV size
 - » Normal LVEF and wall motion
 - » Moderate concentric LVH
 - » No significant valvular disease
 - » Grade 3 diastolic dysfunction

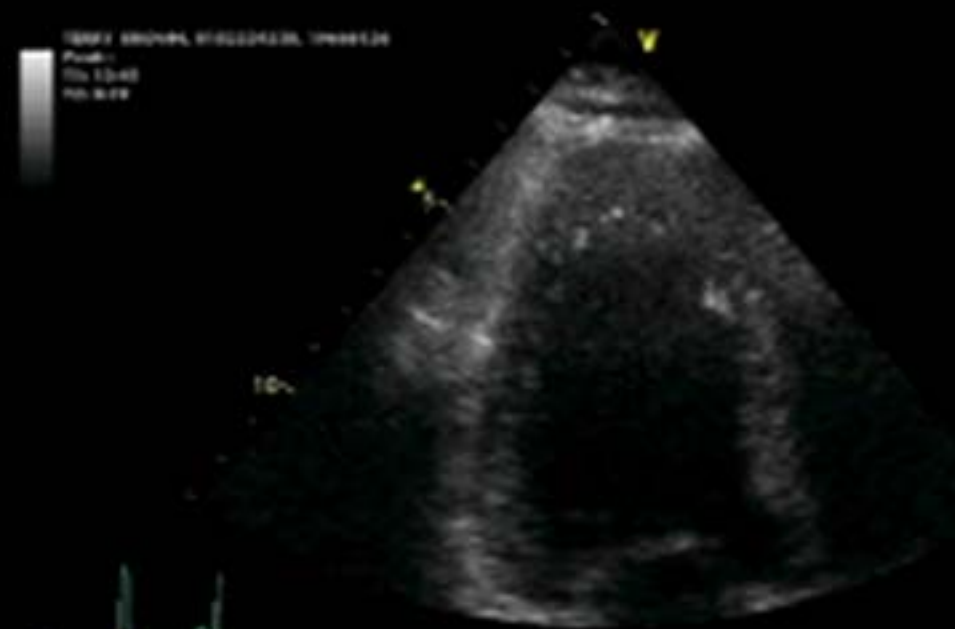
Stress echocardiography

- Stress test:
 - » Bruce protocol
 - » Chest pain at 6 minutes
 - » Total exercise time = 8 minutes (9.4 METs)

Stress echocardiography



REST



STRESS

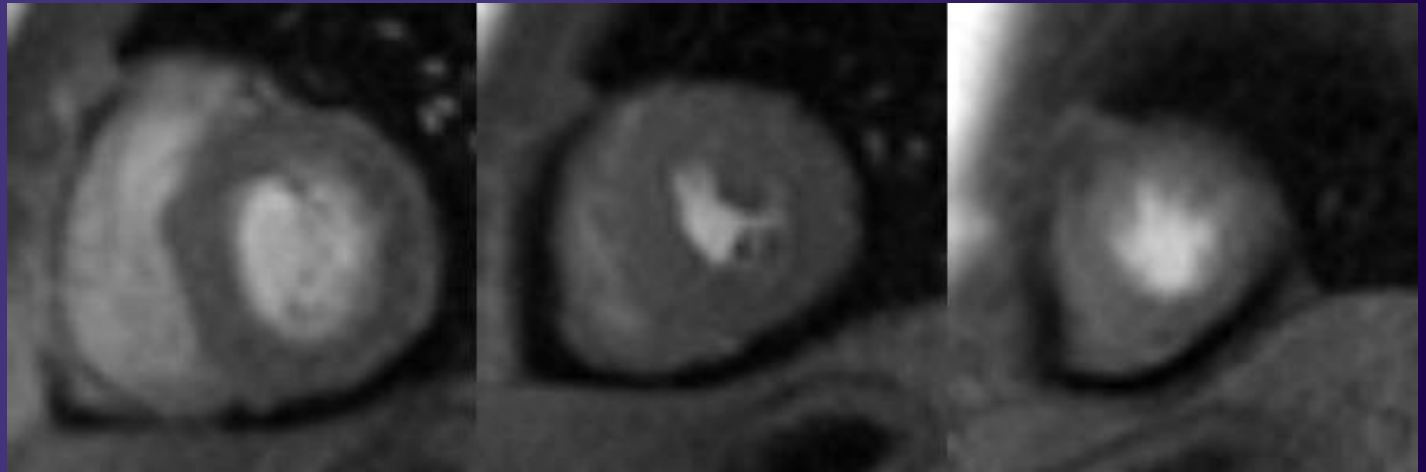
Cardiac catheterization

- Angiographically normal coronary arteries
- Normal hemodynamics

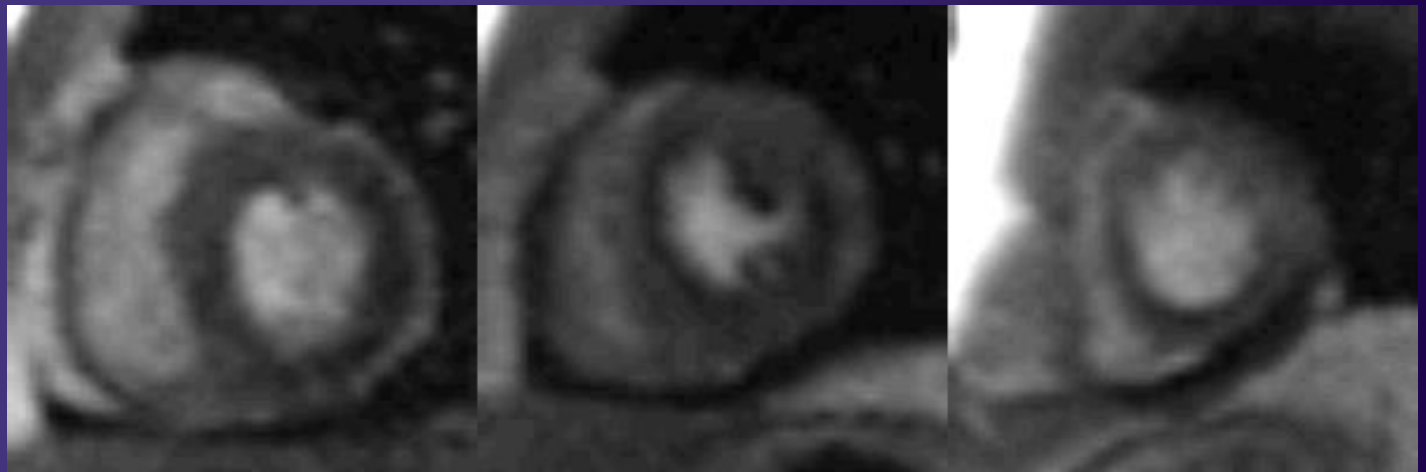


Adenosine Perfusion

Rest

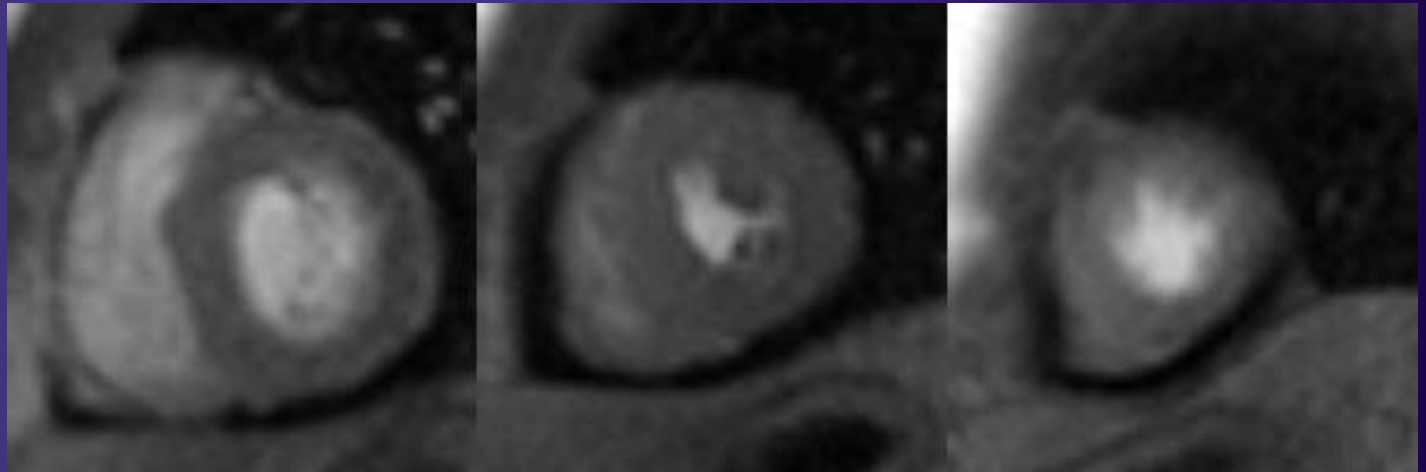


Stress

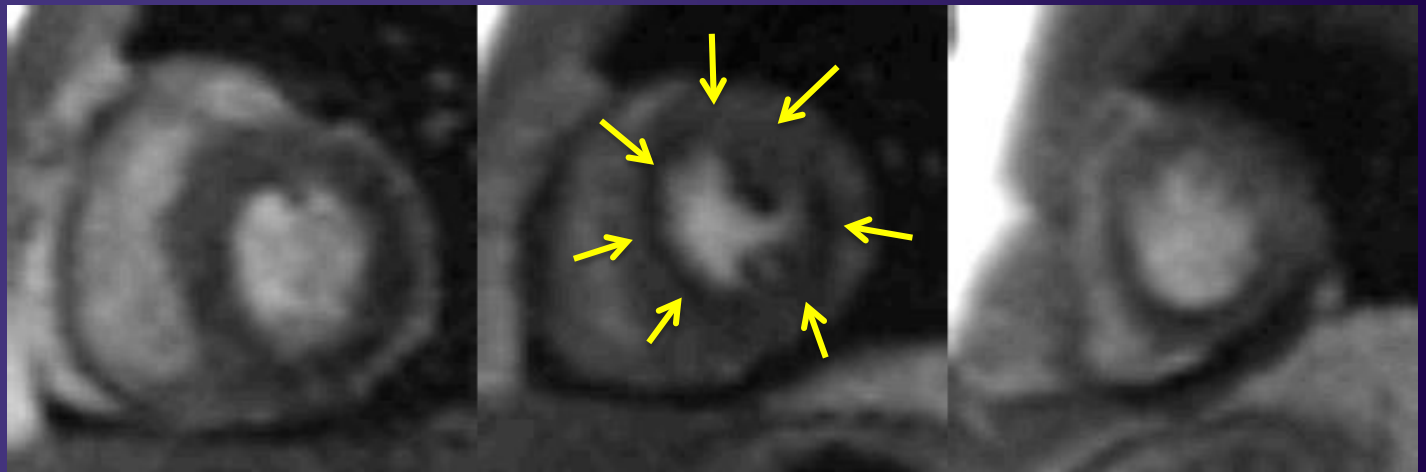


Adenosine Perfusion

Rest



Stress



Summary of MRI findings

- Normal LV size and systolic function
- Moderate concentric LVH
- No focal hyper-enhancement
- Mild mitral regurgitation
- Diffuse reversible subendocardial hypoperfusion with adenosine (in the absence of significant CAD → microvascular dysfunction)

Unifying diagnosis?

- Microvascular ischemia:
 - » Cardiac syndrome X?
 - » May explain exertional dyspnea, chest pain
- What about exertional hemoptysis?
- Is this Hickam's Dictum or can we push forward and satisfy Occam's Razor?

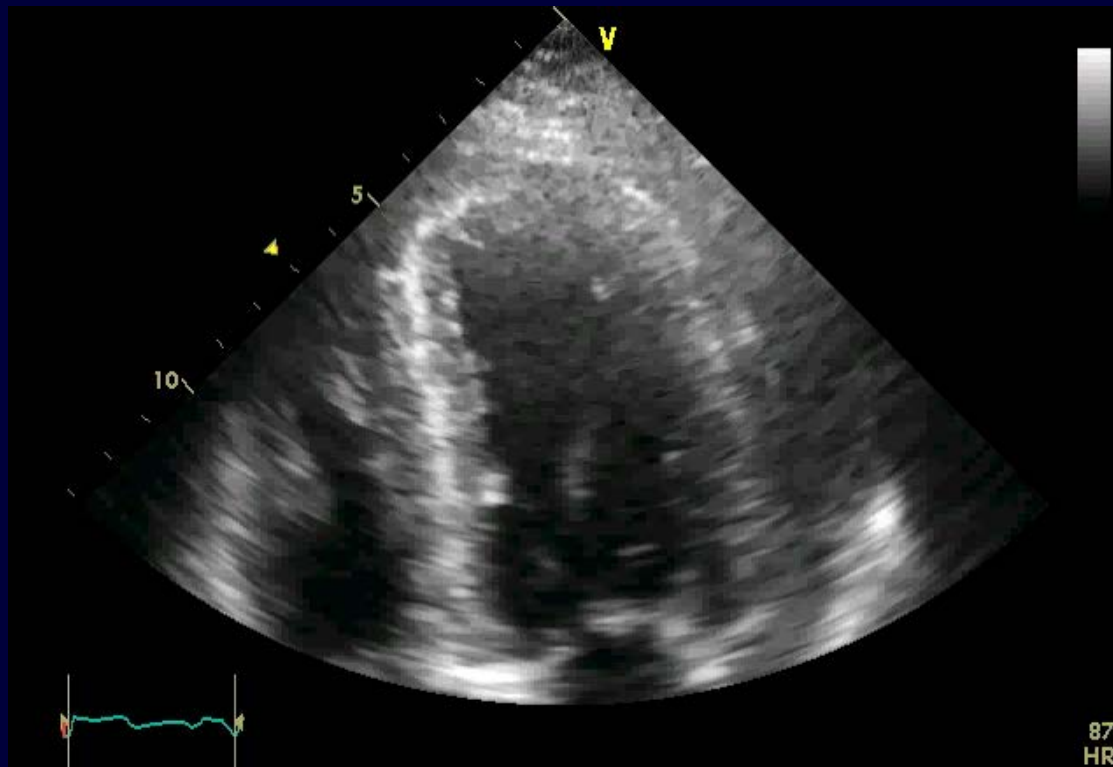
Unifying diagnosis?

- Occam's Razor:
 - » "pluritas non est ponenda sine necessitas"
 - » "plurality should not be posited without necessity"
- Hickam's Dictum:
 - » "Patients can have as many diseases as they damn well please"

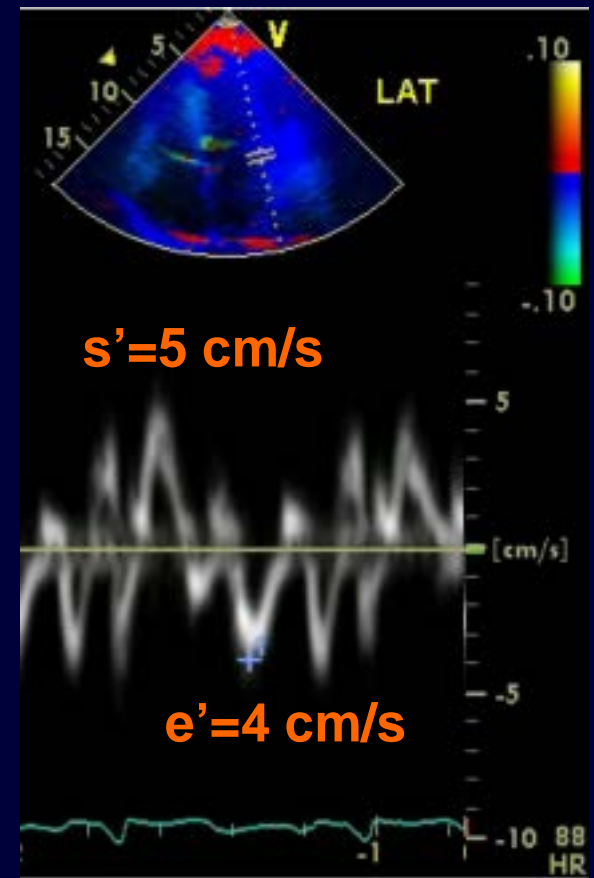
DDx of hemoptysis during intercourse

- Cardiogenic
 - » Heart failure
 - » Mitral stenosis
 - » Coronary artery disease
 - » Systemic hypertension
- Vascular
 - » Pulmonary vascular problem
 - Pulmonary embolism
 - Vasculitis

Another look at the echo...

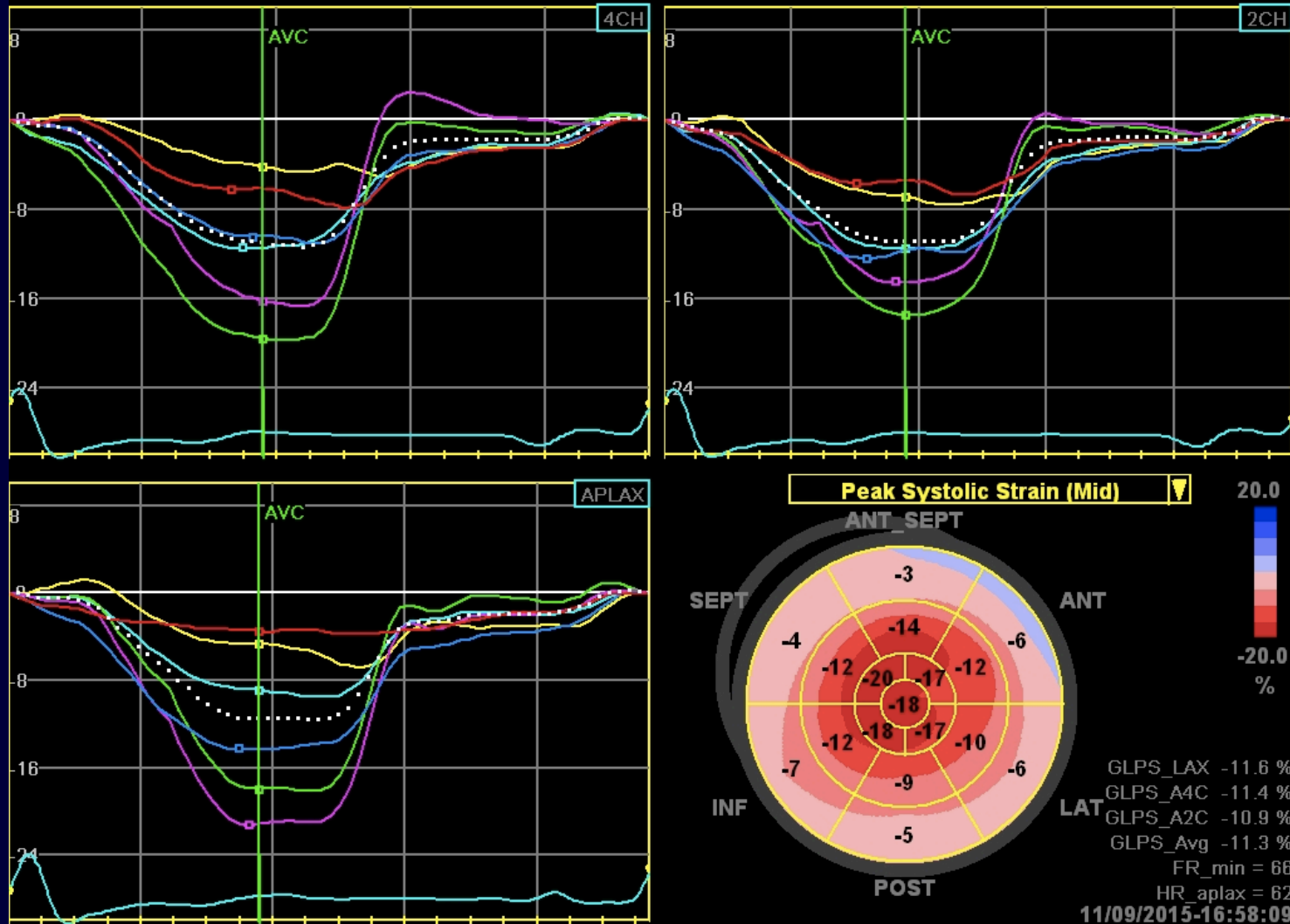


Apical 4-chamber view

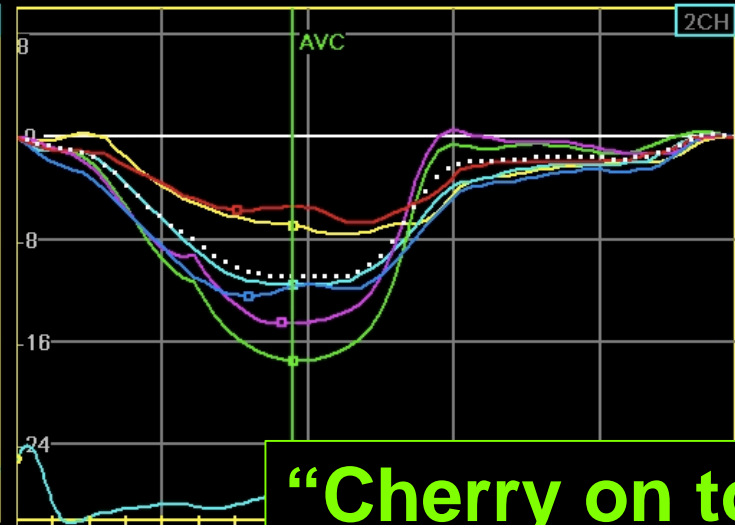
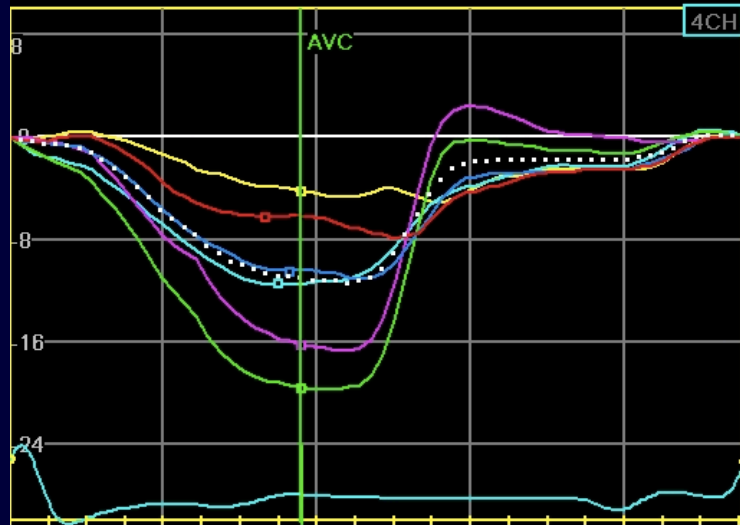


Tissue Doppler

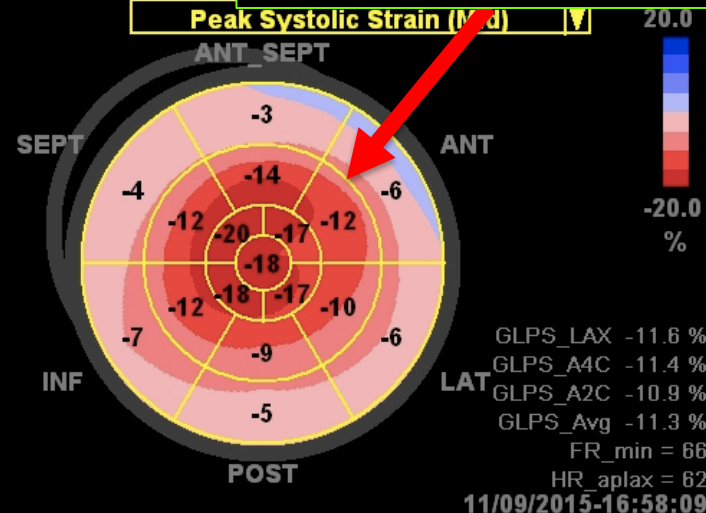
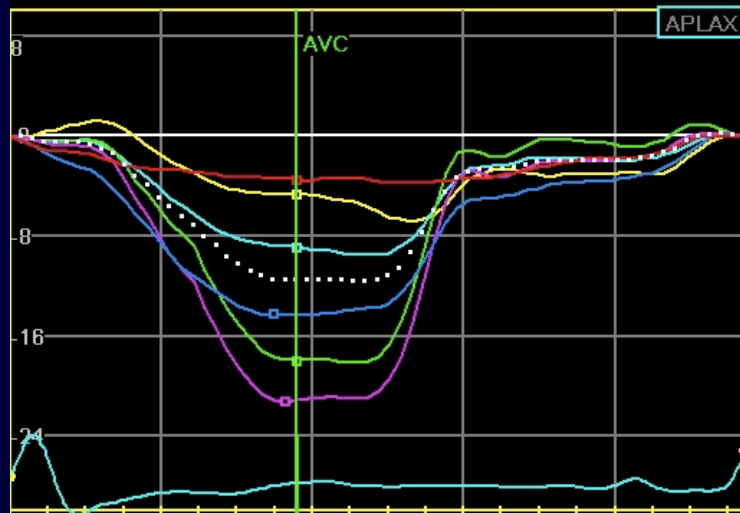
Global longitudinal strain (GLS)



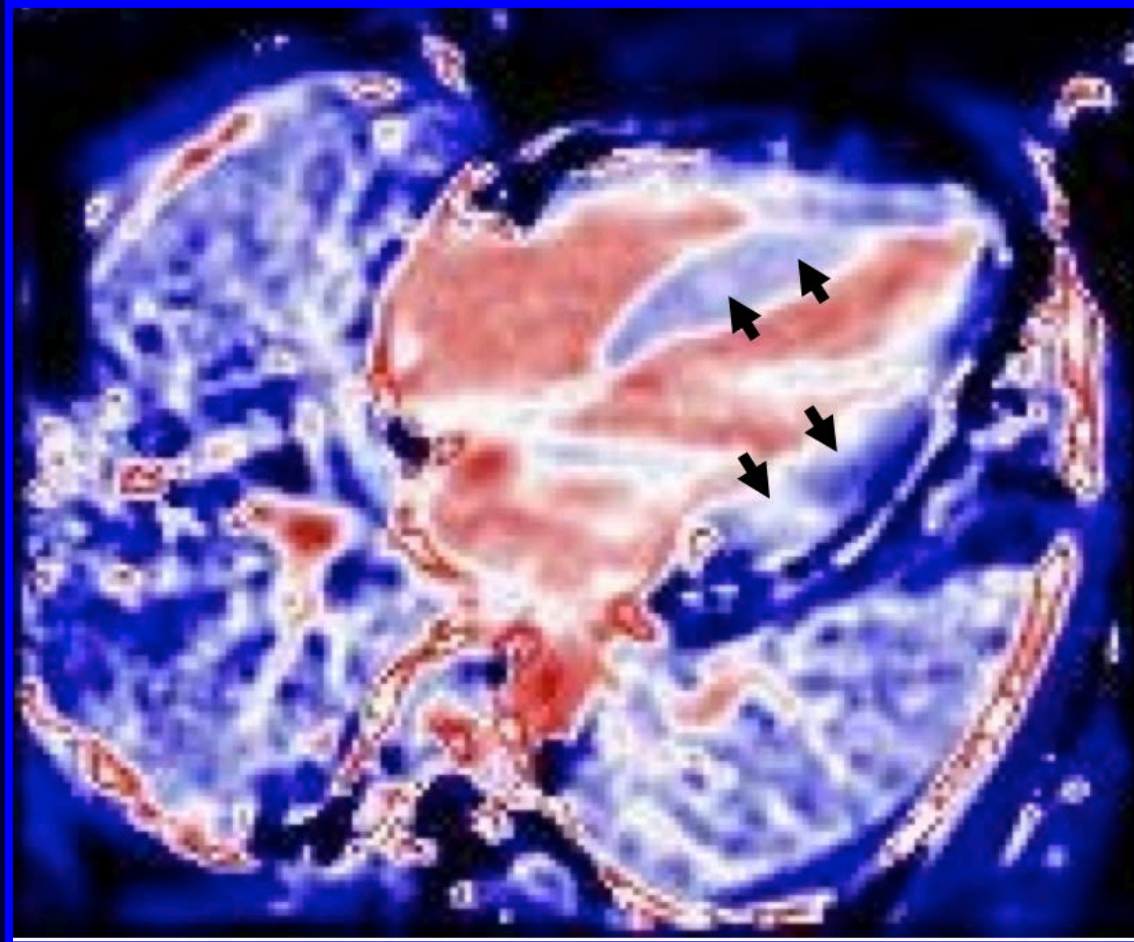
Global longitudinal strain (GLS)



“Cherry on top”



Another look at the cardiac MRI



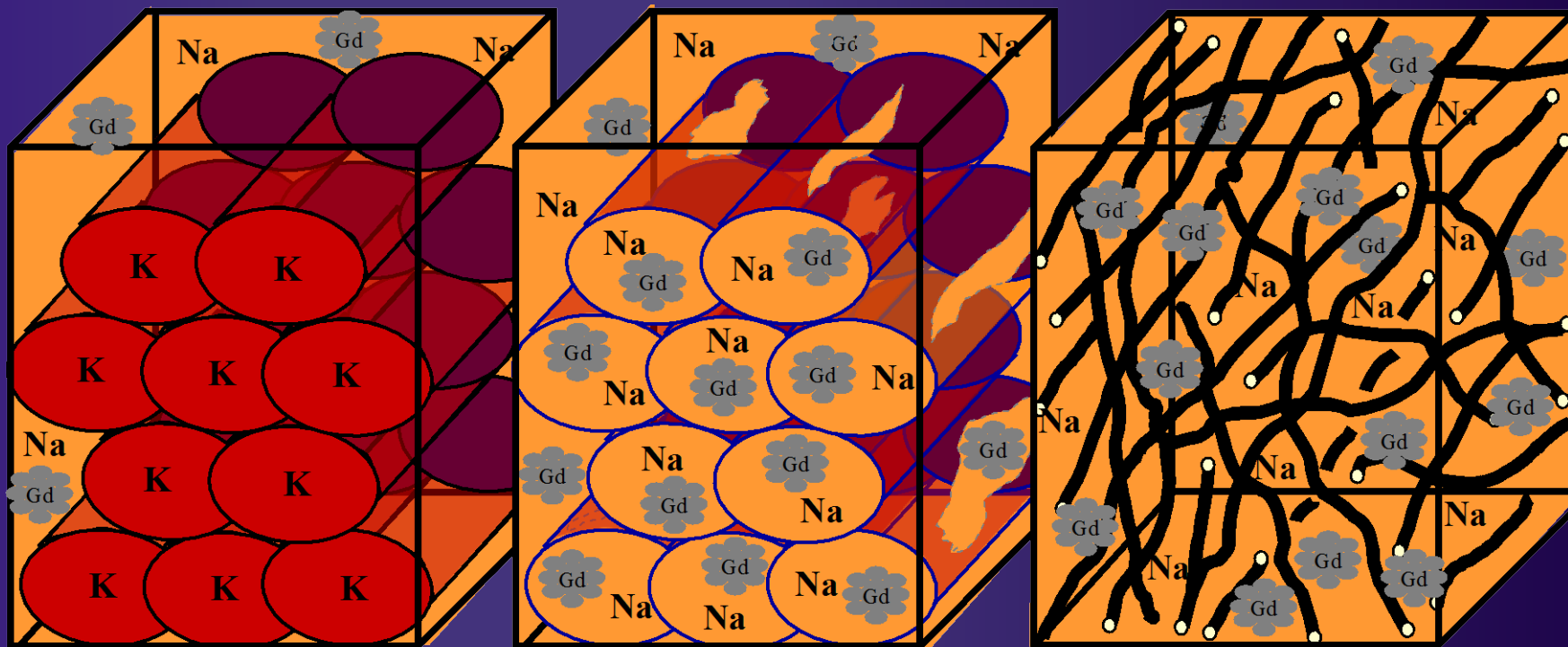
Mechanisms of contrast enhancement in myocardial infarction.



Normal Myocardium

Acute Infarction

Chronic Scar



Intact Cell Membrane

Ruptured Cell Membrane

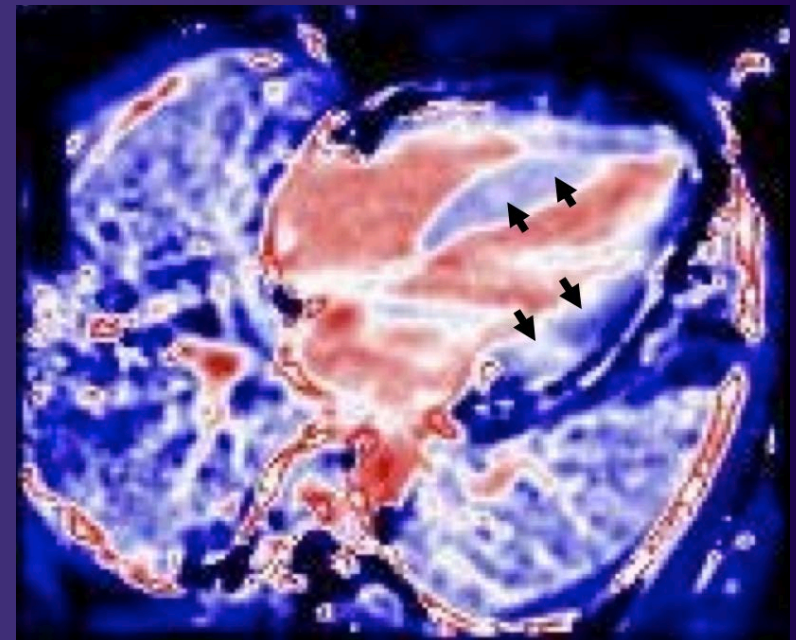
Collagen matrix

Adapted from: Mahrholdt H et al. Eur Heart J 2005;26:1461-1474

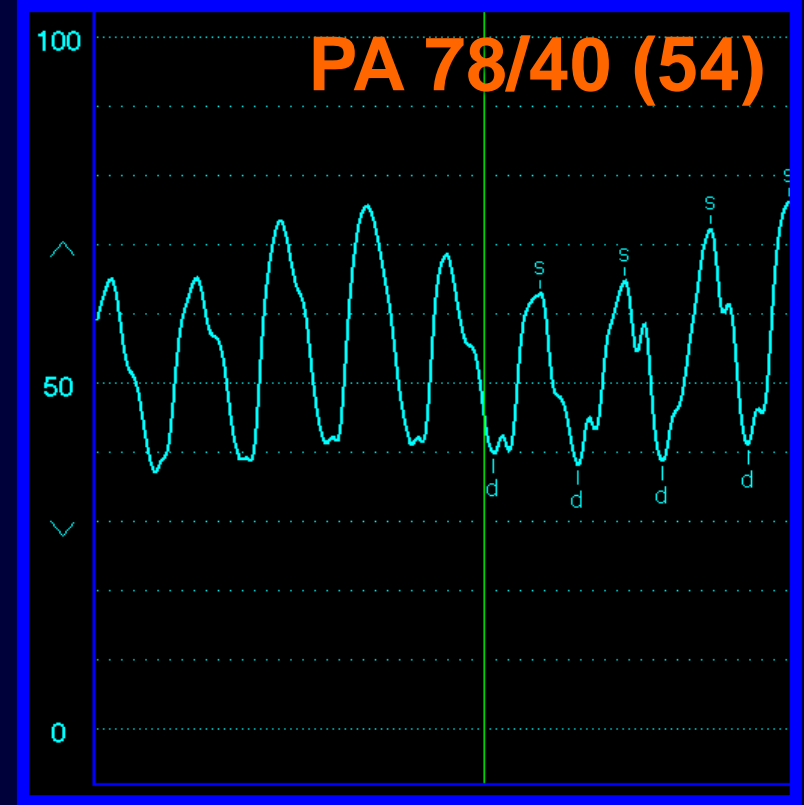
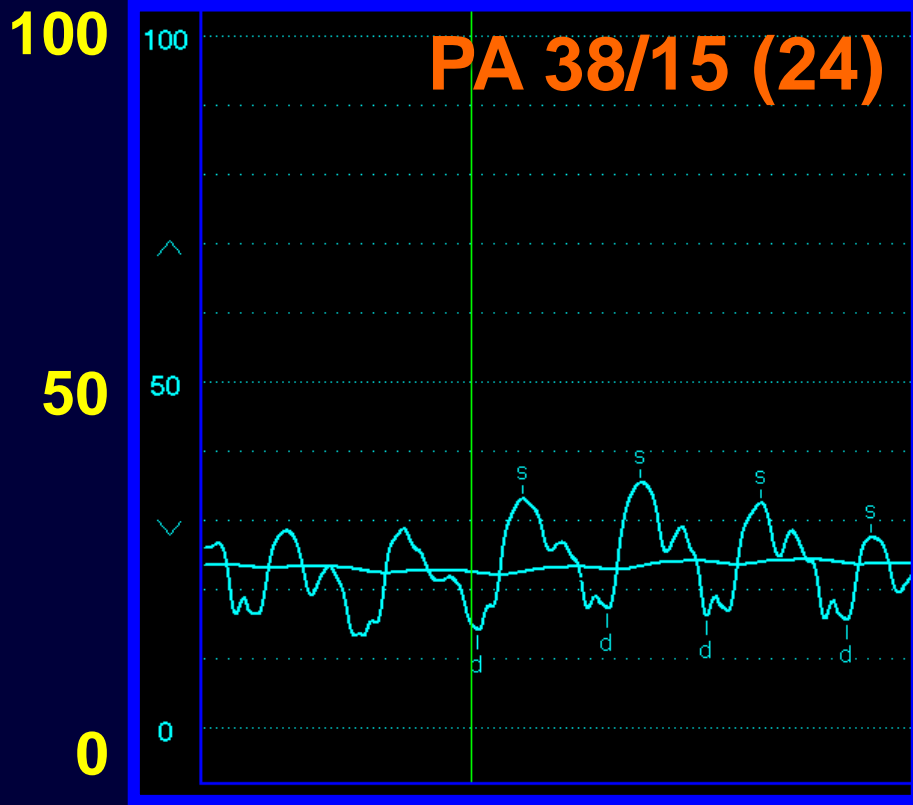


Extracellular Volume Fraction (Ve) in our patient on CMR T1 mapping:

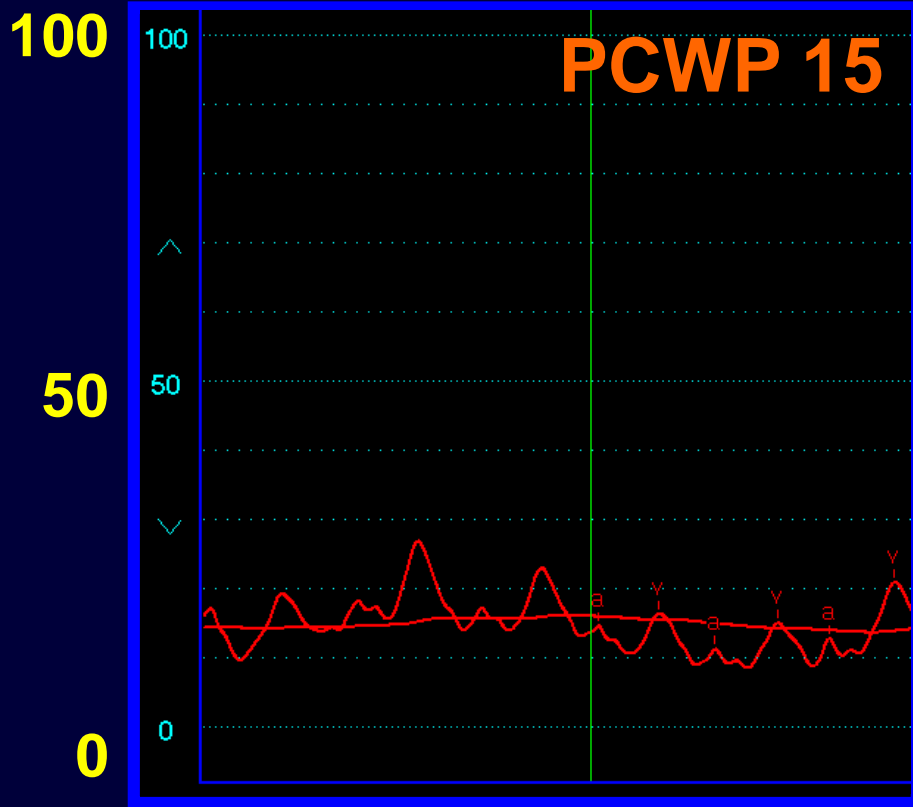
Ve% of Whole Myo	
4CH	43.8%
SA Base	40.4%
SA Mid	37.8%
Normal	< 25%



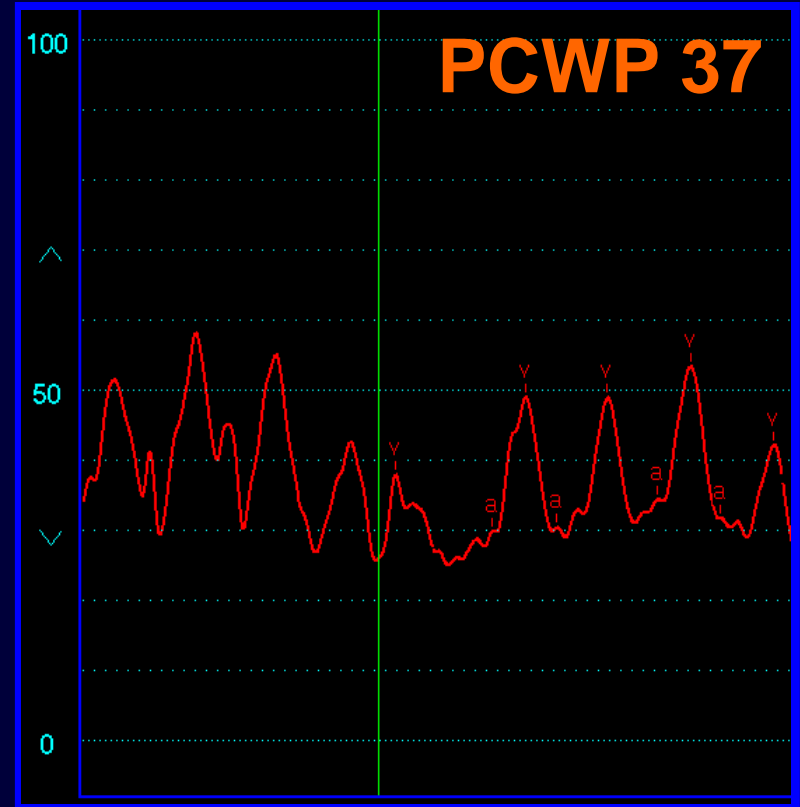
Repeat right heart cath w/exercise



Repeat right heart cath w/exercise



REST

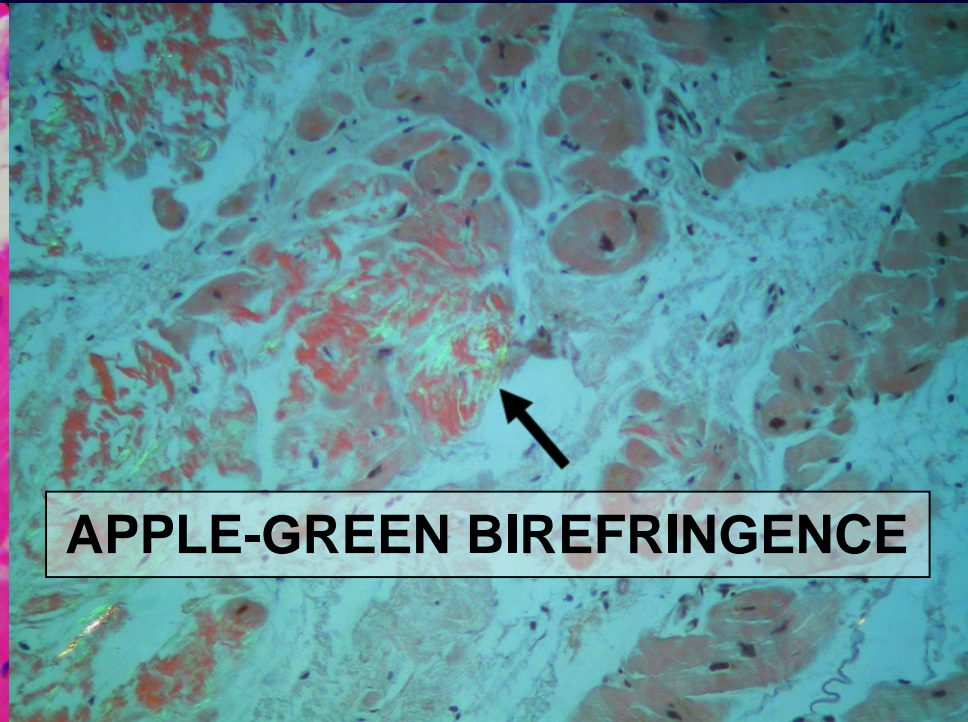
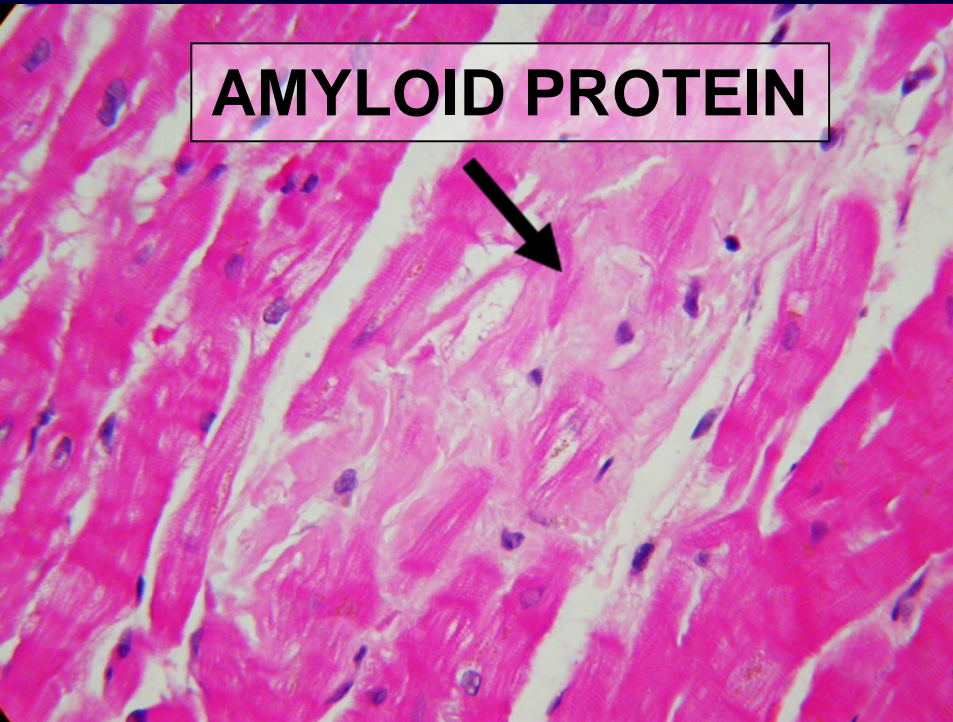


1-MIN. OF EXERCISE

Case summary

- 46-year-old diabetic man with hemoptysis during intercourse, angina, dyspnea
- Pulmonary work-up negative
- Normal LVEF but severely reduced longitudinal systolic and diastolic function
- Increased, diffuse protein infiltration in the myocardium + subendocardial ischemia
- Marked exercise-induced pulmonary venous hypertension due to severe diastolic dysfunction

What's the diagnosis?



Case summary

- Patient treated with:
 - » Bortezomib (Velcade)
 - » Warfarin
 - » Spironolactone
 - » Bumetanide (low dose)
- Marked improvement in functional status
- Underwent autologous stem cell transplantation with uneventful course
- No sign of recurrence of amyloid

Systemic amyloidoses

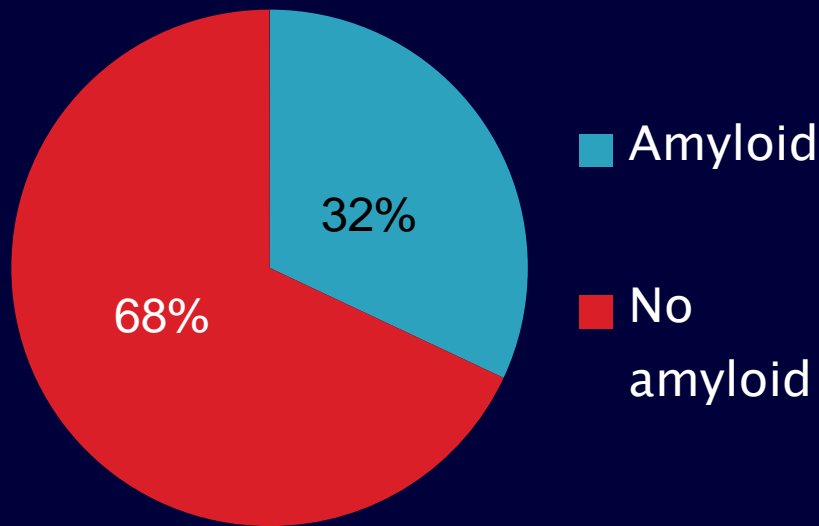
- Group of disorders characterized by extra-cellular deposition of fibrillar protein
- Deposits composed of amyloid fibrils → progressive end-organ dysfunction
- > 20 proteins form amyloid fibrils *in vivo*
- 2 predominant types involve the heart:
 - » AL: typically assoc. w/plasma cell dyscrasia
 - » Transthyretin (TTR)-associated:
 - Hereditary (mutation) and senile (wild-type)

Cardiac amyloid: rare disease?

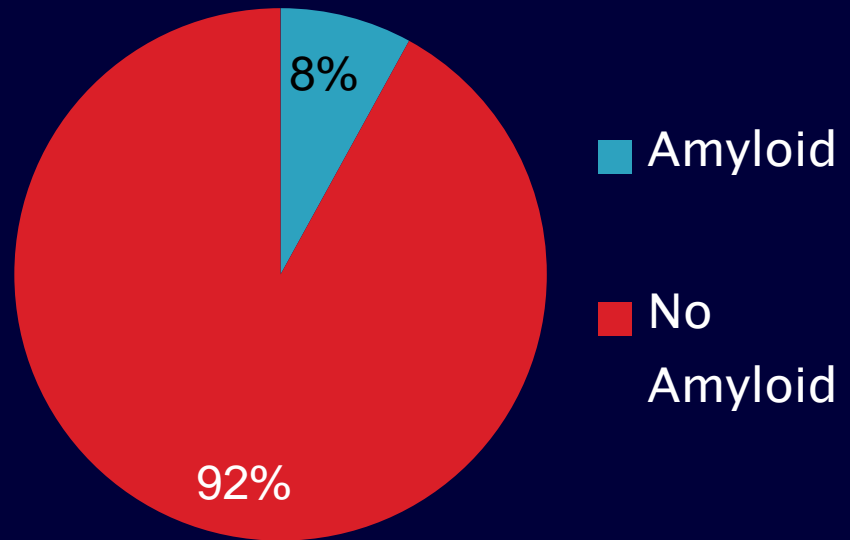
- Annual incidence of systemic amyloid:
 - » 6-10 cases per million in United States
- But...
 - » Amyloidosis likely under-recognized
 - » Transthyretin (TTR) amyloid may be common
 - 3-4% of African Americans carry V122I mutation in *TTR* gene
 - Wild-type (senile) TTR amyloidosis increasing in prevalence

Cardiac amyloid: rare disease?

Age > 75 years



Age < 75 years



In older patients with HF an preserved EF, amyloid deposition is common

Circulation. 2010; 122: A17926

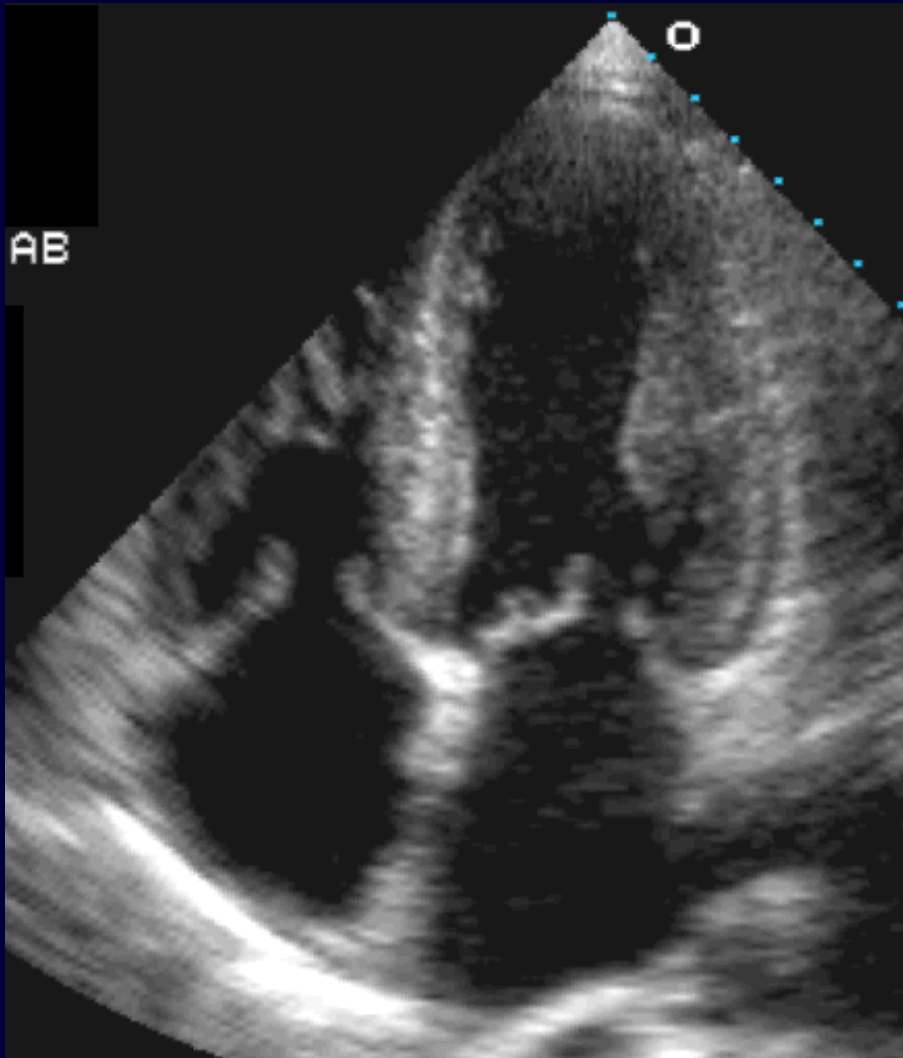
Cardiac amyloidosis

- Primary (AL) amyloid (light chains)
 - » Order serum immunofixation, not SPEP
- Familial (TTR) amyloid
 - » Due to TTR gene mutation (3-4% of AAs have V122I)
 - » Neuropathy, cardiomyopathy
- Secondary (AA) amyloid
 - » Cardiac involvement is rare
- Senile cardiac amyloid
 - » Due to wild-type TTR accumulation

Clinical clues for the diagnosis

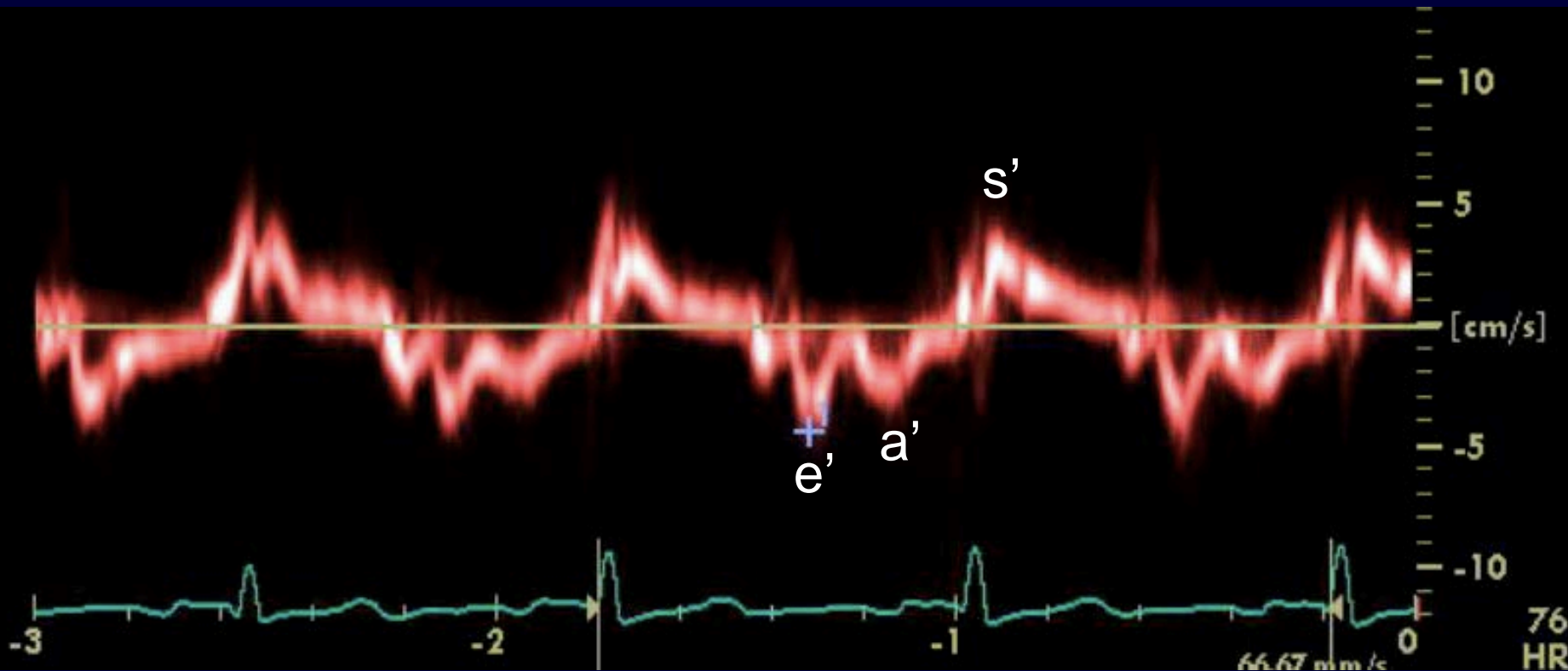
- Bilateral carpal tunnel syndrome
- Macroglossia
- Easy bruising, decreased Factor X levels
- Heart failure with...
 - » Kussmaul's sign
 - » Peripheral neuropathy
 - » Autonomic dysfunction / orthostatic hypotension
 - » Continuous low-level troponin release
- Low BP, low volts, and thick heart

Typical echo findings



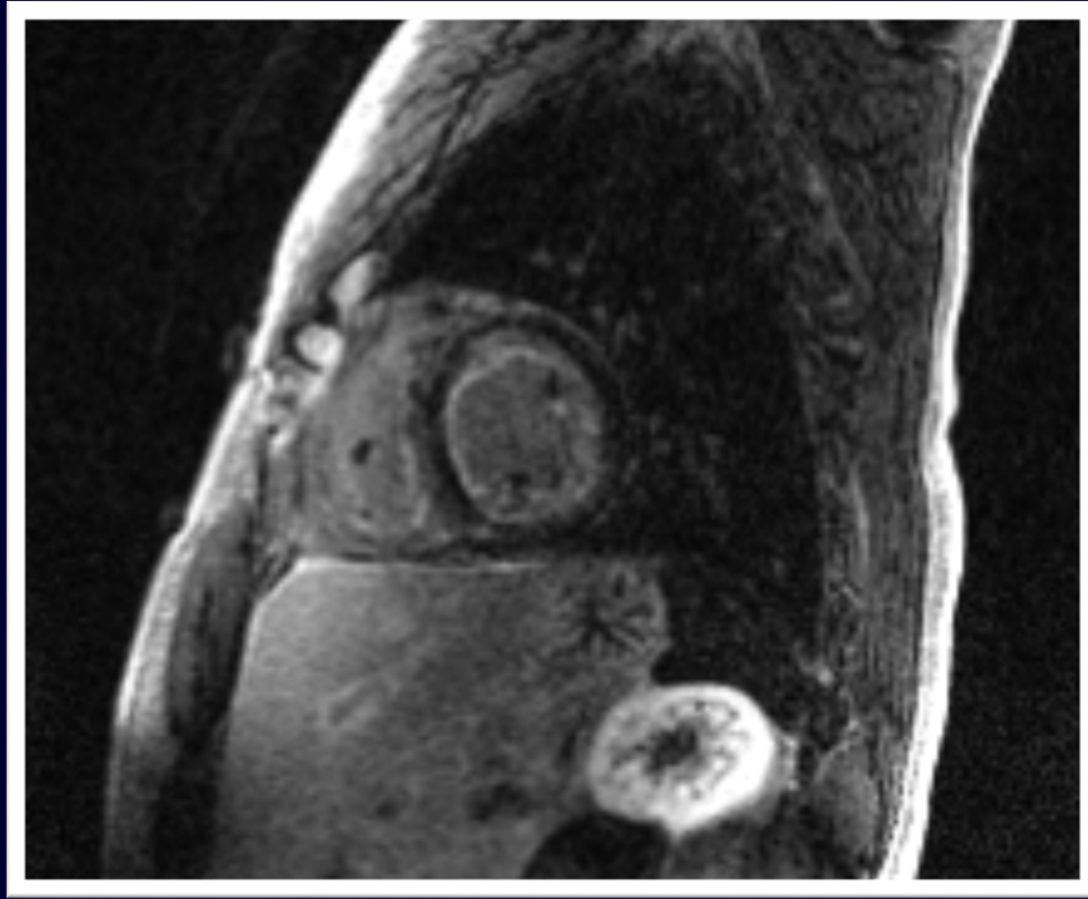
*Loss of longitudinal
cardiac function*

Typical echo findings



Severely reduced longitudinal tissue velocities
“5-5-5 sign”

Typical cardiac MRI findings



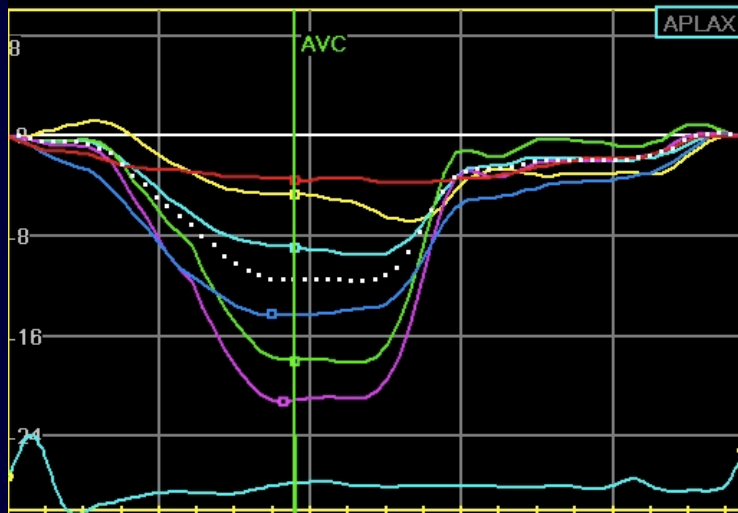
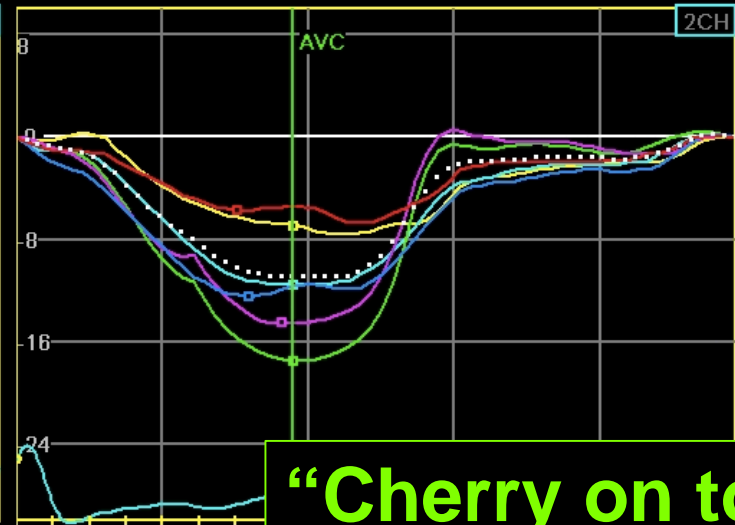
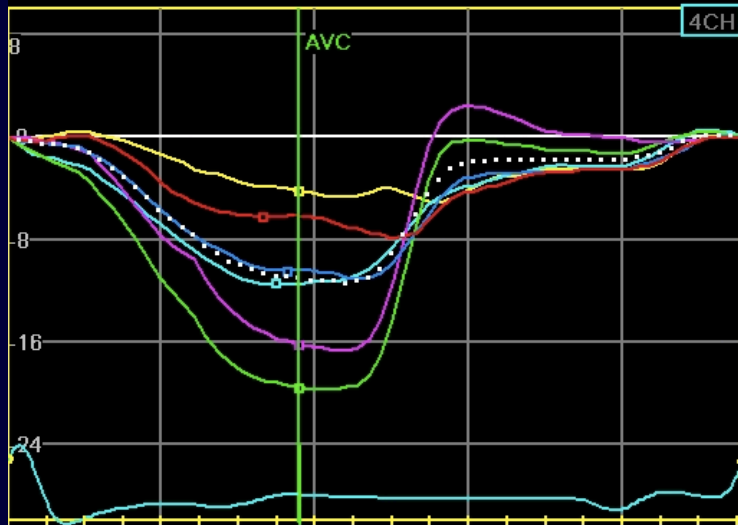
Diffuse subendocardial delayed enhancement

Typical cardiac MRI findings

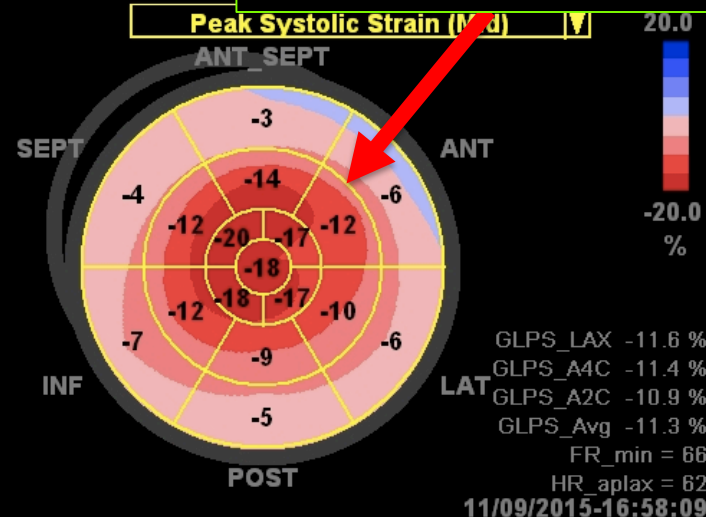


Diffuse subendocardial delayed enhancement

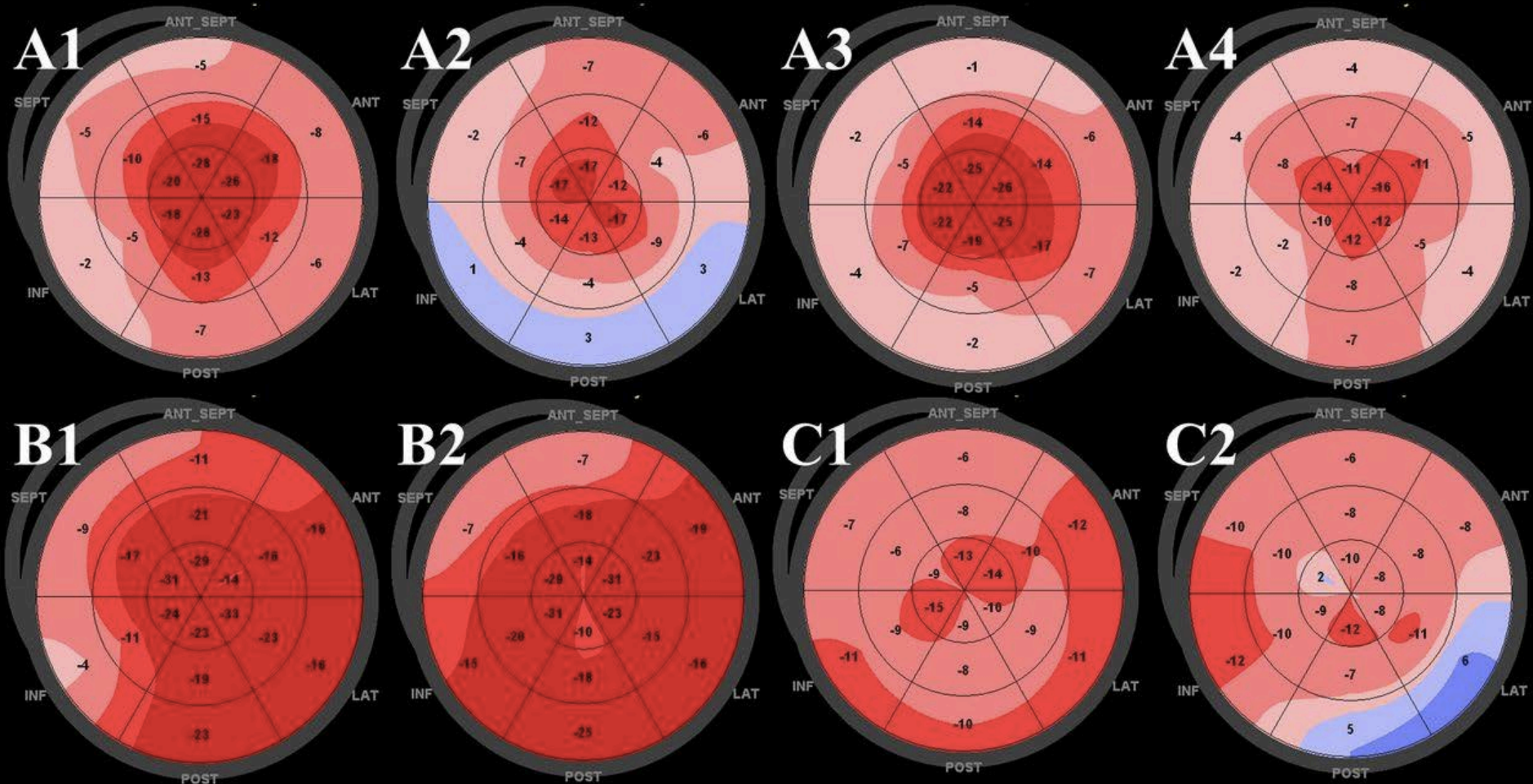
Speckle-tracking: “cherry on the top”



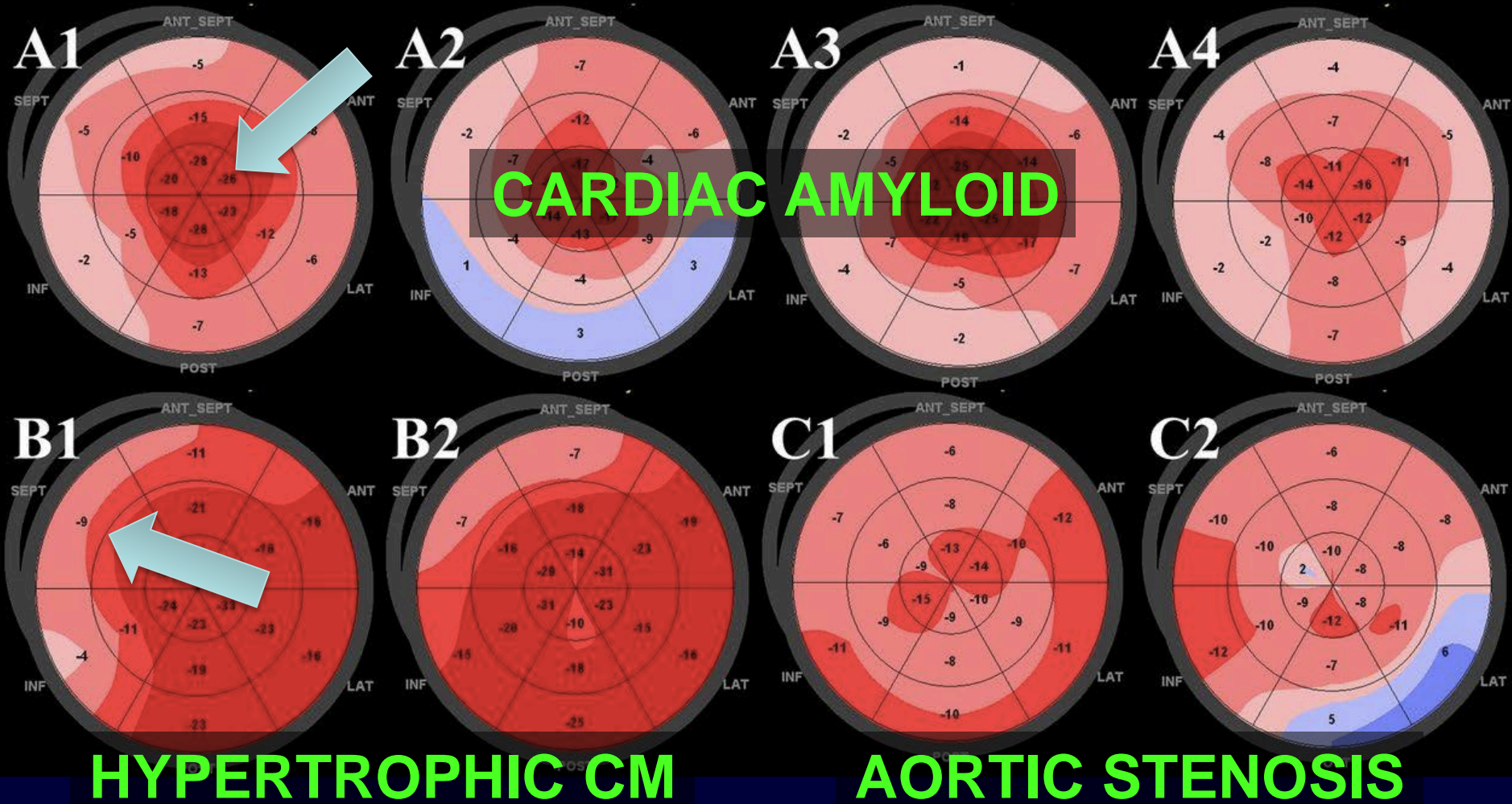
“Cherry on top”



Speckle-tracking: “cherry on the top”



Speckle-tracking: “cherry on the top”



Cardiac amyloidosis: key echo findings



- Severely reduced longitudinal function
 - » TDI e' , a' , and s' typically < 5 cm/s
 - » Absolute global longitudinal strain $< 15\%$ (often $< 10\%$)
- Preserved radial and apical function

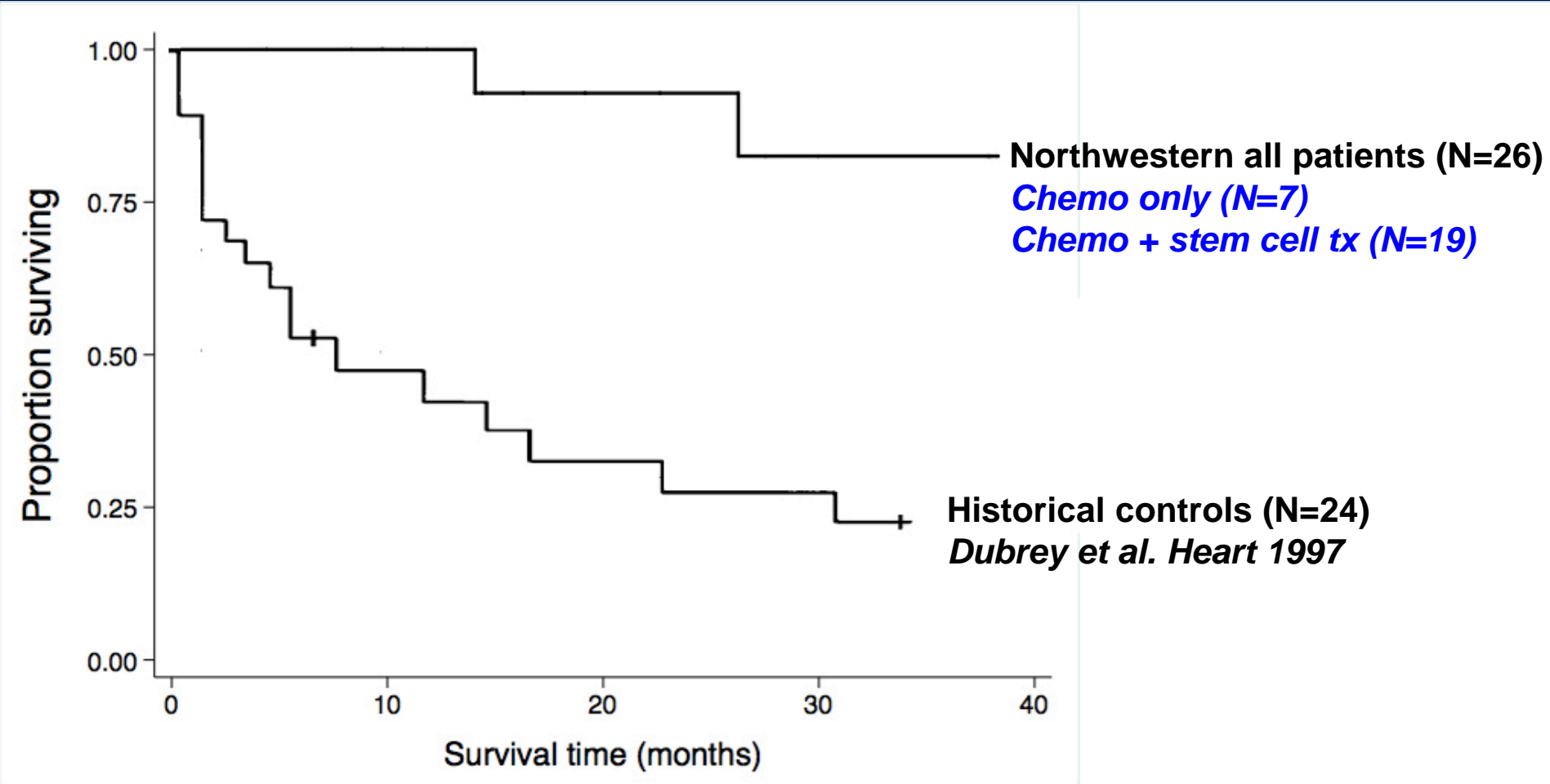
Cardiac amyloid: echo pearls

- “Sparkling texture” on echo:
 - » Still helpful in era of harmonic imaging
 - » Look at renal function: if no severe CKD or ESRD, sparkling appearance (especially with severely decreased longitudinal function), think infiltrative (most commonly amyloid)
- Remember to look at tissue Doppler s' , e' , and a' velocities:
 - » They will be severely reduced (< 5 cm/s) in most cases of cardiac amyloid

Cardiac amyloid can be treated!

- Cardiac amyloid: *not a death sentence*
 - » Primary (AL) amyloidosis:
 - Stem cell transplantation *or*
 - Cardiac transplant followed by stem cell tx
 - » Familial or wild-type TTR amyloidosis:
 - Several novel drugs in pipeline (TTR stabilizers, RNA interference, RNA anti-sense molecules)
 - Phase 3 clinical trials in TTR cardiac amyloid: ATTR-ACT and ENDEAVOUR
 - Heart-liver transplant

Primary (AL) cardiac amyloid: improved survival with stem-cell tx



Take home points

- Amyloidosis is not 1 disease
- Prognosis of amyloidosis varies by organ involvement and type of amyloid
- Echo clues:
 - » Sparkling, granular texture of myocardium
 - » Thick LV out of proportion to ECG voltage
 - » Severely reduced longitudinal systolic/diastolic function
 - » “Cherry on the top” on speckle-tracking
- *Cardiac amyloid: not a death sentence*



thank you!