



HFpEF

Heart Failure with Preserved Ejection Fraction

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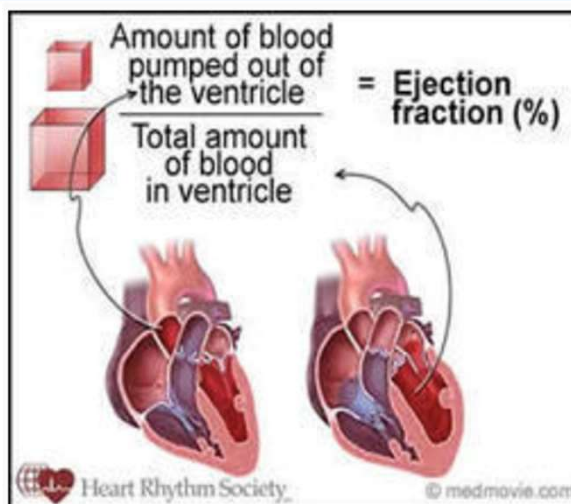


Disclosures: None



EJECTION FRACTION

- Developed by Physiologists in 1950's as a measure of contractility under CONSTANT loading conditions
- NORMAL = 55% to 70%
- LVEF changes with:
 - Preload
 - Afterload
 - Volume
 - Contractility



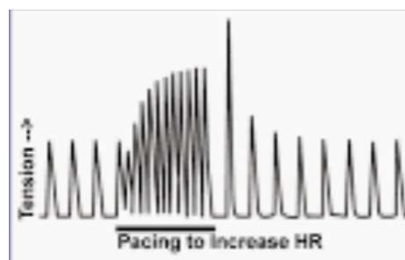
NORMAL HEART PHYSIOLOGY

- Ventricular contraction involves a “Twisting” and “Untwisting” action
- Mitral Annulus moves up and down
- Creates a SUCTION effect which facilitates Rapid LV Filling in early diastole.
- The “TREPPE” or STAIRCASE effect:
As Heart Rate Increases there is a stair step Increase in Contractility.



NET EFFECT

- As HR goes up:
- Contractility Goes Up
- SUCTION increases
- Early Diastolic Filling is accelerated
- LV and Pulmonary Wedge pressures stay LOW



LVEF DOES NOT DEFINE “HEART FAILURE”

- Echocardiographic studies have shown that only HALF of patients with LVEF less than 50% are symptomatic

(McDonagh TA, et al. Symptomatic and Asymptomatic Left Ventricular Dysfunction in an Urban Population. Lancet. 1997; 350-829)

- Multiple studies have demonstrated that roughly HALF of patients with clinically diagnosed “Heart Failure” have NORMAL LVEF

(Vasan RS, et al. Congestive Heart Failure in Subjects With Normal Versus Reduced Left Ventricular Ejection Fraction. J Am Coll Cardiol 1999; 33: 1948)



ASYMPTOMATIC DIASTOLIC DYSFUNCTION

- ECHO measures of “Diastolic Dysfunction” alone does not define HFpEF

- One study of 2042 patients > 45 years old demonstrated that 28% of asymptomatic patients had ECHO derived evidence of Diastolic Dysfunction. This is considered Stage “B” by ACC/ AHA Guidelines.

(Redfield MM, et al. Burden of systolic and Diastolic Ventricular Dysfunction in the Community. JAMA. 2003; 289: 194)

- The presence and severity of “Diastolic Dysfunction” by ECHO increases with Age and may be a precursor to development of Heart Failure



CLINICAL DIAGNOSIS OF “CONGESTIVE HEART FAILURE”

Framingham Criteria: 2 Major or 1 Major and 2 Minor

	Major	Minor
HPI	PND or orthopnea	DOE
	Rales	Nocturnal cough
PE	HJR	Tachycardia
	S3	Ankle edema
	JVD (or elevated CVP)	Hepatomegaly
Imaging	CXR pulmonary edema	CXR engorged pulm vessels
	Cardiomegaly	Pleural effusion
Empiric!	10lb weight loss with diuretics	Decreased vital capacity

(Yancy, et al. 2013 ACCF/AHA Heart Failure Guideline)



CATEGORIES OF HEART FAILURE

HFrEF: Heart Failure with Reduced Ejection Fraction: LVEF < 40%

HFpEF: Heart Failure with Reduced Ejection Fraction: LVEF > 50%

(Yancy, et al. 2013 ACCF/AHA Heart Failure Guideline)

HFmrEF: Heart Failure with Mid Range Ejection Fraction: LVEF 41-49%

(Ponikowski P, et al. 2016 ESC Guidelines. European Heart Journal, Vol 37, Issue 27, 14 July, 2016. P 2129-2200)



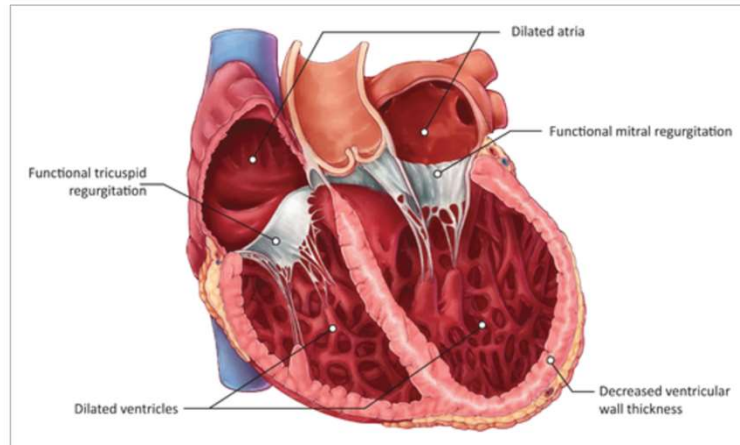
“HFrEF” (Heart Failure with Reduced Ejection Fraction)

CHARACTERISTICS

- Dilated Left Ventricle
- Eccentric Hypertrophy
- LVEF < 40%
- Pulmonary Edema

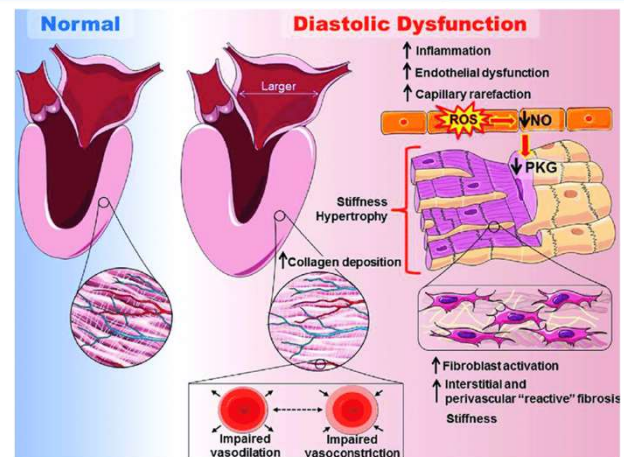
PROVEN TREATMENTS

- Beta Blockers
- Ace Inhibitors / ARB
- Neprilysin Inhibitors
- Aldosterone Inhibitors
- Digoxin
- AICD / Biventricular Pacing



STRUCTURAL CHANGES IN HFpEF

- Chamber Remodeling
 - Increased Relative Wall thickness & LV Mass
 - Normal End Diastolic Ventricular Volume
 - Increased Left Atrial Volume
- Cardio Myocyte Remodeling
 - Increased myocyte Hypertrophy (Myocytes thicker and shorter)
 - Matrix Inflammation and fibrosis
 - Increased Collagen Deposition
 - Increased metalloproteinases

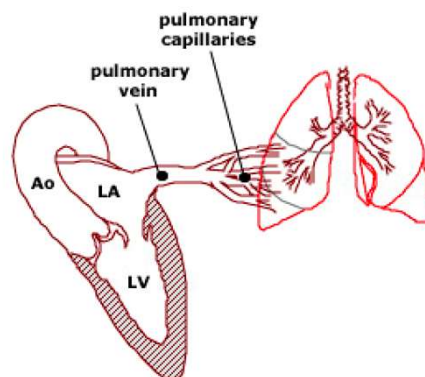


FUNCTIONAL CHANGES IN HFpEF

- Decreased Myocardial Relaxation
- Decreased Early LV Filling and shift to Late Diastolic Filling
- Increased dependence on Left Atrial Contraction
- Increased LV Stiffness and reduced LV Distention
- Increased Diastolic Pressure in Left Ventricle; Left Atrium and Pulmonary Veins

ALL CHANGES EXACERBATED BY:

- EXERCISE
- TACHYCARDIA
- AFIB (Loss of Atrial Kick)



At end Diastole the LV; LA and Pulmonary Veins Effectively form a common chamber. Pressure Gets transmitted to the pulmonary capillaries. (Up To Date)



DYSPNEA ON EXERTION MOST COMMON SYMPTOM IN HFpEF

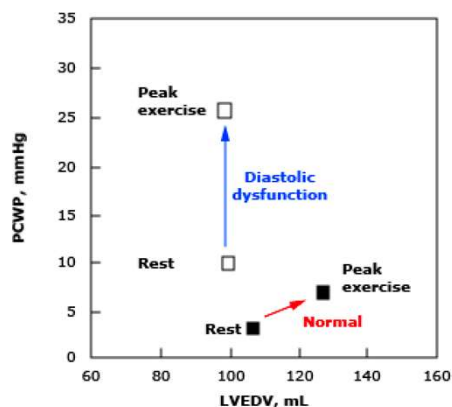
- Decreased Diastolic Filling time
- Decreased Early Left Ventricular Filling
- Increased Left Ventricular Stiffness
- Increased Left Ventricular; Left Atrial and pulmonary vein pressures

❖ Right Heart Cath:

- PCWP > 15 at rest
- PCWP > 25 with Exercise

Kitzman DW, Higginbotham MB, Cobb FR, et al,
J. Am. Coll. Cardiol. 1991; 17; 1065
(As referenced in "Up to Date")

Pulmonary Capillary Wedge Pressure increases dramatically
In patients with HFpEF during Exercise



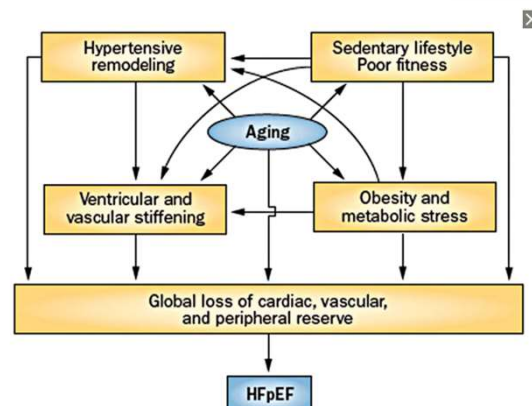
OTHER CHARACTERISTICS OF HFpEF

- Pulmonary Hypertension
 - 70 to 80% of HFpEF patients have Pulmonary HTN
- Right Ventricular Systolic Dysfunction
 - 20-30% develop Right Ventricular Dysfunction
- Atrial Fibrillation
 - AFIB is present at some point in 2/3 of patients
- Decreased vasodilator response to Exercise
- Chronotropic Incompetence (Inability to raise HR with Exercise)



CO-MORBID CONDITIONS

- AGE >60
 - Disease of Elderly
- HTN
- OBESITY
- DIABETES
- CAD (50% prevalence)
- KIDNEY DISEASE
- SLEEP APNEA
- SEDENTARY LIFESTYLE

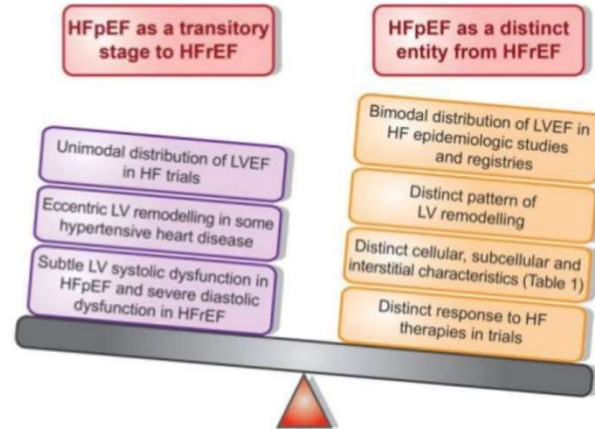


Interaction of factors resulting in symptomatic HFpEF

The interaction between risk factors, cardiac aging and loss of cardiovascular reserve, which results in the development of symptomatic HFpEF. Based on Nature Reviews Cardiology. 2014;11:507. Used with permission.



Arguments for heart failure with preserved ejection fraction as a transitory stage to heart failure with reduced ejection fraction (left) vs. heart failure with preserved ejection fraction as a distinct entity from heart failure with reduced ejection fraction (right).



Michel Komajda, and Carolyn S.P. Lam Eur Heart J
2014;35:1022-1032

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European
Heart Journal



	Clinical Variable	Values	Points
H₂	H heavy	Body mass index > 30 kg/m ²	2
	H ypertensive	2 or more antihypertensive medicines	1
F	Atrial F ibrillation	Paroxysmal or Persistent	3
P	P ulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	E lder	Age > 60 years	1
F	F illing Pressure	Doppler Echocardiographic E/e' > 9	1
H₂FPEF score			Sum (0-9)
<div> Total Points <div>0123456789</div> </div>			
<div> Probability of HFpEF <div>0.20.30.40.50.60.70.80.90.95</div> </div>			

Borlaug, Reddy, et al



USING H₂FPEF SCORE to Diagnose HFpEF

Low H₂FPEF Score (0 to 1): < 25% probability of HFpEF

Intermediate H₂FPEF Score (2 to 5): 40 – 80% probability of HFpEF

- BNP > 100 pg/ml, OR
- N-terminal proBNP > 300 pg/ml, AND
- NO SIGNIFICANT LUNG DISEASE PRESENT
- ❖ Otherwise: Consider Right Heart Catheterization
(PCWP > 15mm at rest or >25 mm with exercise)

High H₂FPEF Score (6 or greater): > 90% probability of HFpEF

(Reddy YNV, et al. A Simple, Evidence-Based Approach to Help Guide Diagnosis of Heart Failure With Preserved Ejection Fraction. Circulation 2018; 138:861)



NORMAL BNP Does Not Necessarily Exclude HFpEF

(BNP < 100 pg/ml or N-Terminal Pro BNP < 300 pg/ml)

- BNP levels are typically LOWER in HFpEF than in HFrEF.
- BNP is more reflective of Left Ventricular Wall Stress than Filling Pressures. Wall Stress is typically less in HFpEF due to Hypertrophy.
- Obesity (Common in HFpEF) is associated with decreased levels of BNP
- In one study: 30% of patients with HFpEF had BNP < 100 pg/ml

(Oktay A and Shah S. Diagnosis and Management of Heart Failure with Preserved Ejection Fraction. Curr Cardiol Rev. 2015 Feb; 11(1): 42-52)



MUST EXCLUDE THESE DIAGNOSES

CARDIOMYOPATHIES WITH PRESERVED LVEF

- Restrictive Cardiomyopathy
 - Amyloid
 - Hemochromatosis
- Hypertrophic Cardiomyopathy

VALVULAR HEART DISEASE

- Mitral Stenosis or Regurgitation
- Aortic Stenosis or Regurgitation

RIGHT HEART FAILURE

- Primary Pulmonary Hypertension
- Right Ventricular Infarction
- Arrhythmic Right Ventricular Cardiomyopathy

PERICARDIAL DISEASE

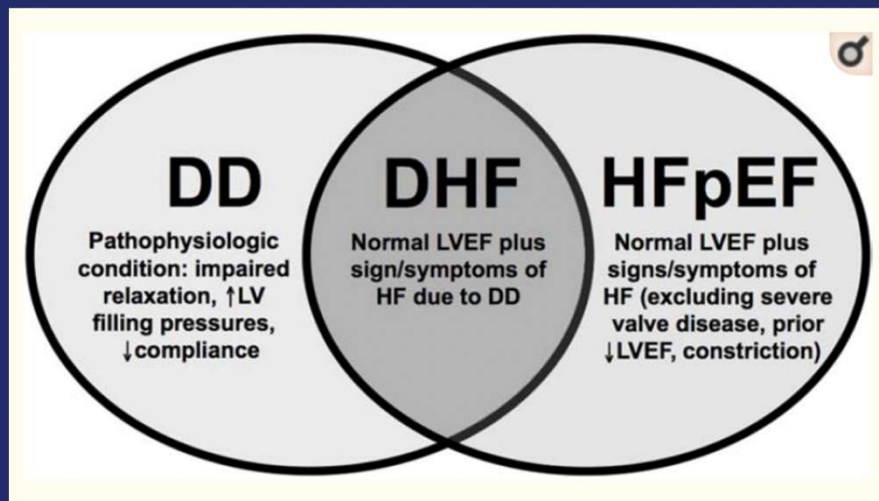
- Constrictive Pericarditis

OBSTRUCTIVE LESIONS

- Atrial Myxoma
- Pulmonary Vein Stenosis

HIGH OUTPUT FAILURE

TRANSIENT LV SYSTOLIC DYSFUNCTION

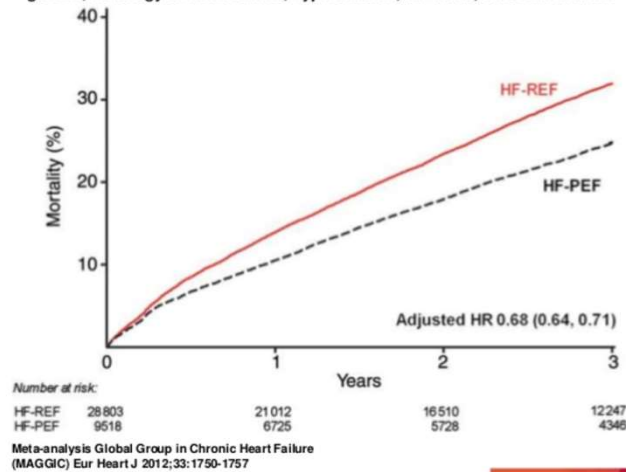


Heart Failure + LVEF > 50% + Diastolic Dysfunction
MINUS Everything Else = HFpEF



PROGNOSIS

Mortality for patients with HF-PEF (heart failure with preserved left ventricular ejection fraction) and HF-REF (heart failure with low left ventricular ejection fraction), adjusted for age, gender, aetiology of heart failure, hypertension, diabetes, atrial fibrillation.

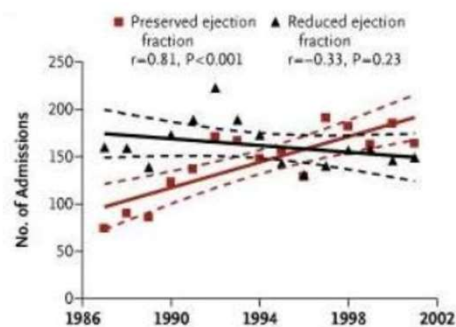


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European Heart Journal



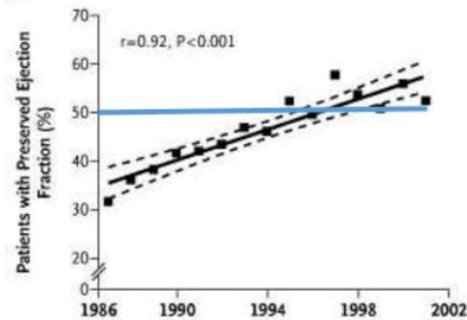
Admissions for HFPEF vs HFREF



Owan TE et al. N Engl J Med 2006;355:251-259.



Increasing proportion of HFpEF



Owan TE et al. N Engl J Med 2006;355:251-259.



TREATMENT OF HFpEF

- CONTROL HYPERTENSION
 - Guideline directed management
- DIURETICS (Judiciously) and SODIUM RESTRICTION
 - Symptom guided management
 - Avoid Over Diuresis (Excess pre load reduction may led to hypotension)
- TREAT CAD / ISCHEMIA
 - High Prevalance of CAD. Ischemia worsens Diastolic Dysfunction
- TREAT ATRIAL FIBRILLATION
 - Control or prevent AFIB. HR control if AFIB persists
- TREAT COMORBID CONDITIONS
 - DM; OBESITY; SLEEP APNEA



ALDOSTERONE INHIBITORS

The “TOPCAT” TRIAL

- 3445 patients with HFpEF followed for 3.3 years (Spironolactone vs Placebo)
- Mild reduction in event rate (18.6% vs 20.4%)
- SUBGROUP ANALYSIS:
 - Patients with BNP > 100pg/ml or NT Pro BNP > 360 pg/ml
 - Combined Endpoint Reduced (15.9% vs 23.6%)
 - Hospitalizations Reduced (11.2% vs 16.9%)
 - Mortality Reduced (8.2% vs 12%)

ACC / AHA Heart Failure Guidelines:

Recommend Aldosterone or Eplerenone for patients with HFpEF AND elevated BNP
Who have adequate Renal Function with close follow up of Potassium.

(PITT B, Pfeffer MA, et al. Spironolactone for Heart Failure With Preserved Ejection Fraction.
N Engl J Med 2014; 370: 1383)



CARDIAC REHAB/EXERCISE TRAINING

- Several Clinical Trials have shown that Exercise Training may improve exercise capacity and quality of life in patients with HFpEF
- Exercise Training may improve Vascular Vasodilator Response to Exercise
- Exercise Training may help with Weight Loss

(Pandey A, et al. Exercise Training in Patients With Heart Failure and Preserved Ejection Fraction:
Meta-Analysis of Randomized Control Trials. Circ Heart Fail. 2015; 8: 33.)



THINGS THAT DON'T HELP

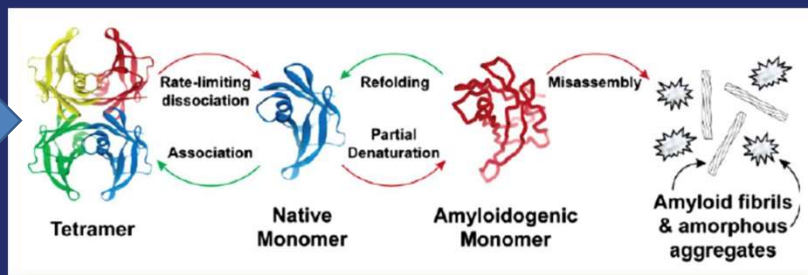
- BETA BLOCKERS (No Mortality Benefit)
 - Use as needed for HTN; or CAD
- ACE INHIBITORS (No Mortality Benefit)
 - Use for HTN if renal function good
- ANGIOTENSIN RECEPTOR BLOCKERS
 - "CHARM" and "PRESERVE" Trials: No Benefit
- SILDENAFIL (PDE-5 Inhibitors) (For Pulmonary HTN)
 - "RELAX" Trial showed No Benefit
- DIGOXIN
 - No Benefit
- NITRATES
 - No Benefit
- ARNI (Angiotensin Receptor Neprilysin Inhibitors)
 - INVESTIGATIONAL

(Yancy, et al. 2013 ACCF/AHA Heart Failure Guideline)



Transthyretin (PreAlbumin) Break Down

"TAFAMIDIS"
Binds to Tetramer
And Stabilizes it



- Tetramer Protein made in the Liver which binds to Thyroxine
- Tetramer becomes unstable and breaks in to Monomers that dissolve in to "fibrils"
- Amyloid Fibrils deposit in Cardiac Tissue and Nerve Tissue causing Amyloidosis
- Hereditary Type is due to genetic defect coding for Tetramer
- Wild Type is due to OLD AGE causing defective Tetramer Formation (Most Common Type)



Transthyretin Amyloid Cardiomyopathy (ATTR-CM)

- Progressive Cardiac Amyloidosis that causes Restrictive Cardiomyopathy
- Mimics HFpEF Characteristics
- Frequently underdiagnosed or missed
- Up to 13% of Cases diagnosed as HFpEF are caused by TTR Amyloidosis
- Autopsy studies show 25% of patients over 80 have Amyloid Deposits in their heart
- New treatment available with “TAFAMIDIS” if started early enough

(Witteles R, et al. Screening for Transthyretin Amyloid Cardiomyopathy in Everyday Practice
J Am Coll Cardiol HF 2019; 7: 709-16)



Characteristics of Transthyretin Amyloid Cardiomyopathy

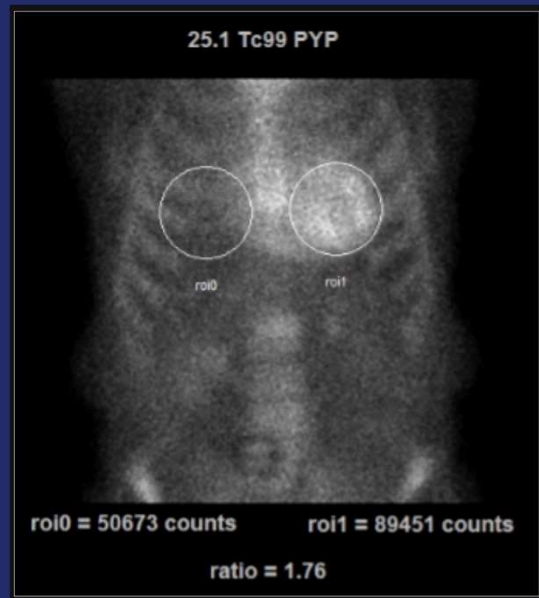
- OLD AGE: M > 65 F > 70
- ECHO (Looks Like HFpEF)
 - LVH. Wall thickness > 14 mm
 - Normal LV volume and LVEF > 50%
 - Thickening of Valves and Atrial Septum
 - Dilated Atria
- ECG
 - Low Voltage QRS (Despite LVH on ECHO)
 - AV Block and Conduction Disease
- POLY NEUROPATHY
 - Bilateral Carpal Tunnel Syndrome
 - Autonomic Neuropathy (Orthostatic Hypotension)



^{99m}Tc Technetium-Pyrophosphate Imaging Transthyretin Cardiac Amyloidosis

- Measure Activity in Region of Interest of HEART
- Measure Activity in Region of Interest of LUNG
- RATIO of HEART to LUNG > 1.5
Diagnostic for TTR Amyloid

Falk RH, et al. How to Image Cardiac Amyloidosis
Circ Cardiovasc Imaging 2014; 7:552-62.



THE END

Thank You for Your Attention

