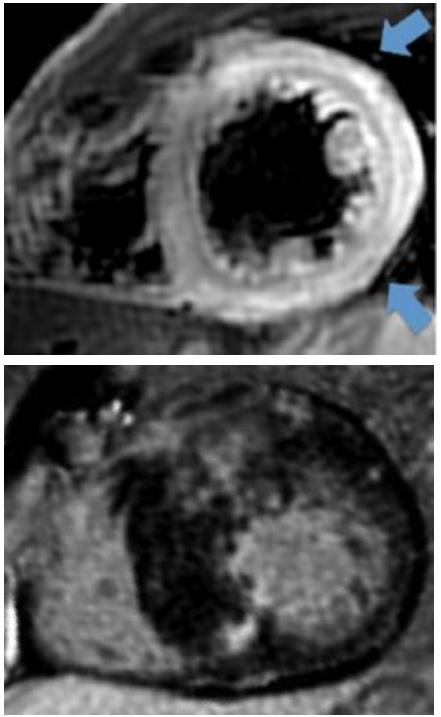
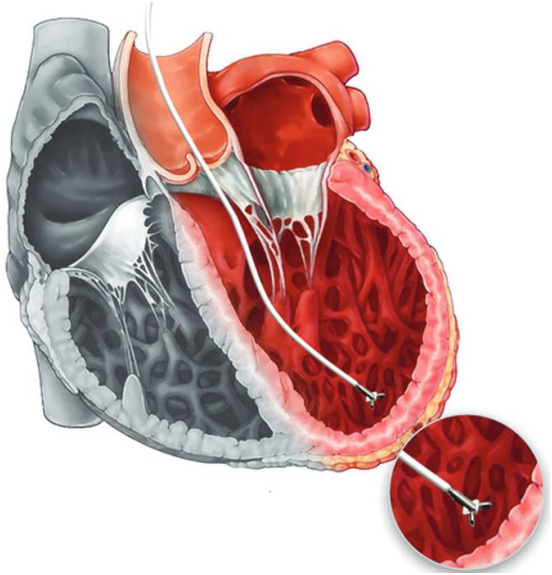
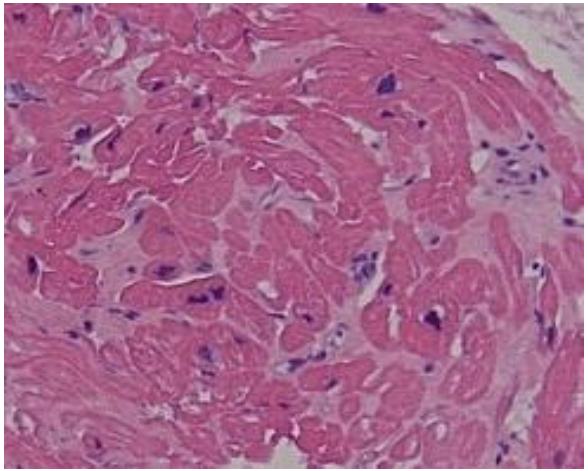
“Hartbiopten bij hartalen patienten”

Continuing Nursing Education; NVHVV; Scholing 16 april 2024
“Interventiecardiologie en Hartfalen, een keten- en combinatie van zorg”





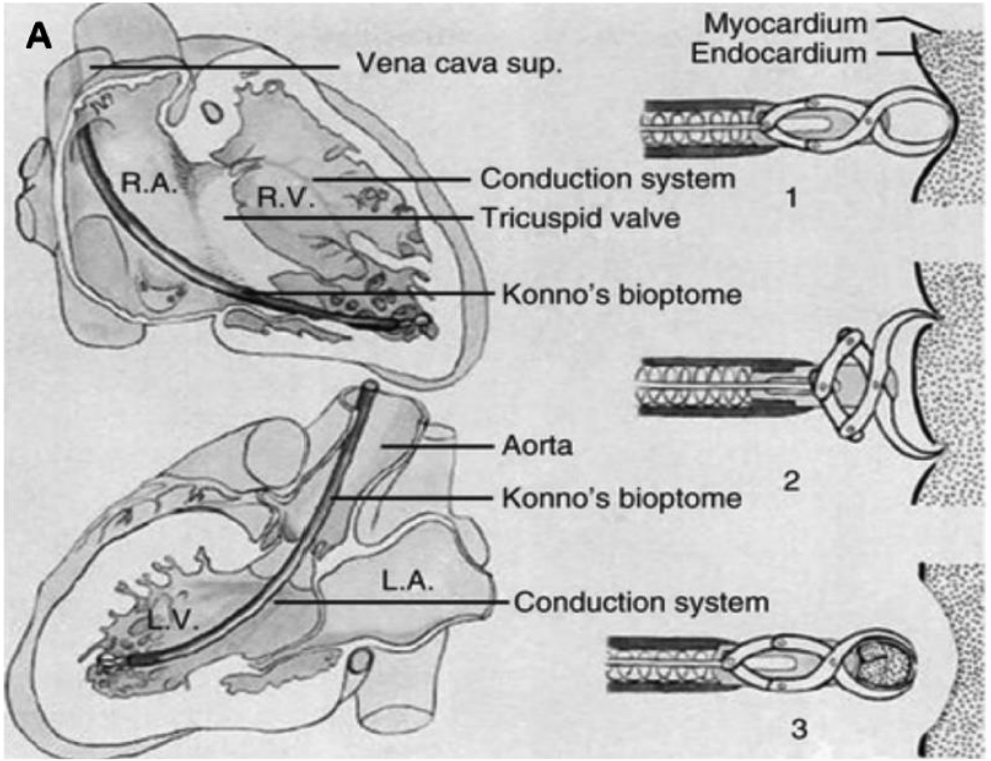


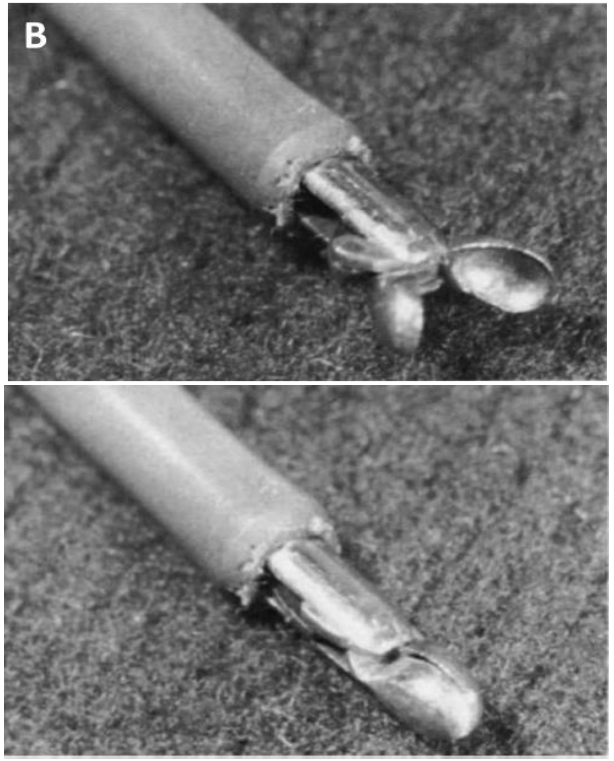
Loek van Heerebeek, Cardiologist, MD, PhD, MSc, FESC

Disclosures

(Potentiële) belangenverstrengeling	Geen / Zie hieronder
Voor bijeenkomst mogelijk relevante relaties met bedrijven	Bedrijfsnamen
Sponsoring of onderzoeksgeld	Astrazeneca, Bayer, Novartis, Pfizer, Boehringer Ingelheim
Honorarium of andere (financiële) vergoeding	Astrazeneca, Bayer, Boehringer Ingelheim, Novartis, Vifor
Aandeelhouder	-
Andere relatie, namelijk …	-

Endomyocardial biopsy





Konno S, Sakakibara S. Dis Chest 1963;44:345

Endomyocardial biopsy - Guidelines

European Heart Journal (2007) **28**, 3076–3093
doi:10.1093/eurheartj/ehm456

AHA/ACCF/ESC scientific statement

The role of endomyocardial biopsy in the management of cardiovascular disease

A Scientific Statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology
Endorsed by the Heart Failure Society of America and the Heart Failure Association of the European Society of Cardiology

INDICATIONS FOR ENDOMYOCARDIAL BIOPSY

- HTx rejection surveillance
- Myocarditis
- Cardiomyopathies
- Drug-related cardiotoxicity
- Amyloidosis
- Infiltrative and storage disorders
- Cardiac tumours

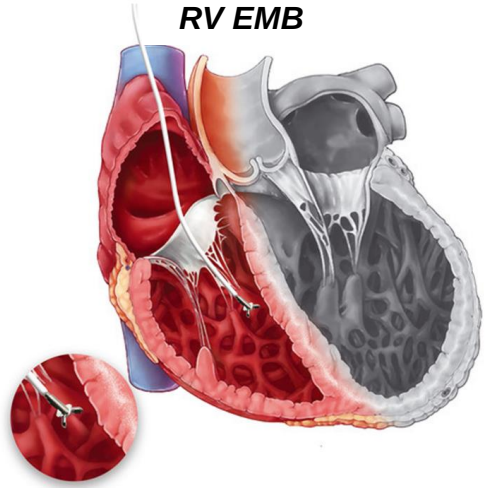
European Journal of Heart Failure (2021)
doi:10.1002/ejhf.2190

POSITION PAPER

Heart Failure Association of the ESC, Heart Failure Society of America and Japanese Heart Failure Society Position statement on endomyocardial biopsy

Endomyocardial biopsy – Access and procedural guidance

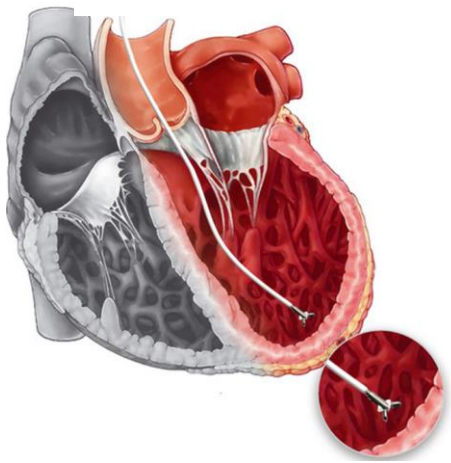
RV EMB



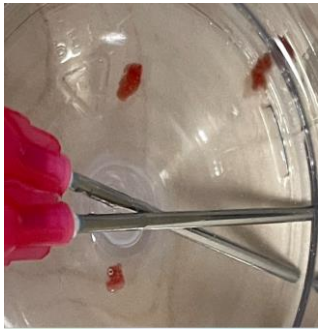
Venous access route
(i.e. femoral, brachial, jugular)

>

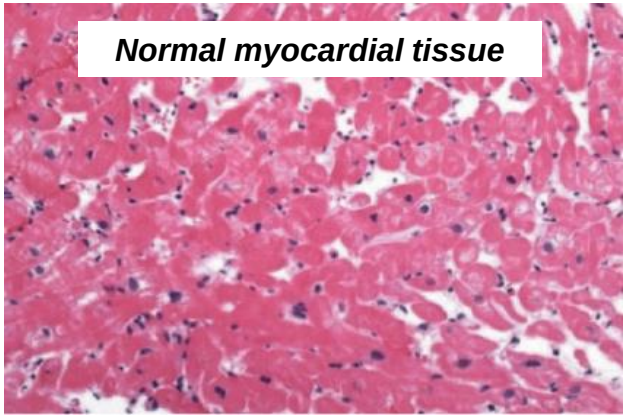
LV EMB



Arterial access route
(i.e. femoral, radial)



≥ 5 samples



Procedural guidance - Cathlab

***Heart rhythm**
***Blood pressure**
***Oxygen monitoring**
***INR ≤1.5-1.8**
***Aspirin**
***Platelet count >50x10^9/L**

Seferovic PM et al. Eur J Heart Fail 2021

Endomyocardial biopsy – Complications and contraindications

Complications

Major complications

Death (0–0.07%)
Cardiac perforation/haemopericardium/tamponade (0–6.9%)
Pneumothorax/air embolism (0–0.8%)
Thromboembolism (0–0.32%)
Valvular trauma (0.02–1.1%)
Severe arrhythmias/atrioventricular block (0–11%)

Minor complications

Chest pain (transient) (0–1.8%)
Deep vein thrombosis (0.23–3.8%)
Puncture site haematoma/nerve palsy (0–0.64%)
Hypotension/vaso-vagal syncope (0–4.3%)
Arterial trauma/vascular damage/fistulae (0.32–2.8%)

Contraindications

Absolute contraindications

- Intracardiac thrombus
- Ventricular aneurysm
- Severe tricuspid, pulmonary or aortic stenosis
- Aortic and tricuspid mechanical prosthesis

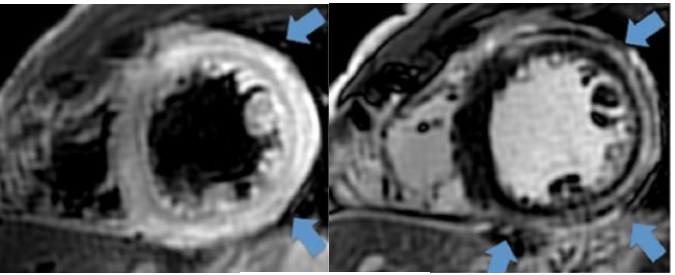
Relative contraindications

- Active bleeding
- Infection and fever
- Infective endocarditis
- Pregnancy
- Recent cerebrovascular accident/TIA (<1 month)
- Uncontrolled hypertension
- Thin ventricular wall (for the biopsy of the myocardium)
- Coagulopathy
- Contrast media hypersensitivity[a]
- Uncooperative patient

Seferovic PM et al. Eur J Heart Fail 2021, May 19

Endomyocardial biopsy – Indications

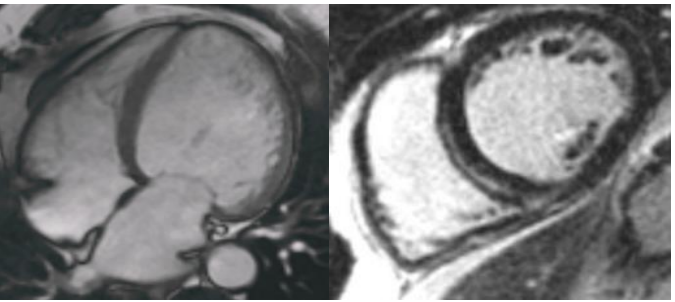
Myocarditis



****Fulminant or acute myocarditis with acute HF/LV dysfx and/or rhythm disorders***

****Suspected myocarditis in HD stable pts***

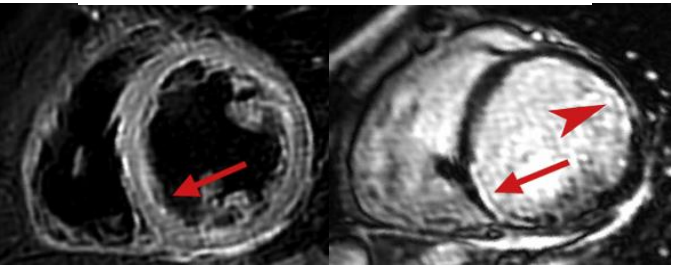
DCM



****DCM recent onset with moderate/severe LV dysfx and refractory to therapy***

****Suspected myocarditis in HD stable pts***

ICI-induced myocarditis

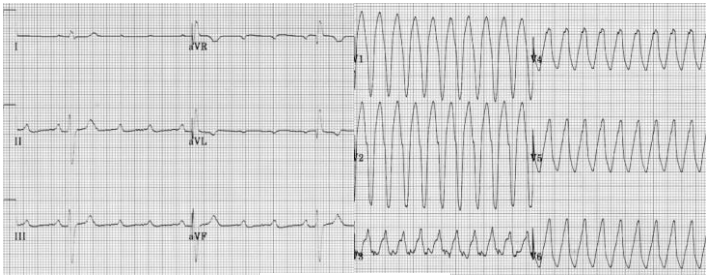


****Suspected Immune Checkpoint Inhibitor mediated cardiotoxicity with LV dysfx and/or arrhythmias within 4 cycles of therapy***

Seferovic PM et al. Eur J Heart Fail 2021, May 19

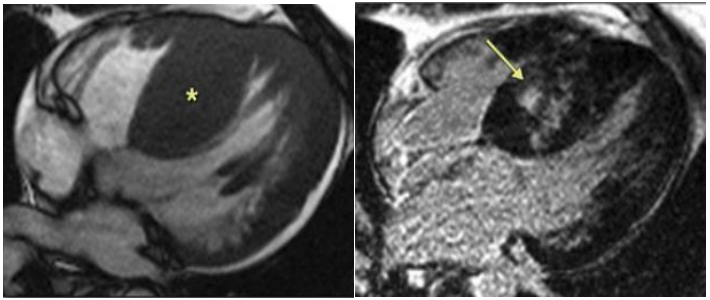
Endomyocardial biopsy – Indications

Conduction disorders/VA eci



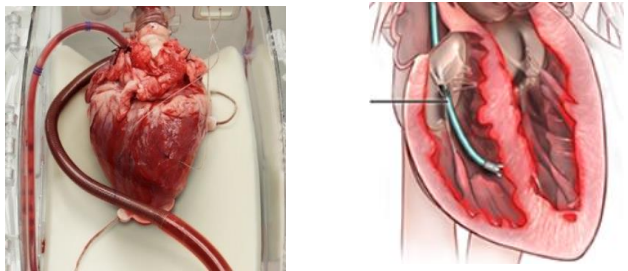
****High degree AVB or VA eci refractory to treatment without obvious cardiac disease or minimal structural abnormalities***

HCM



****Unexplained restrictive or hypertrophic CMP (i.e. Amyloidosis, sarcoidosis, hemochromatosis, glycogen storage disease, Fabry)***

Cardiac transplant surveillance



****Routine surveillance after heart Tx***

Seferovic PM et al. Eur J Heart Fail 2021, May 19

EMB to investigate underlying etiology in unexplained HF

Pts admitted with unexplained HF who underwent EMB (n=851) at Johns Hopkins (‘00-’09). Role of EMB in according to clinical scenario (ESC ‘07 EMB guideline) in establishing diagnosis of underlying etiology and effect on therapeutic strategy.

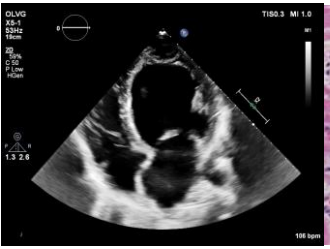
Table 2. Number and Percentage of Biopsies Performed for 14 Clinical Scenarios

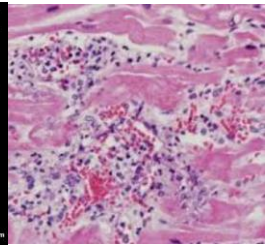
Scenarios	Clinical Scenarios (Class of Recommendation, Level of Evidence)	No.	% of Total
1	New-onset heart failure of <2 wk duration associated with a normal-sized or dilated left ventricle and hemodynamic compromise (I, B)	109	12.8
2	New-onset heart failure of 2 wk to 3 mo duration associated with a dilated left ventricle and new ventricular arrhythmias, second- or third-degree heart block, or failure to respond to usual care within 1 to 2 wk (I, B)	29	3.4
3	Heart failure of >3 mo duration associated with a dilated left ventricle and new ventricular arrhythmias, second- or third-degree heart block, or failure to respond to usual care within 1 to 2 wk (IIa, C)	26	3.1
4	Heart failure associated with a DCM of any duration associated with suspected allergic reaction and/or eosinophilia (IIa, C)	9	1.1
5	Heart failure associated with suspected anthracycline cardiomyopathy (IIa, C)	24	2.8
6	Heart failure associated with unexplained restrictive cardiomyopathy (IIa, C)	286	33.6
7	Suspected cardiac tumors (IIa, C)	4	0.5
8	Unexplained cardiomyopathy in children (IIa, C)	29	3.4
9	New-onset heart failure of 2 wk to 3 mo duration associated with a dilated left ventricle, without new ventricular arrhythmias or second- or third-degree heart block, which responds to usual care within 1 to 2 wk (IIb, B)	100	11.7
10	Heart failure of >3 mo duration associated with a dilated left ventricle, without new ventricular arrhythmias or second- or third-degree heart block, which responds to usual care within 1 to 2 wk (IIb, C)	134	15.7
11	Heart failure associated with unexplained HCM (IIb, C)	28	3.3
12	Suspected ARVD/C (IIb, C)	62	7.3
13	Unexplained ventricular arrhythmias (IIb, C)	8	0.9
14	Unexplained atrial fibrillation (III, C)	3	0.4

ARVD/C indicates arrhythmogenic right ventricular dysplasia/cardiomyopathy; and DCM, dilated cardiomyopathy.

Bennett MK et al. Circ Res 2013;6:676; Cooper LT et al. JACC 2007;50:1914

EMB to investigate underlying etiology in unexplained HF

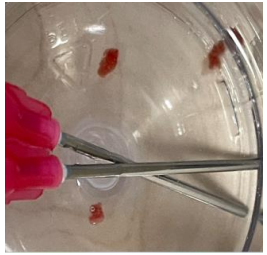




EMB provided diagnosis in:

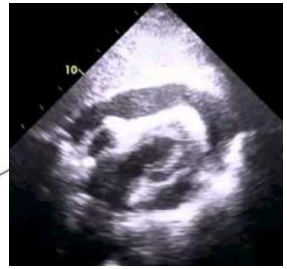
39%

(mostly myocarditis)



Mean biopsies/pt:

5.6



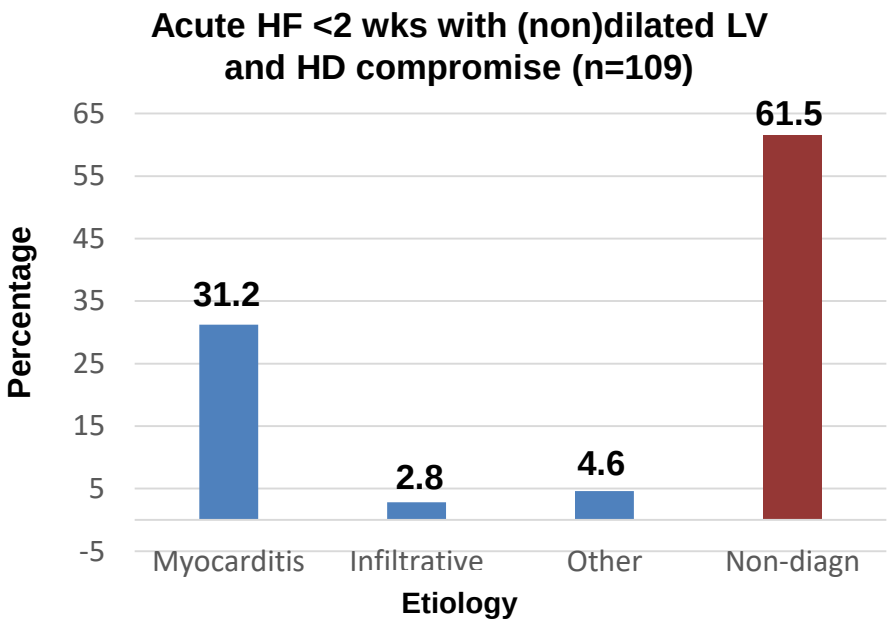
Complications

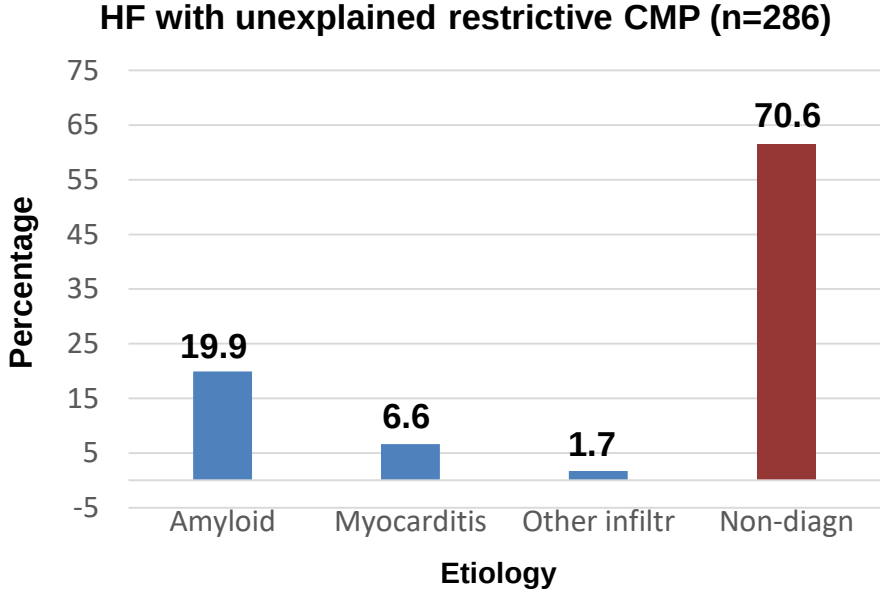
EMB induced change of therapy in:

16 (1.8%)

Of which 8 PE/tamponade

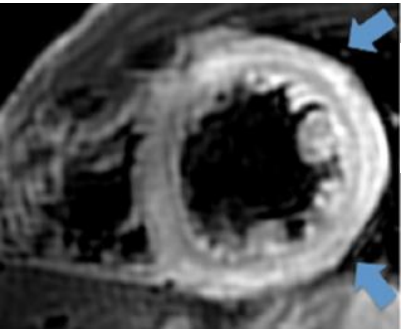
30%





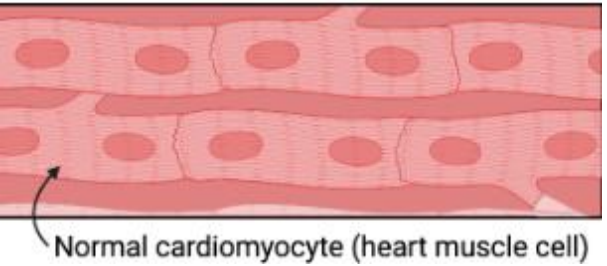
Bennett MK et al. Circ Res 2013;6:676

Myocarditis

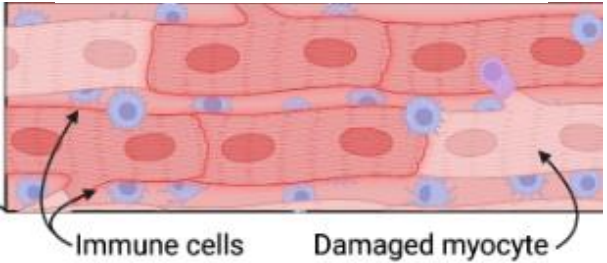


Myocarditis: any heightened humoral or cellular immune response in the heart with clinical presentation ranging from chest pain or mild dyspnea to acute cardiogenic shock. Up to 20% of myocarditis pts may subsequently develop chronic inflammatory dilated CMP

Normal myocardium



Myocarditis – inflammation

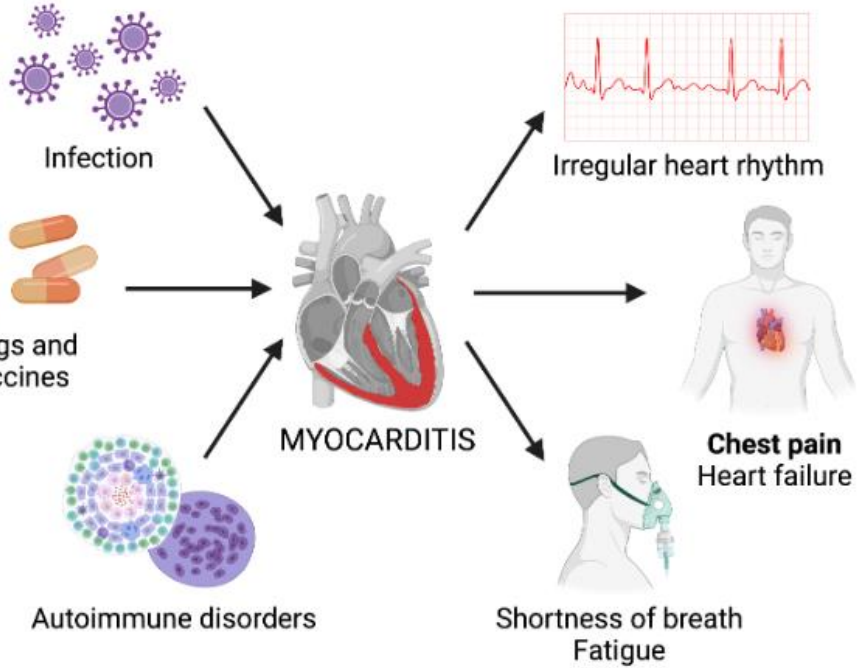


CAUSES

Infections
- Viruses
- Bacteria
- Parasites

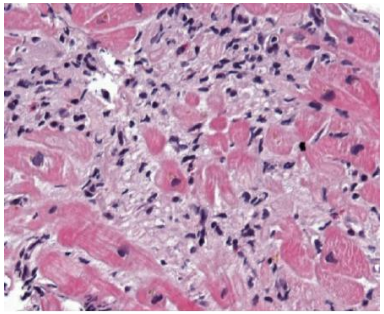
Drugs & vaccines
- Cancer therapies (e.g. immune checkpoint inhibitors)
- Clozapine
- COVID-19, smallpox vaccine

Autoimmune diseases
- Lupus
- Sarcoidosis
- Organ-specific (e.g. IBS)



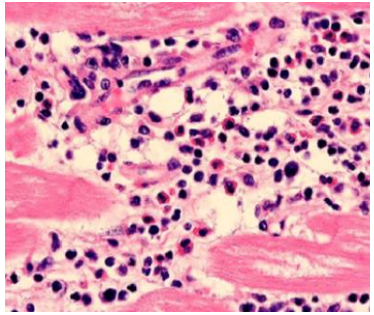
Endomyocardial biopsy – Myocarditis

Lymfocytic myocard.



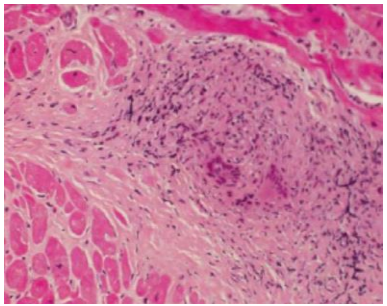
Viral infection
Autoimmunity
Drug-toxicity

Eosinophilic myocard.



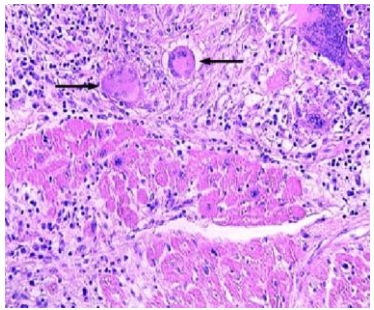
Eosinophilic infiltrate + periperhal blood eosinophilia

Granulomatous myocard.



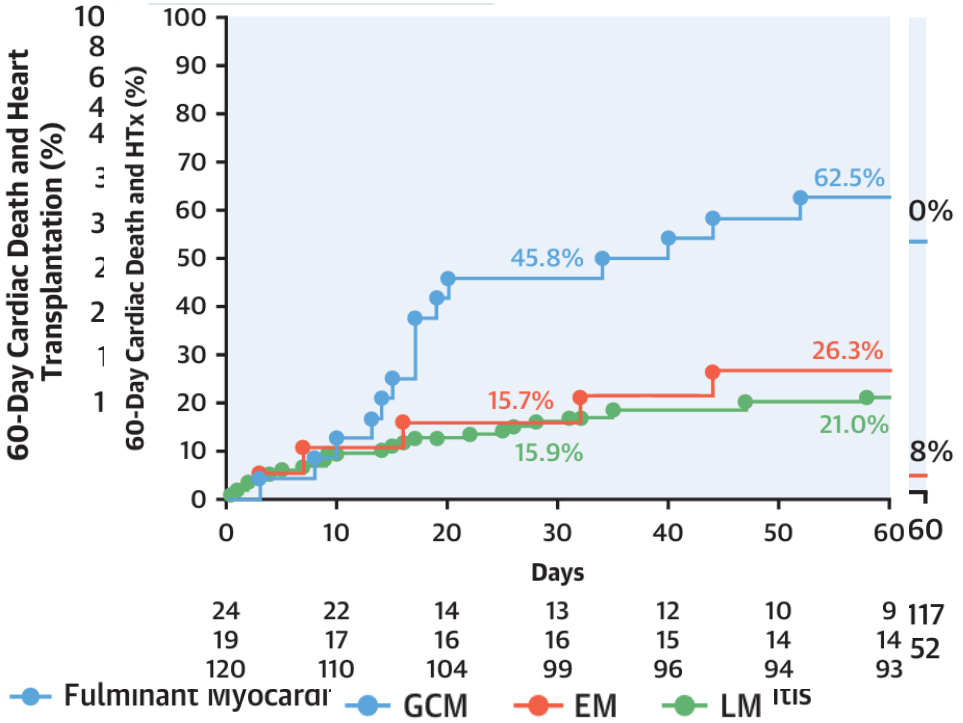
Sarcoidosis

Giant cell myocard.



Rare (1% of acute myocarditis); fulminant

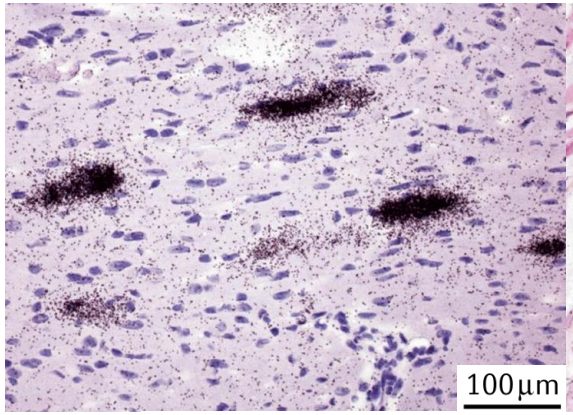
Pts with histologically proven acute myocarditis (n=220) presenting with LV systolic dysfx. Prognosis in pts with fulminant (n=165) vs non-fulminant (n=55) myocarditis →Endpoint: cardiac death or heart Tx



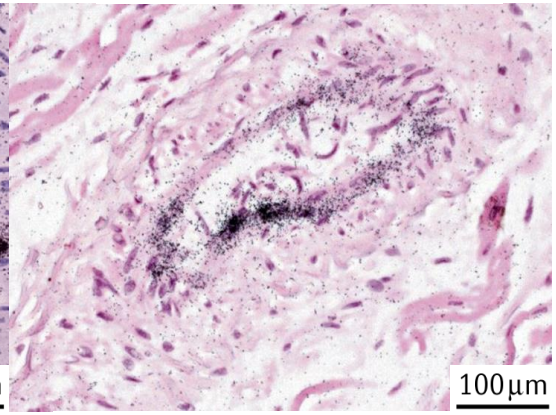
Ammirati E et al. JACC 2019;74:299

Viral myocarditis

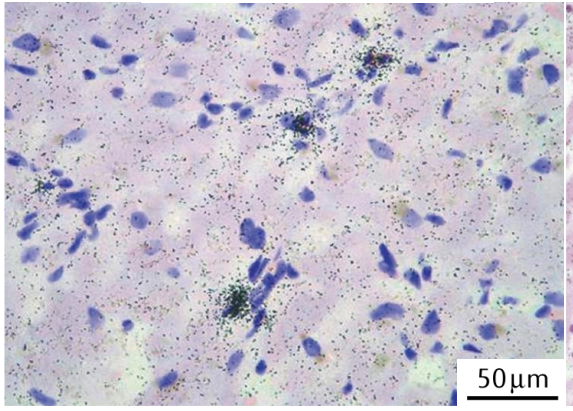
Enterovirus RNA



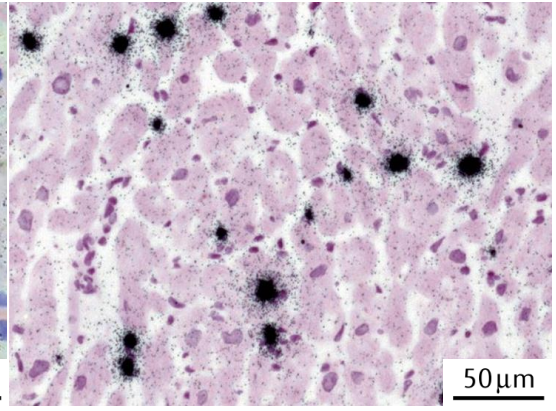
Parvovirus B19 DNA



HHV 6 DNA



Epstein Barr virus RNA



ssDNA

Parvovirus B19

dsDNA

Adenovirus
CMV
EBV
HHV 1&2
HBV
HHV-6
Varicella

+ssRNA

Coxsackie
Dengue
HHV 1&2
HAV
HCV
HIV
Polio
Rubella
SARS-CoV2
Zika

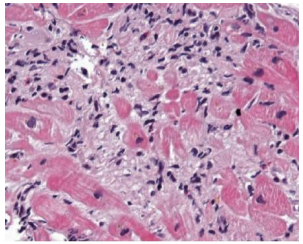
-ssRNA

Ebola
Hanta
Parainfluenza
Influenza A&B
Mumps
RSV

Tschope C et al. Nat Rev Cardiol 2021;18:169

Badrinath A et al. Front Microbiol 2022;13:1030440

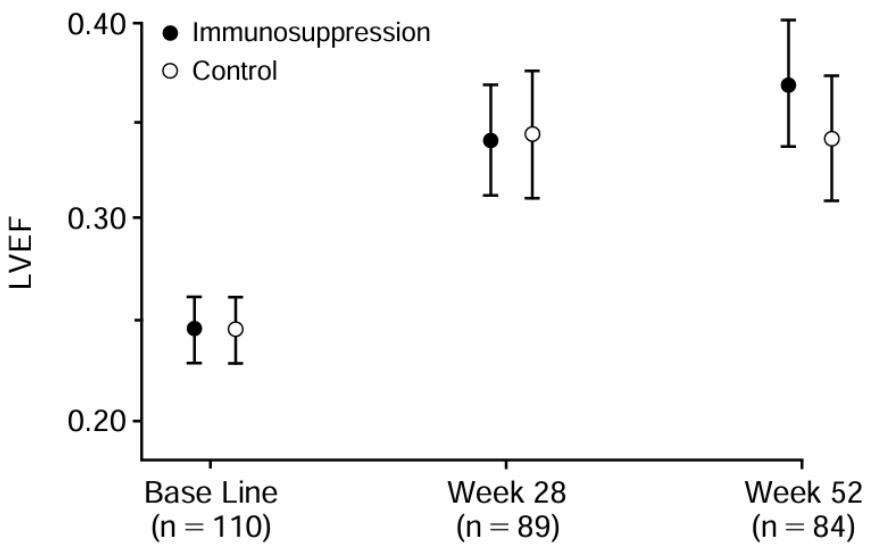
Viral myocarditis

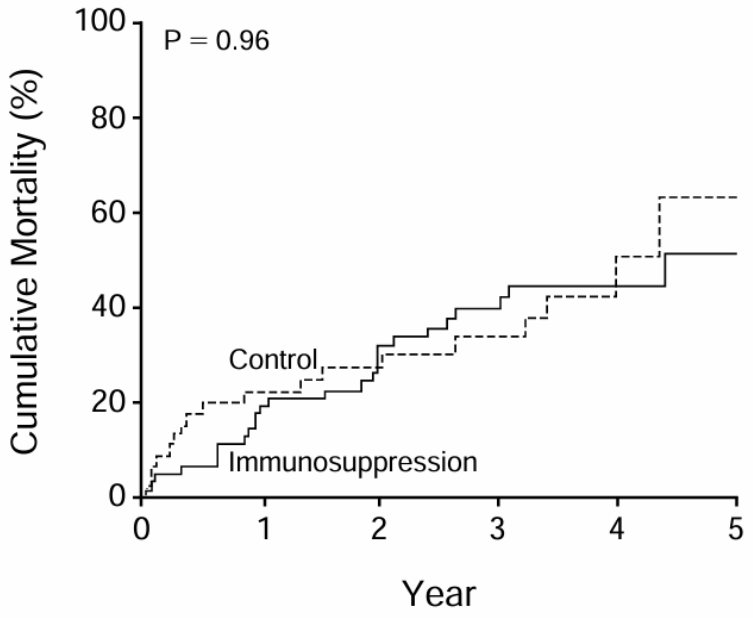
Stage	***Acute***	***Subacute***	***Chronic***
Infection			
	***Active viral replication *Rapid innate immune system response**	***Infiltration of inflamm cells followed by viral clearance *Autoimmune-mediated cardiac injury**	***Persistent viral infection *Potential low level viral replication *Ongoing immune response**
Symptoms			
	***Chest pain;dyspnea; HF *Elevated Troponins, inflammation**	***Prolonged (>1 mth) CV symptoms, such as chestpain, dyspnea, palpitations, etc.**	***Longterm symptoms *Heart failure**
Outcomes			
	***Myocyte necrosis *Potential resolution if viral clearance is achieved**	***Myocyte inflammation *Continued myocyte damage/necrosis**	***Low grade inflammation *CM damage/remodeling *Potential development of DCM**

Badrinath A et al. Front Microbiol 2022;13:1030440

Immunosuppressive therapy in general myocarditis

Pts with histological diagnosis of myocarditis (n=111) and LVEF <45% randomized to usual care (UC) therapy vs immunosuppression (prednison with either cyclosporine or azathioprine) on top of UC for 24 wks. →Prim EP: change in LVEF at 28 wks





Immuno-suppression	64	49	37	23	12	0
Control	47	32	23	16	6	0

Mason JW et al. NEJM 1995;333:269

Endomyocardial biopsy – Myocarditis

Controversial if there is benefit of immunosuppressive therapy in myocarditis
→EMB study with serial EMB procedures to assess effect of immunosuppressive therapy in lymfocytic myocarditis

652 pts with EMB

↓

112 with lymfocytic myocarditis

↓

41 with refractory HF despite conventional Rx

↓

6 mths treatment

Prednisone + Azathioprine

EMB at 1 + 6 mths

21 responded with improved LVEF

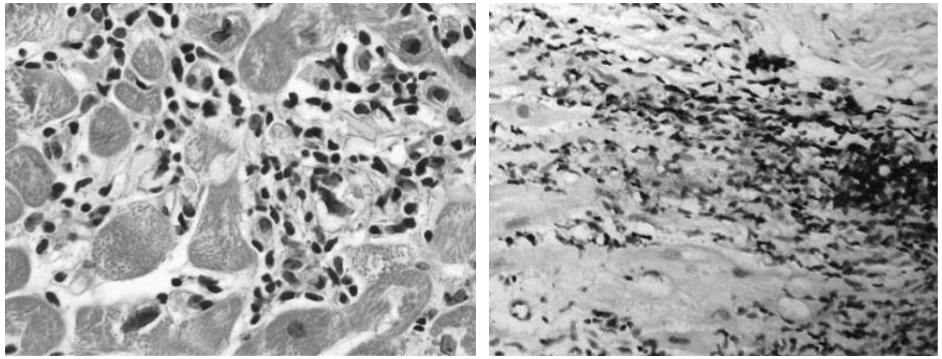
20 no response with progression to DCM

3 cardiac Tx and 5 died

EMB analysis

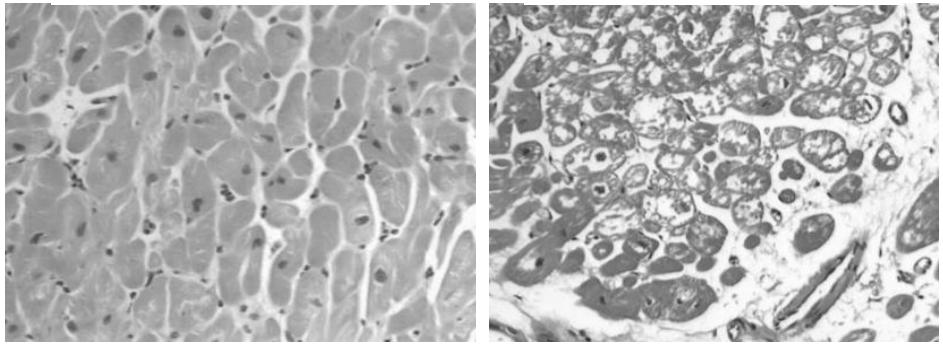
EMB analysis: Responders had cardiac auto-antibodies and absence of viral genome

Acute lymfocytic myocarditis



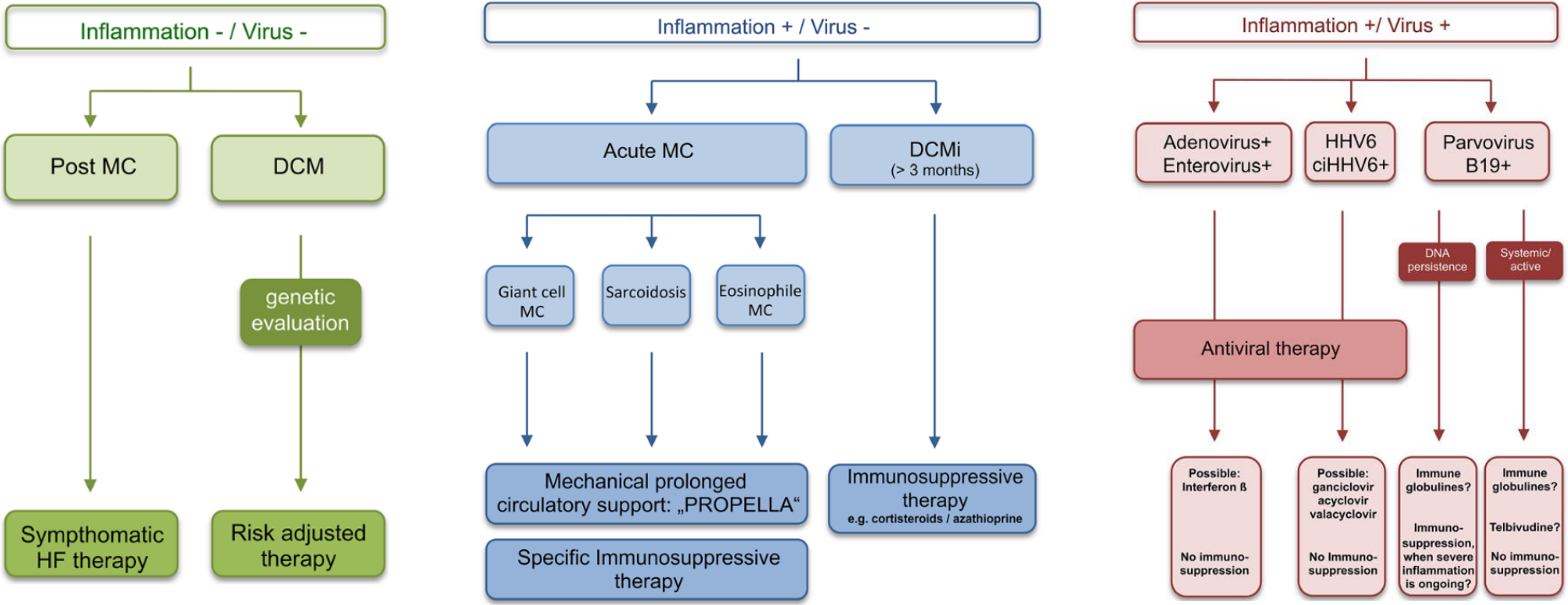
Healed at FUP EMB

DCM at FUP EMB



Frustaci A et al. Circulation 2003;107:857

Potential therapeutic options Based on Endomyocardial Biopsy results from patients with suspected Complicated Myocarditis

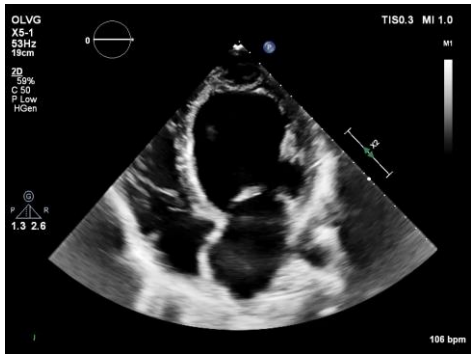


Tschope C et al. Nat Rev Cardiol 2021;18:169

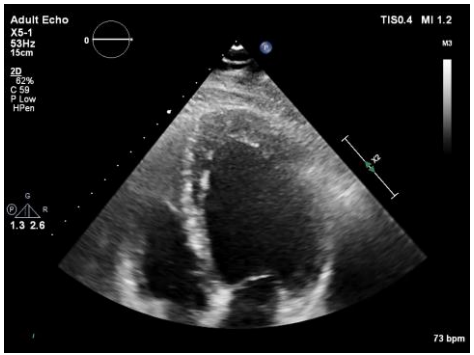
Heart Failure (HF) phenotypes

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF ≤40%	LVEF 41–49%[b]	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides[c]

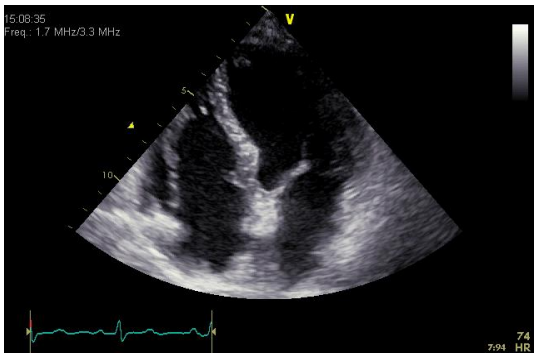
HFrEF



HFmrEF



HFpEF



Management of patients with HFrEF

- ACE-I/ARNI[a]
- Beta-blocker
- MRA
- Dapagliflozin/Empagliflozin
- Loop diuretic for fluid retention

(Class I)

Ivabradine (Class IIa)

Vericiguat (Class IIb) | **Digoxin (Class IIb)** | **Hydralazine/ISDN (Class IIb)**

Management of patients with HFmrEF

Diuretics for fluid retention (Class I)

Dapagliflozin/ Empagliflozin (Class I)

ACEI/ARNI/ARB (Class IIb) | MRA (Class IIb) | Beta-blocker (Class IIb)

Management of patients with HFpEF

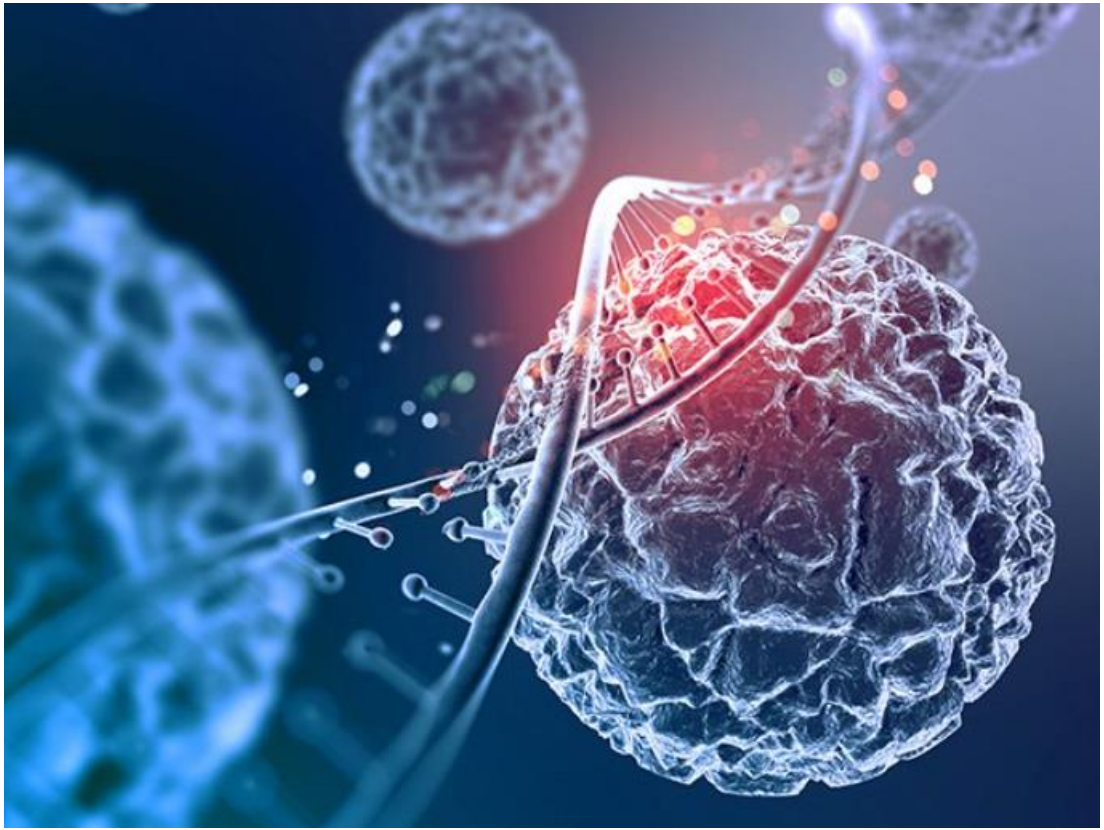
Diuretics for fluid retention (Class I)

Treatment for aetiology, CV and non-CV comorbodities (Class I)

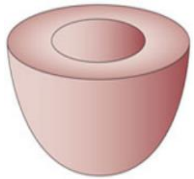
Dapagliflozin/ Empagliflozin (Class I)

ESC guidelines Heart Failure Eur Heart J 2021

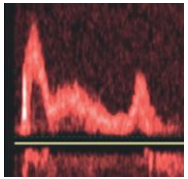
Pathophysiology



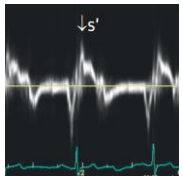
HFpEF – (much) more than just LV diastolic and cardiac dysfunction



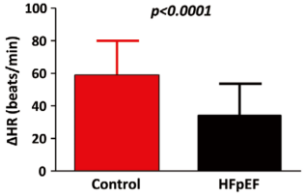
Concentric LVH remodeling



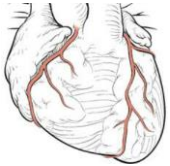
Diastol dysf



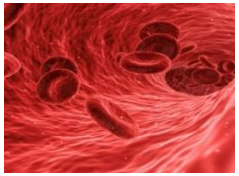
Systol dysf



Chronotropic incomp

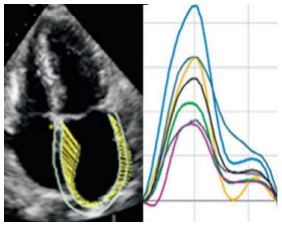


MVD



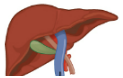
Endothelial dysfx

Comorbidities



LA dysfunction

RAAS



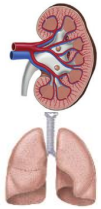
Angiotensinogen

Renin

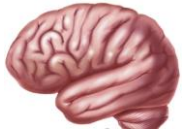
Ang I

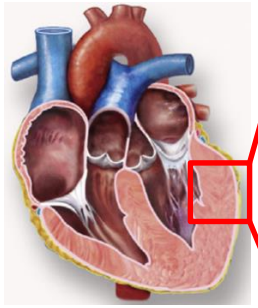
ACE

Ang II



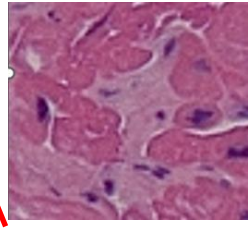
SNS

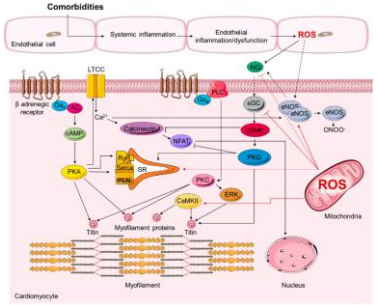




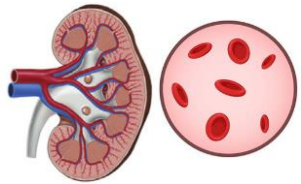
HFpEF

Myocardial structural and functional abnormalities



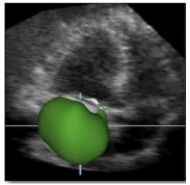


Budde H et al. Front Physiol 2022

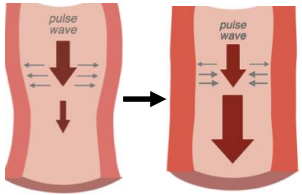


CKD

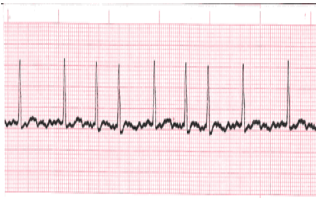
Anemia



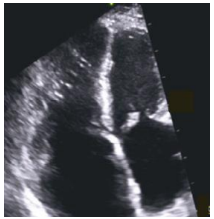
LA remodeling



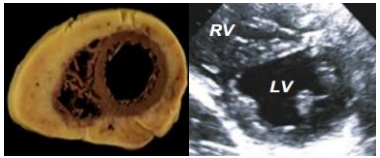
Arterial stiffness



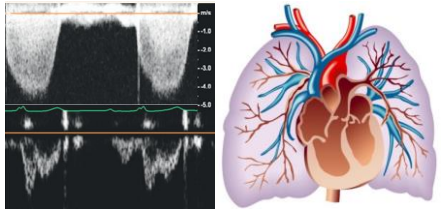
Atrial fibrillation



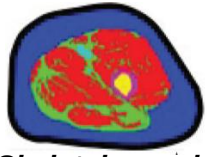
RV dysfx



Ventric. interdependence



Pulmonary HT and PVD

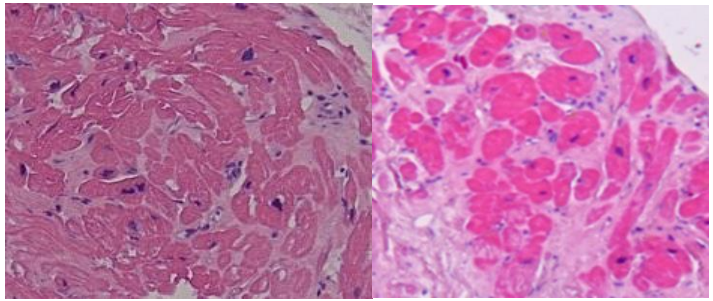


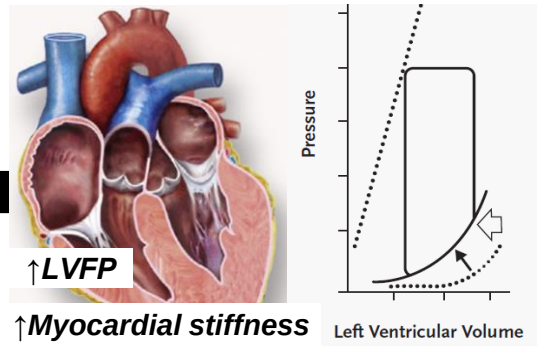
Skeletal muscle dysfx/sarcopenia

Determinants of ↑ myocardial stiffness in HFpEF

*HFpEF

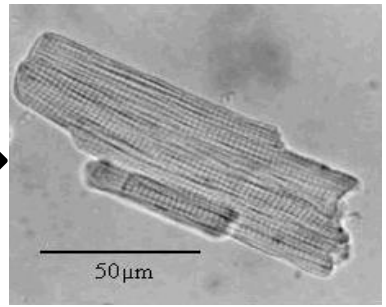
Extracellular matrix remodeling



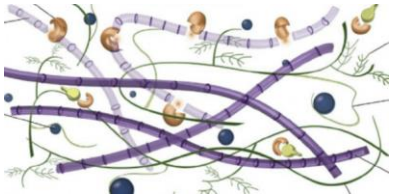


↑*Myocardial stiffness*

Cardiomyocyte dysfunction



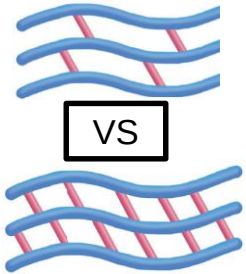
***ECM constituents**



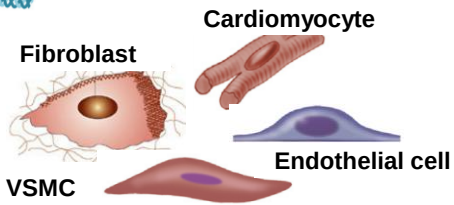
***Glycoproteins**
***Proteoglycans**
***Collagen types (1 vs 3)**

***Collagen synthesis vs degradation (MMPs; TIMPs)**

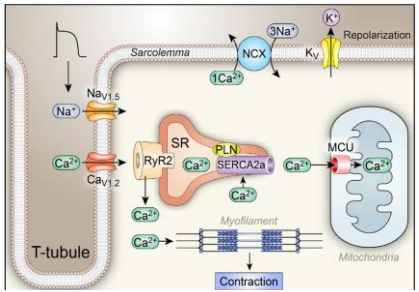
***Collagen crosslinking**



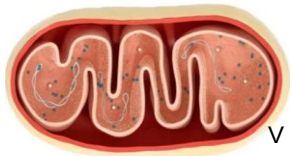
***Multicellular crosstalk**



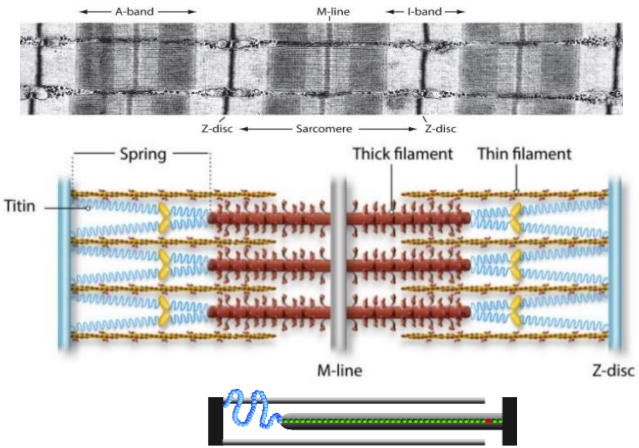
***Impaired relaxation**



***Mitochondrial dysfunction**



***Myofilamentary/sarcomeric changes**



V Heerebeek L. Circulation 2006; v Heerebeek L. Circulation 2008; v Heerebeek L. Circulation 2012; Franssen C. JACC HF 2016

HFpEF: a heterogeneous syndrome

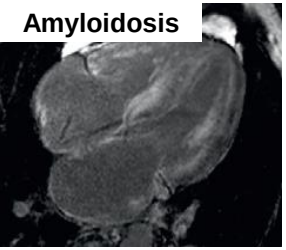
HFpEF

1) HF symptoms 2) LVEF ≥ 50% 3) Diastol dysfunction; NT-proBNP; Struct. abnorm. (LVH; LAE)

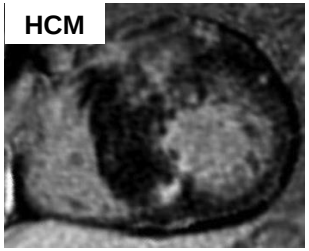
HFpEF "masqueraders"

Cardiomyopathies

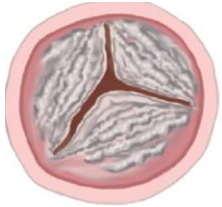
Amyloidosis



HCM

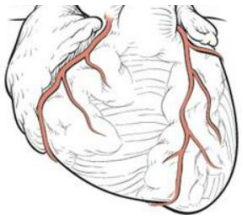


Valvular HD



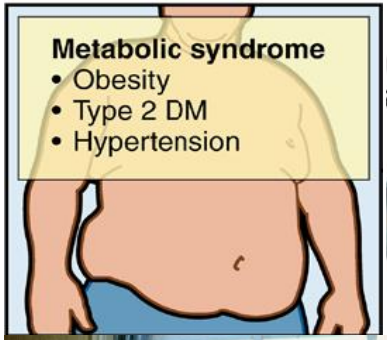
Sarcoidosis

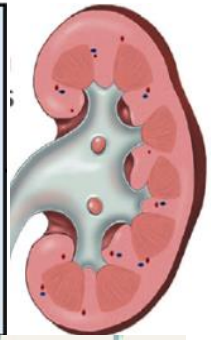
Coronary disease

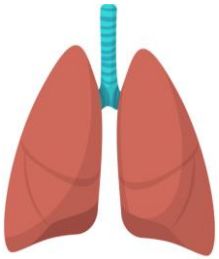


PAH;LD+cor pulmonale

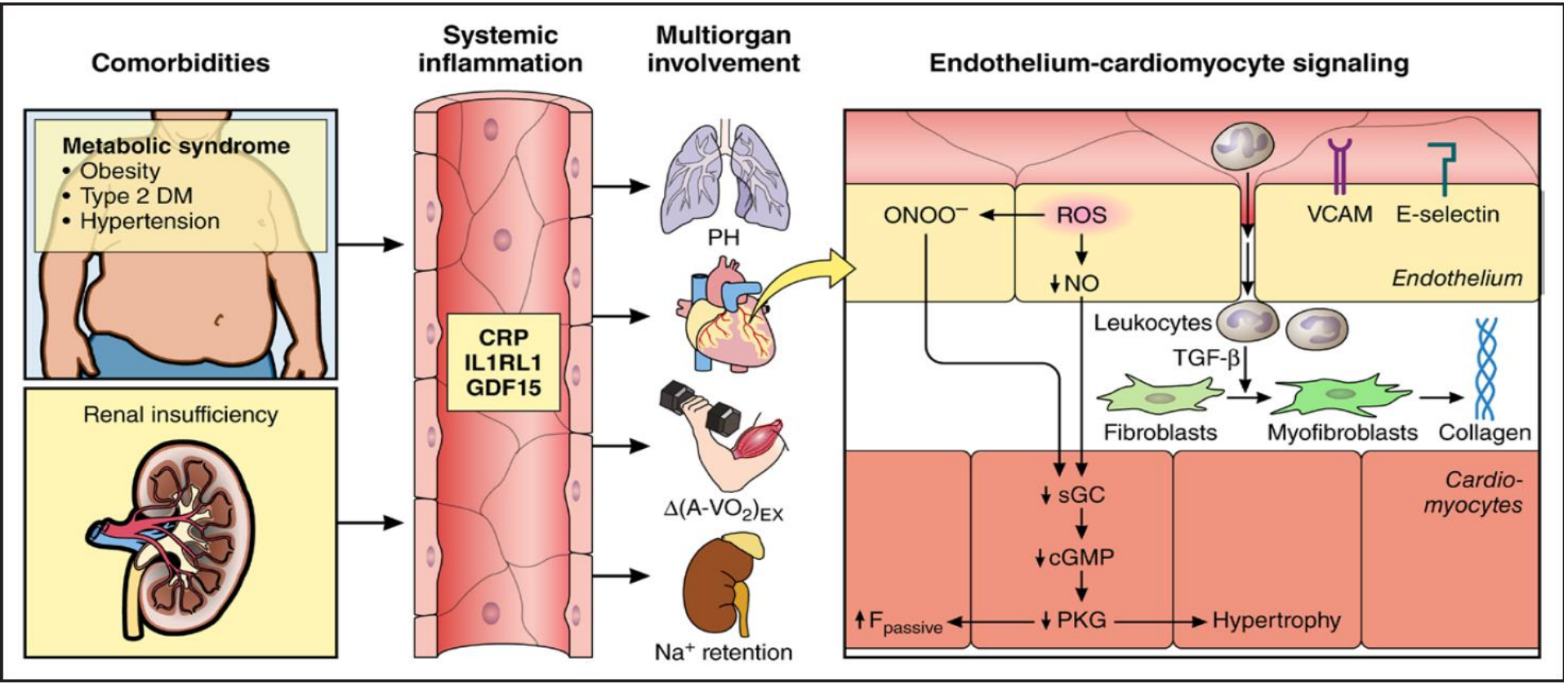
"Garden variety" HFpEF (comorbidities)







Comorbidities induce structural and functional remodeling in HFpEF through coronary endothelial inflammation

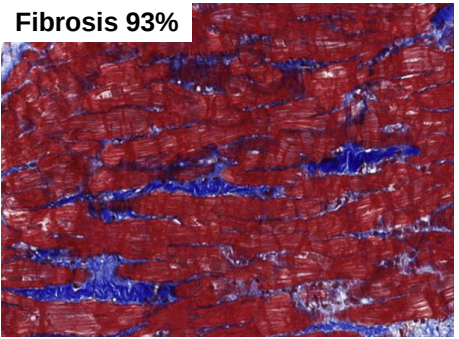


Shah S…van Heerebeek L, Paulus WJ. Circulation 2016;134:73

Endomyocardial biopsy (EMB) – in HFpEF

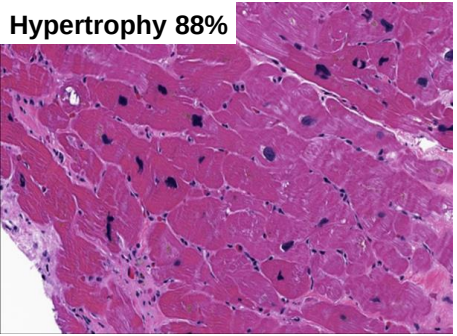
HFpEF patients (n = 108; LVEF ≥50%); Age 66 yrs; 61% women; BMI 37 kg/m2; 62% previous HF hosp referred to Johns Hopkins (‘14-’18) for RHC and RV EMB

Fibrosis 93%



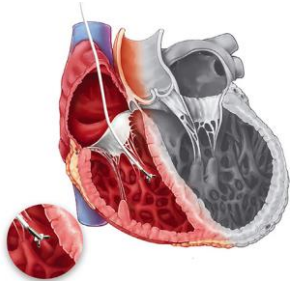
***66% mild fibrosis**
***27% moderate/severe fibrosis**
***7% no fibrosis**

Hypertrophy 88%

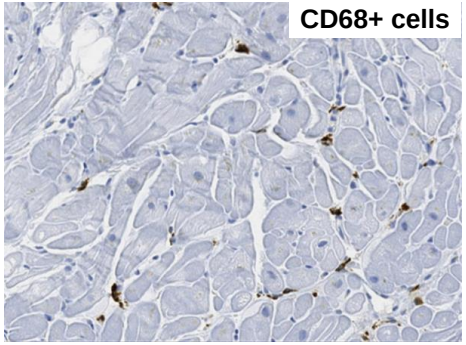


***45% mild hypertrophy**
***43% moderate/severe hypertrophy**
***12% no hypertrophy**

RV EMB

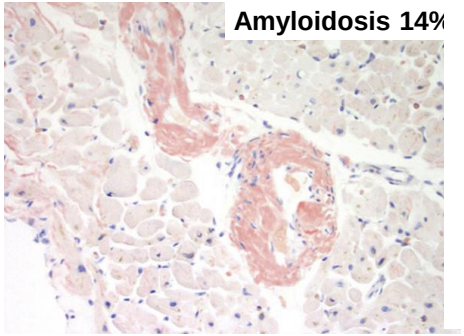


CD68+ cells

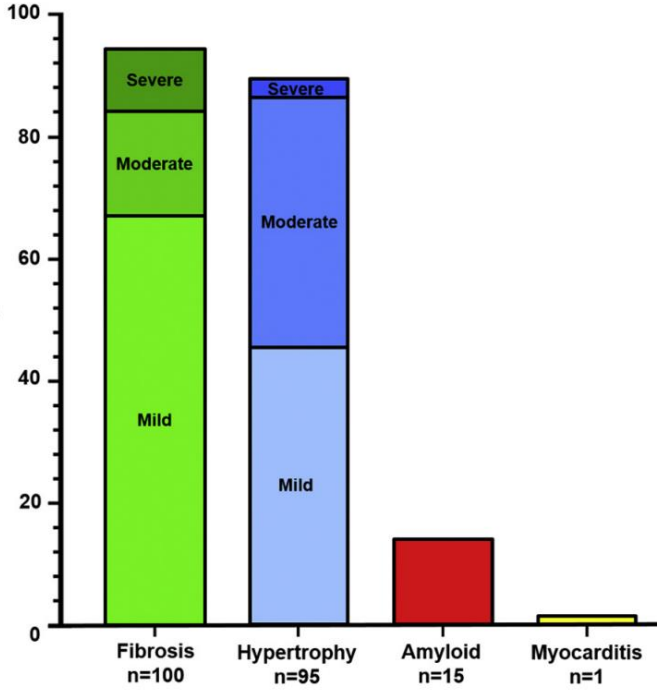


1.9x greater than controls

Amyloidosis 14%

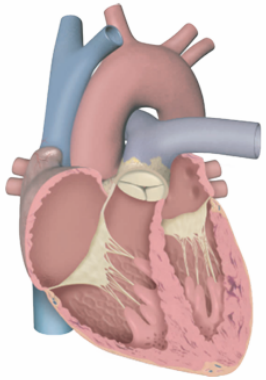


Cardiac amyloidosis in 15 patients (14%)
of which 7 cases were <u>unsuspected</u> prior to EMB



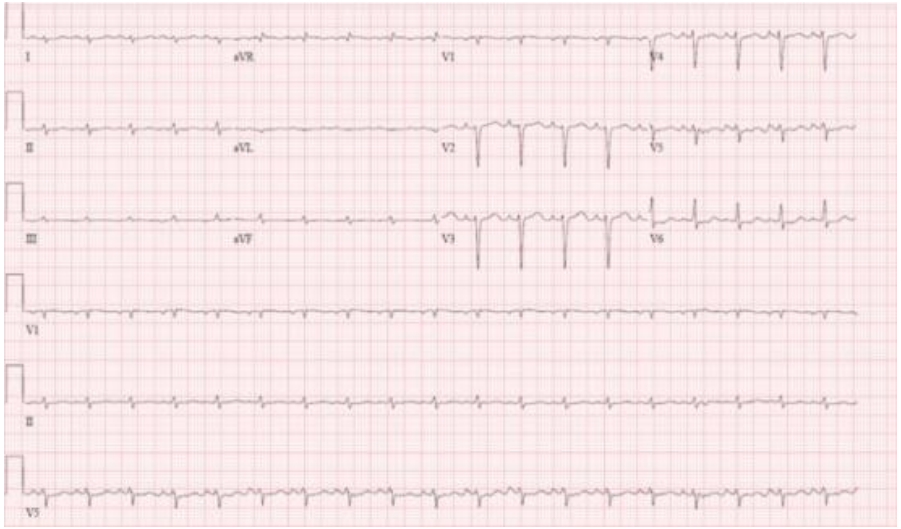
Hahn VS et al. JACC Heart Fail 2020;8:712

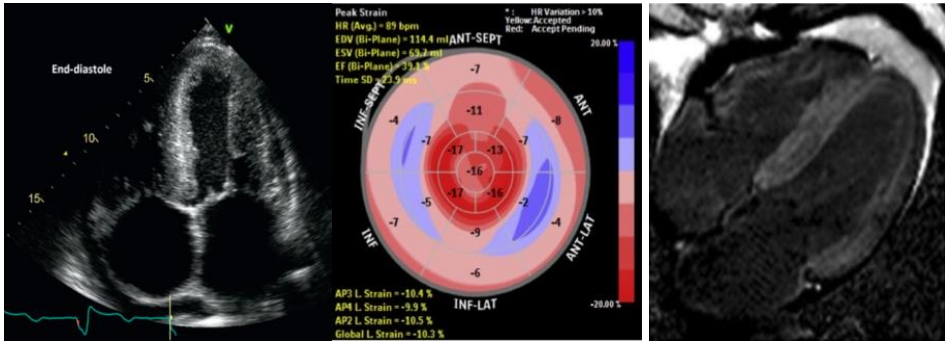
Cardiac Amyloidosis – Red flags and diagnostic findings



Left ventricular wall thickness ≥12 mm + ≥1 of

- Heart failure in ≥65 years
- Aortic stenosis in ≥65 years
- Hypotension or normotensive if previously hypertensive
- Sensory involvement, autonomic dysfunction
- Peripheral polyneuropathy
- Proteinuria
- Skin bruising
- Ruptured biceps tendon
- Bilateral carpal tunnel syndrome
- Subendocardial/transmural LGE or increased ECV
- Reduced longitudinal strain with apical sparing
- Decreased QRS voltage to mass ratio
- Pseudo Q waves on ECG
- AV conduction disease
- Possible family history of ATTR
- Chronically increased troponin levels
- Known multiple myeloma or MGUS

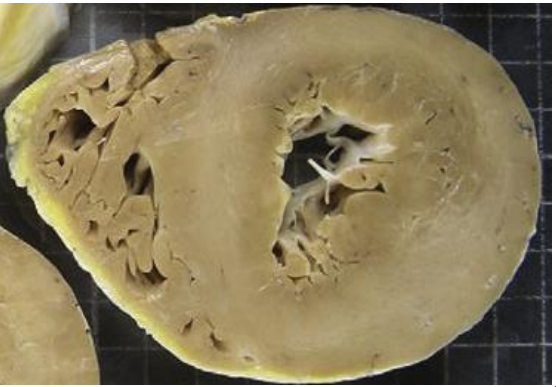




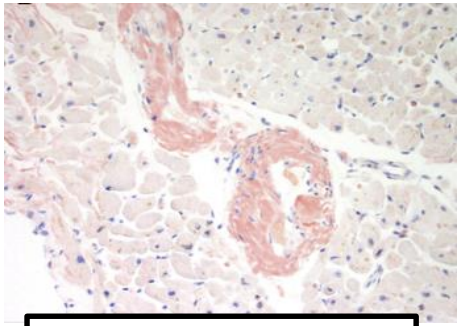
Arbelo E et al ESC guidelines 2023 Eur Heart J 2023;44:3503

Cardiac Amyloidosis – (Histo)pathology

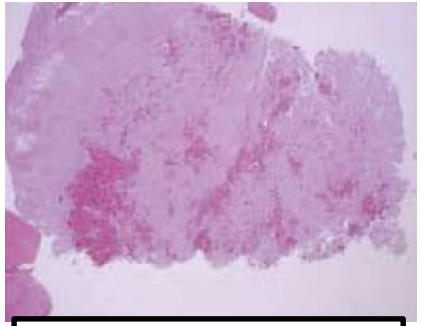
Gross pathology



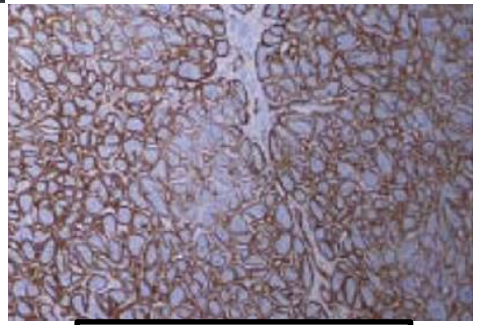
Histopathology



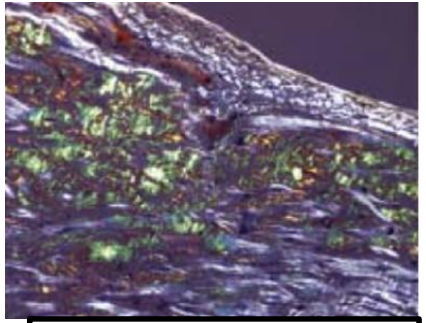
Congo Red



Hematoxylin eosin

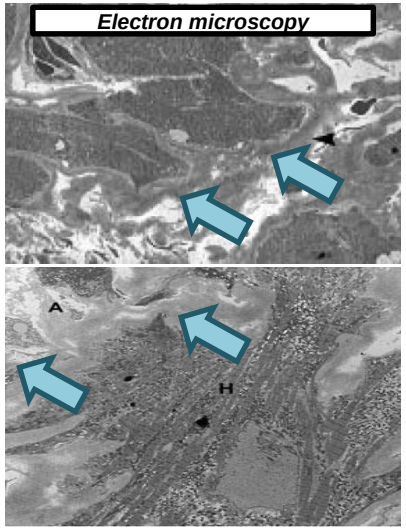


Immunohistochemistry



Polarized light microscopy

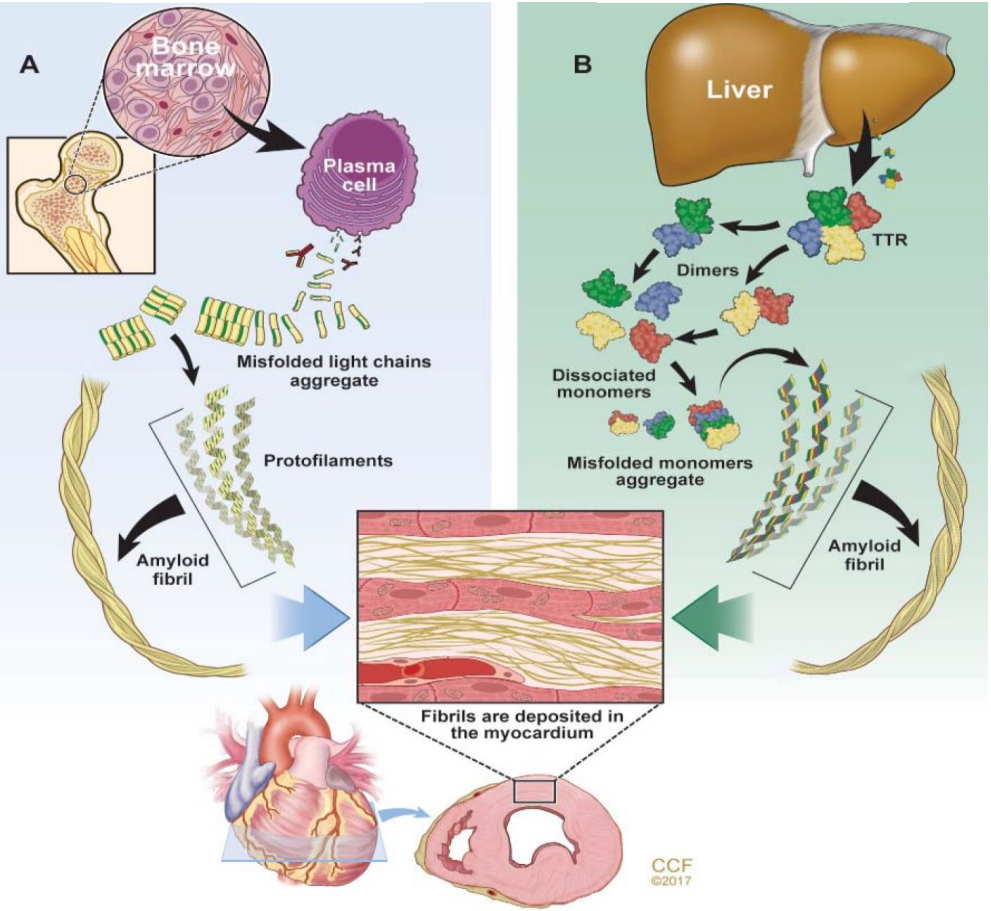
Electron microscopy



Ternacle J et al. JACC 2019;74:2638

Ruberg JACC 2019; Hahn JACC HF 2020; Mudhar J Clin Pathol 2001

AL amyloidosis **TTR amyloidosis**

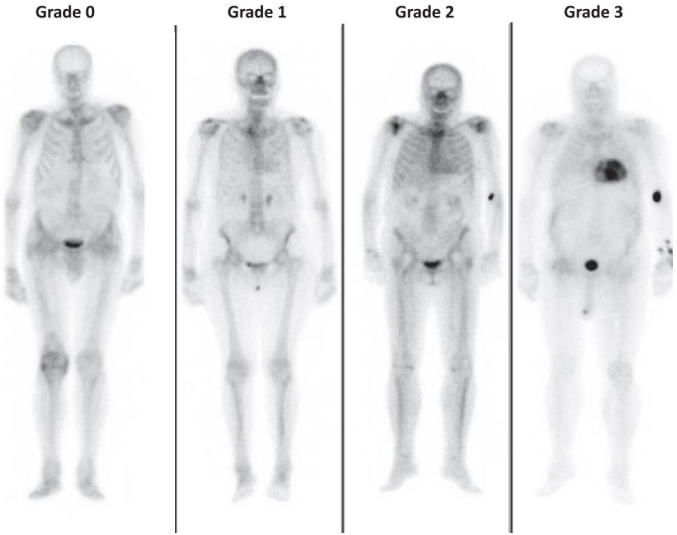


Donnelly JP et al. Cleveland Clin J Med 2017;84:12

AL amyloidosis

Haematologic tests
(serum free-light chain quantification & serum and urine immunofixation)

TTR amyloidosis

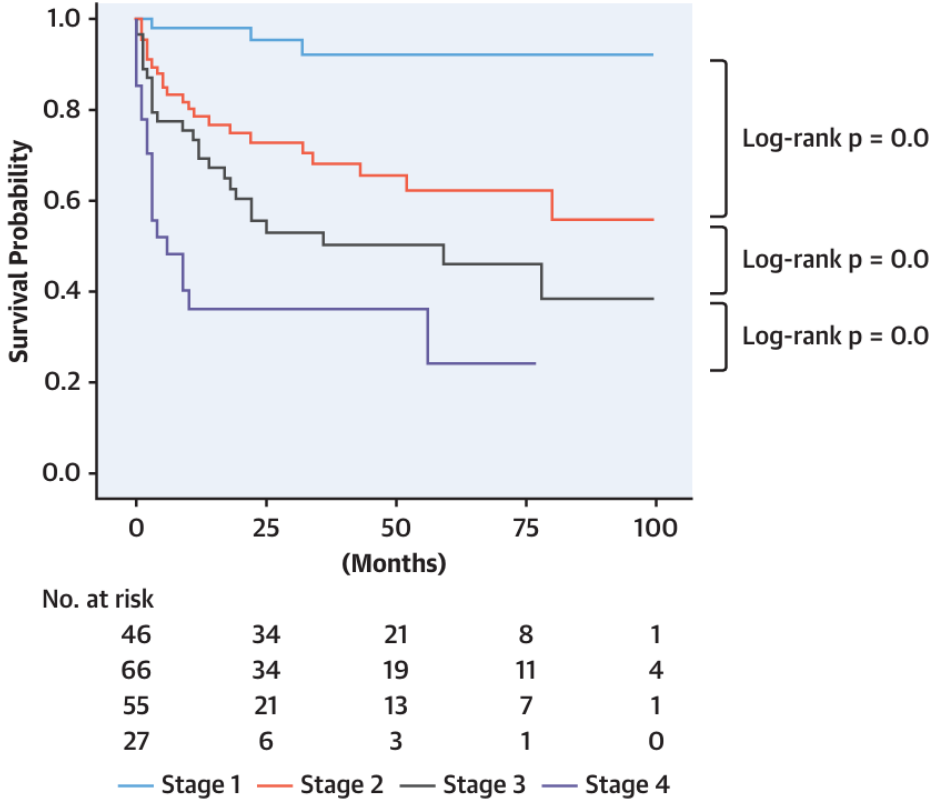


^{99m}Tc-DPD/PYP/HMDP
Scintigraphy with SPECT

Garcia-Pavia P et al Eur Heart J 2021;42:1554

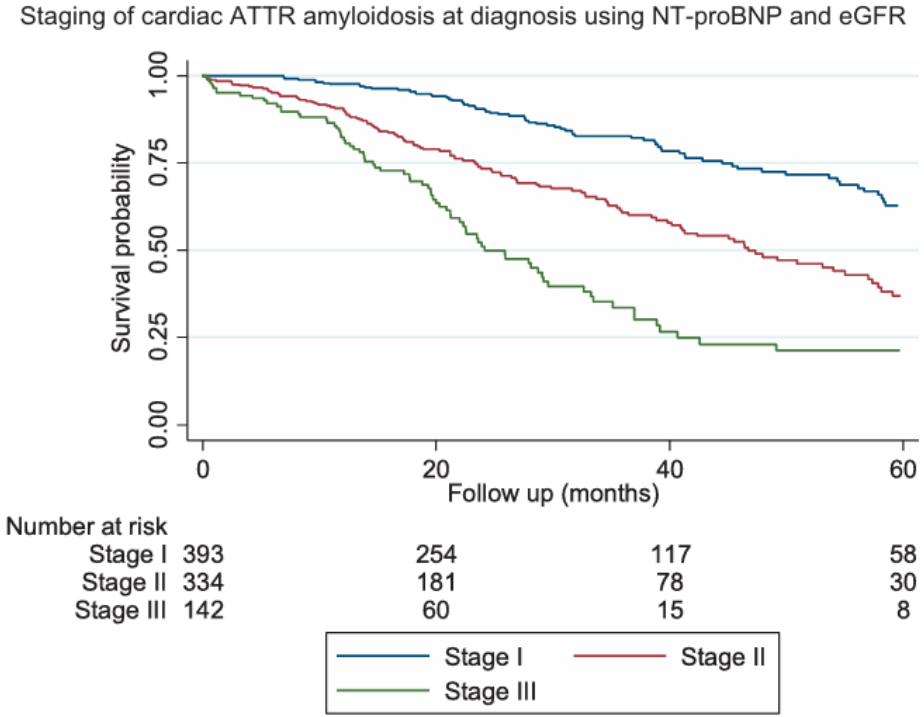
Cardiac Amyloidosis – Prognosis

Survival in AL amyloidosis



Barrett CD et al. JACC Heart Fail 2019;7:958

Survival in TTR amyloidosis



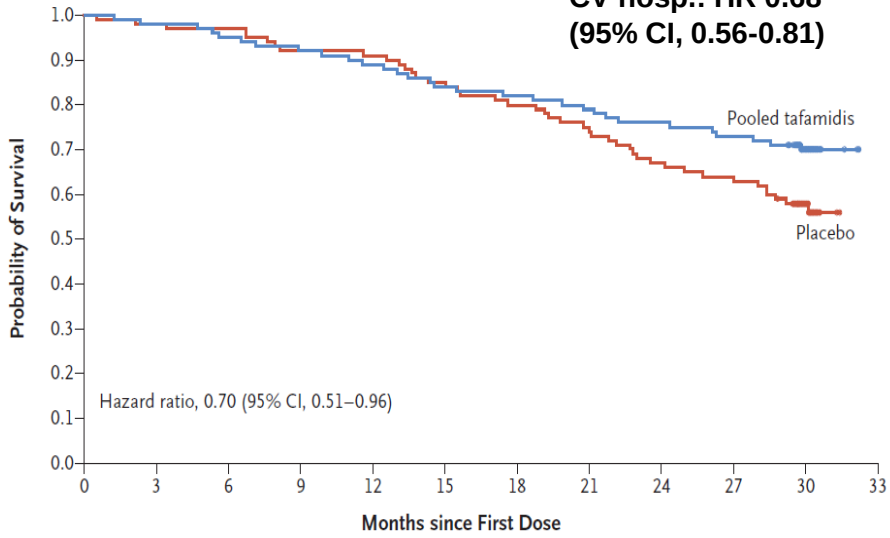
Gillmore JD et al. Eur Heart J 2018;39:2799

Amyloid cardiomyopathy – Treatment: Tafamidis (stabilize tetramer)

ATTR-ACT: ATTR CMP pts (n=441) randomized 2:1:2 tafamidis (80 mg), tafamidis (20 mg) vs placebo or 30 mths %;
Prim EP: All cause mortality and CV hosp
Secondary EP: 6 MWD and KCCQ

B Analysis of All-Cause Mortality

CV hosp.: HR 0.68 (95% CI, 0.56-0.81)

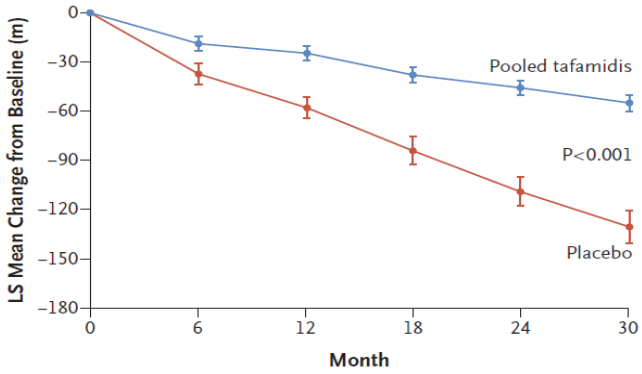


No. at Risk (cumulative no. of events)

Pooled tafamidis	264 (0)	259 (5)	252 (12)	244 (20)	235 (29)	222 (42)	216 (48)	209 (55)	200 (64)	193 (71)	99 (78)	0 (78)
Placebo	177 (0)	173 (4)	171 (6)	163 (14)	161 (16)	150 (27)	141 (36)	131 (46)	118 (59)	113 (64)	51 (75)	0 (76)

Maurer MS et al. NEJM 2018;379:1007

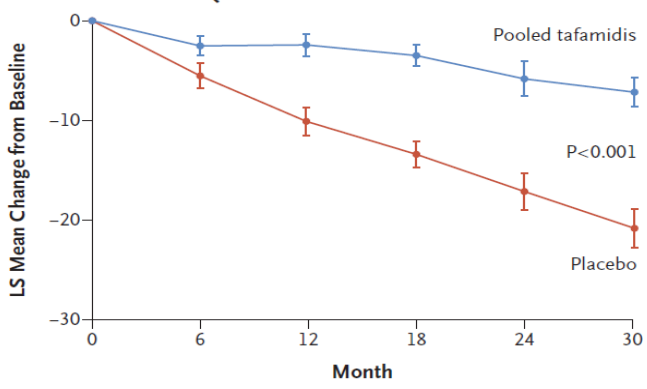
A Change from Baseline in 6-Minute Walk Test



No. of Patients

Tafamidis	264	233	216	193	163	155
Placebo	177	147	136	111	85	70

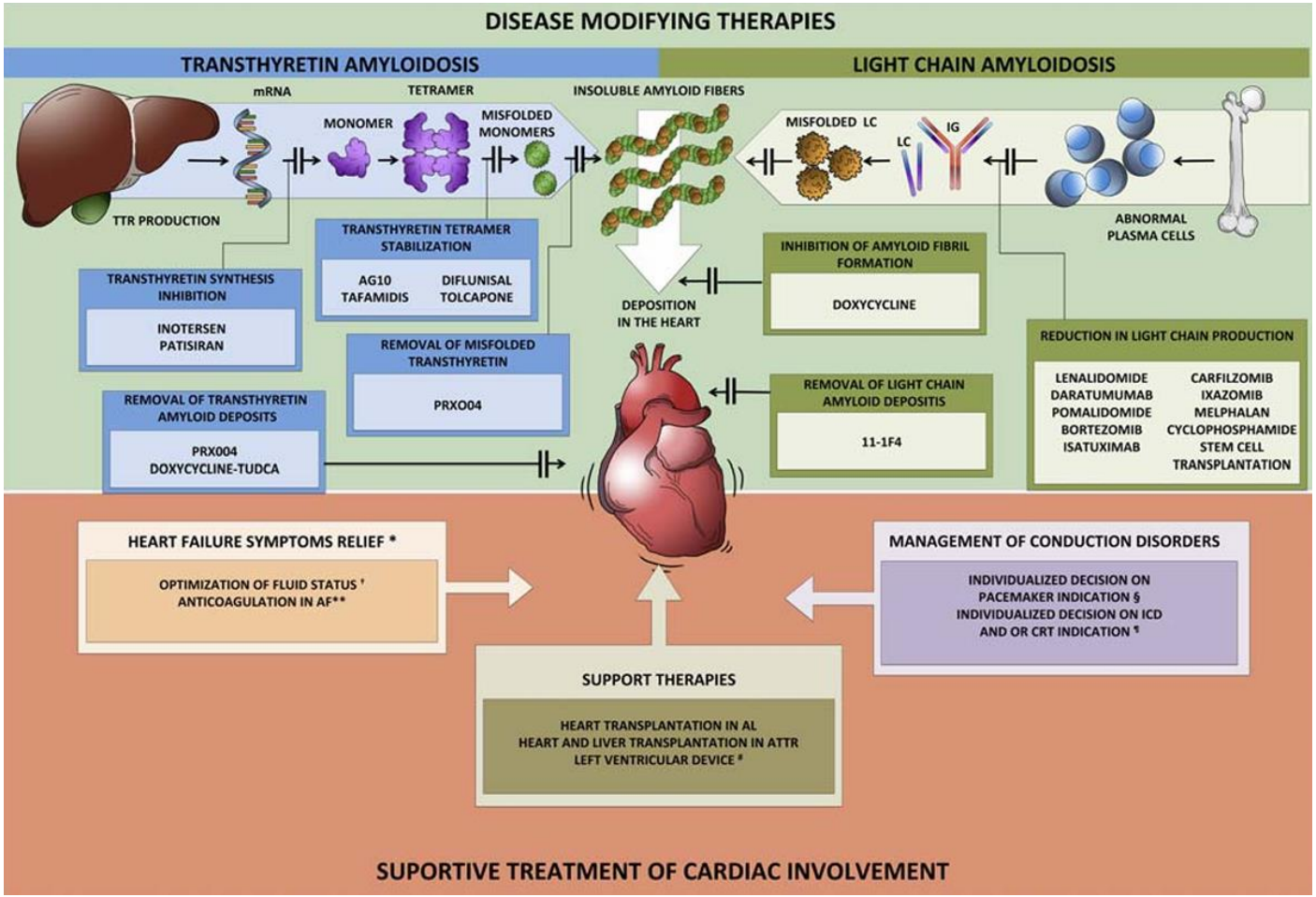
B Change from Baseline in KCCQ-OS



No. of Patients

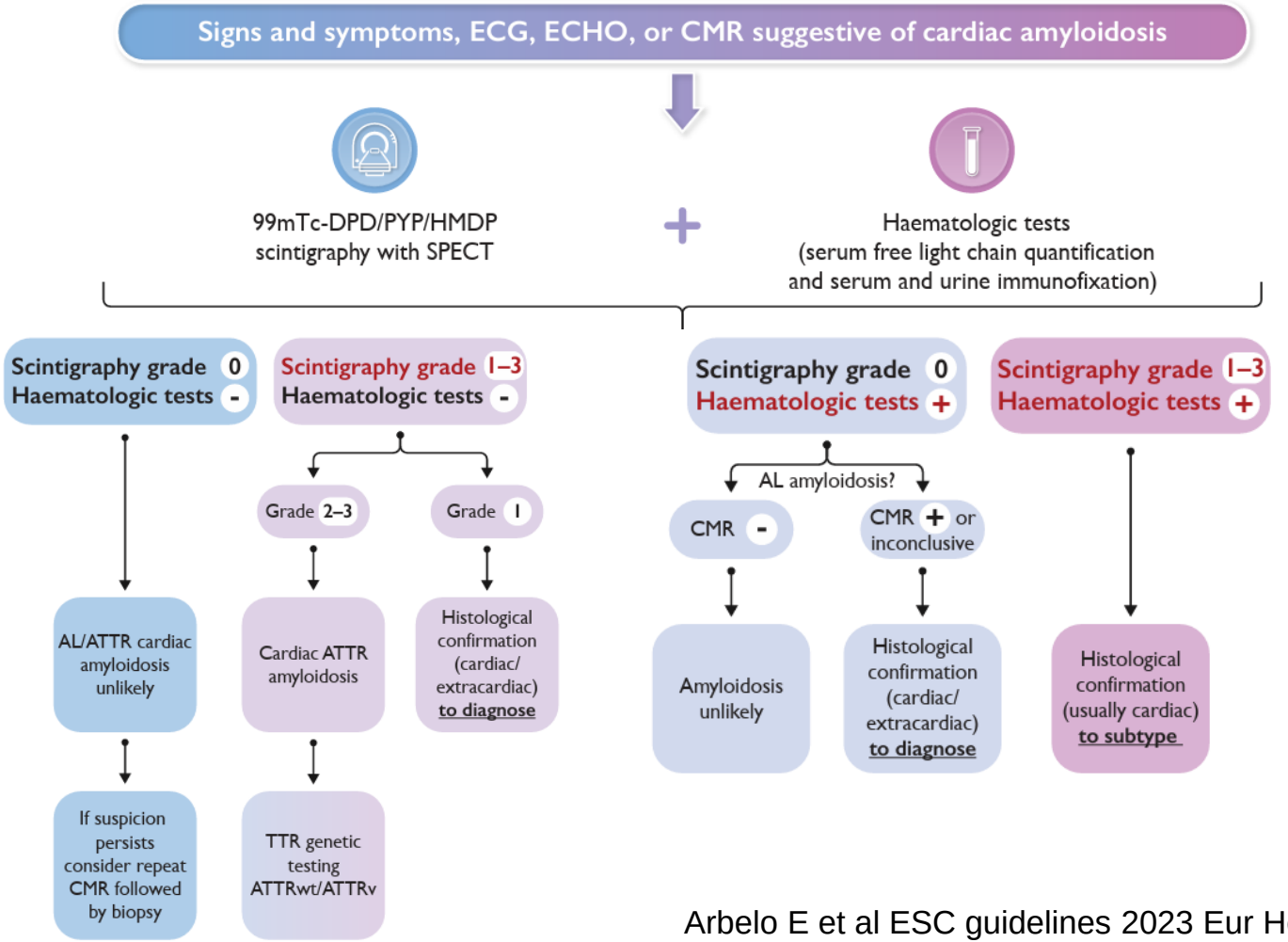
Tafamidis	264	241	221	201	181	170
Placebo	177	159	145	123	96	84

Cardiac amyloidosis – Treatment



Scarlatelli-Macedo AV et al Curr Treatment Options in Oncol 2020;21:36

Cardiac Amyloidosis

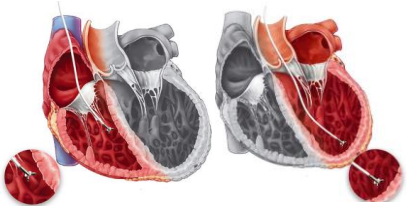


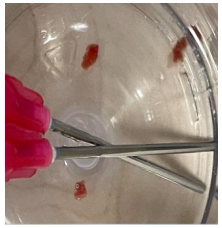
Arbelo E et al ESC guidelines 2023 Eur Heart J 2023;44:3503

Cardiac biopsy

Procedural aspects

RV EMB **LV EMB** **≥5 biopsies**



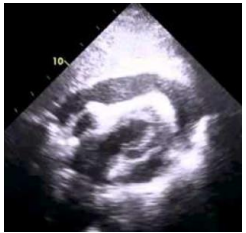


Indications

INDICATIONS FOR ENDOMYOCARDIAL BIOPSY

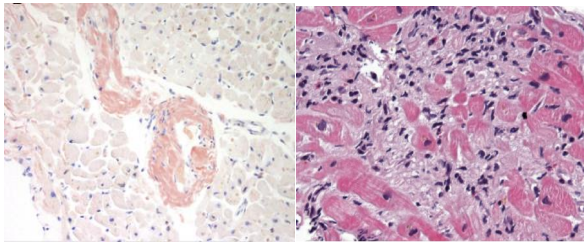
- HTx rejection surveillance
- Myocarditis
- Cardiomyopathies
- Drug-related cardiotoxicity
- Amyloidosis
- Infiltrative and storage disorders
- Cardiac tumours

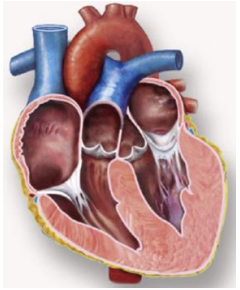
Complications



Contraindications

Diagnosis





In HF eci; EMB can provide diagnosis in:

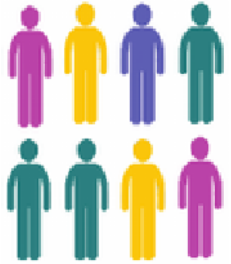
39%

Therapeutic implications

EMB can change therapy in :

30%

Improved personalized care




olvg
onze lieve vrouwe gasthuis