HEART FAILURE

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Improving Lives Together

Kintsugi
To join with gold

15th Century
Japanese practice

A reminder to stay optimistic when things fall apart

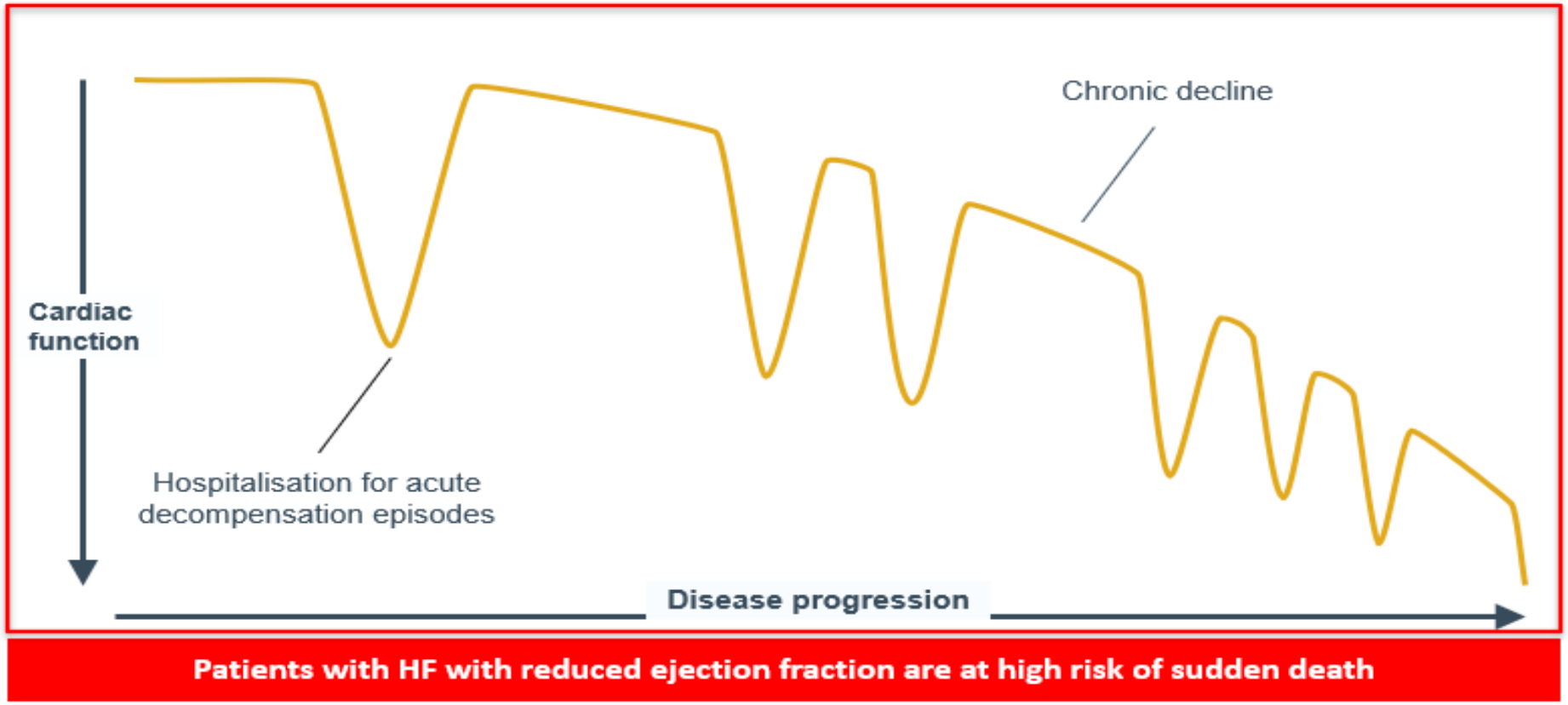
We can heal from our wounds,
embrace our imperfections and become stronger…

…Ancient Japanese Philosophy that helps us accept our flaws

Heart Failure – The Scale of the Problem

- CVD – leading cause of death in the UK and globally, responsible for 1/3 of all deaths each year
- Incidence HF : 1/1000 general population, rising 10% each year
- Prevalence:
  - >1 million confirmed patients in UK
  - 200,000 new diagnoses per year
    - 80% Diagnosed in hospital (40% had symptoms in preceding months)
  - Est 400,000 undiagnosed
  - 1% <65yrs
  - 25% NYHA III/IV
- Prevalence expected to increase by 50% over next 20 years
- >1M inpatient bed days
- 5% of all emergency admissions
- 2% total NHS budget
- 70% of cost = hospital admissions
- High readmission rate – predominantly due to fluid accumulation

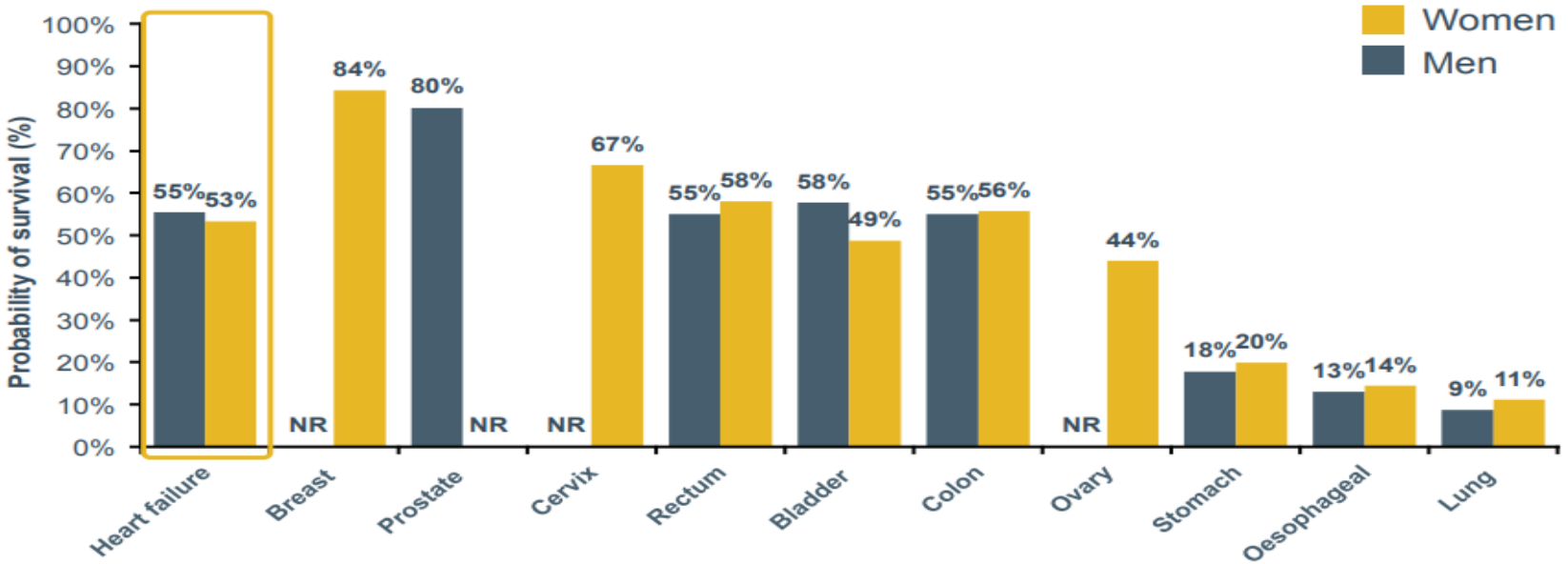
Heart failure: persistent and progressive



Life expectancy

HF should be prioritised to ensure patient outcomes continue to improve

5-year survival for HF is worse than some common cancers[1,2]



Adapted from National HF Audit and Office for National Statistics references.
ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker; NR=not relevant.

ENT16-C063(1) | July 2016

1. National HF audit 2013/14. Available at: www.ucl.ac.uk/nicor/audits/heartfailure/documents/annualreports/hfannual13-14.pdf.
2. Office for National Statistics. Summary: Cancer Survival in England: Patients Diagnosed, 2006–2010 and Followed up to 2011.

Entresto™ sacubitril/valsartan

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Quality of Life

- Lower physical functioning
- Lower mental functioning
- Lower social functioning
- Poor mental health
- Less energy
- Poor health perception

What is Heart Failure?

A clinical syndrome due to changes in cardiac structure and/or function, resulting in reduced cardiac output or elevated intra-cardiac pressures, which cause a constellation of clinical symptoms and signs

- Asymptomatic structural/functional abnormalities are pre-cursors to HF; **symptoms or signs must be present**
- Results from any disorder which impairs the ability of the ventricles to fill with, or eject blood
- Diagnosis is based on:
  - Typical symptoms +/- signs
  - Objective evidence of structural or functional abnormality
  - Elevated levels of natriuretic peptides
- Overall prognosis is poor – 50% mortality at 5 years

Causes of Heart Failure

Ischaemic heart disease is the most common cause

Common

- Coronary artery disease
- Hypertensive heart disease
- Degenerative valvular disease
- Chronic arrhythmias

Less Common

- Congenital Heart Disease
- Cardiomyopathies and myocardial disease
  - DCM
  - HCM
  - RCM
  - ARVC
  - Takotsubo
  - Post-partum
- Myocardial disease
  - Myocarditis
- Pericardial disease
- High output states
  - Thyrotoxicosis
  - Severe anaemia
  - AV fistula
  - Paget's disease
  - Nutritional deficits
    - Beri Beri (Thiamine)
    - Selenium
- Toxins
  - Chemotherapy drugs, immune-modulating drugs
  - Alcohol, cocaine, anabolic steroids
- Infection
  - HIV/AIDS
  - Chagas
- Immune
  - Giant cell myocarditis
  - SLE
  - Eosinophilic myocarditis
- Infiltrative
  - Malignancy, masses
  - Amyloidosis, sarcoidosis, haemachromatosis, storage diseases (e.g. Fabry's)
- Genetic diseases, e.g. muscular dystrophy

Definitions – European Society of Cardiology

- The ESC currently defines three types of heart failure, based on LV ejection fraction:
  - Heart failure with reduced ejection fraction (**HFrEF**)
  - Heart failure with mildly reduced ejection fraction (**HFmrEF**)
  - Heart failure with preserved ejection fraction (**HFpEF**)

- Broadly speaking:
  - **HFrEF:** failure of ventricle to eject blood
  - **HFpEF:** failure of ventricle to fill with blood

- **Left heart failure:** predominantly symptoms of pulmonary congestion
- **Right heart failure:** predominantly symptoms of systemic congestion

Table I Diagnosis of heart failure

The diagnosis of HF-REF requires three conditions to be satisfied:
1. Symptoms typical of HF
2. Signs typical of HF[a]
3. Reduced LVEF
The diagnosis of HF-PEF requires four conditions to be satisfied:
1. Symptoms typical of HF
2. Signs typical of HF[a]
3. Normal or only mildly reduced LVEF and LV not dilated
4. Relevant structural heart disease (LV hypertrophy/LA enlargement) and/or diastolic dysfunction (see Section 4.1.2)

HF = heart failure; HF-PEF = heart failure with 'preserved' ejection fraction; HF-REF = heart failure and a reduced ejection fraction; LA = left atrial; LV = left ventricular; LVEF = left ventricular ejection fraction.
[a]Signs may not be present in the early stages of HF (especially in HF-PEF) and in patients treated with diuretics (see Section 3.6).

Definitions : European Society of Cardiology

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

Symptoms

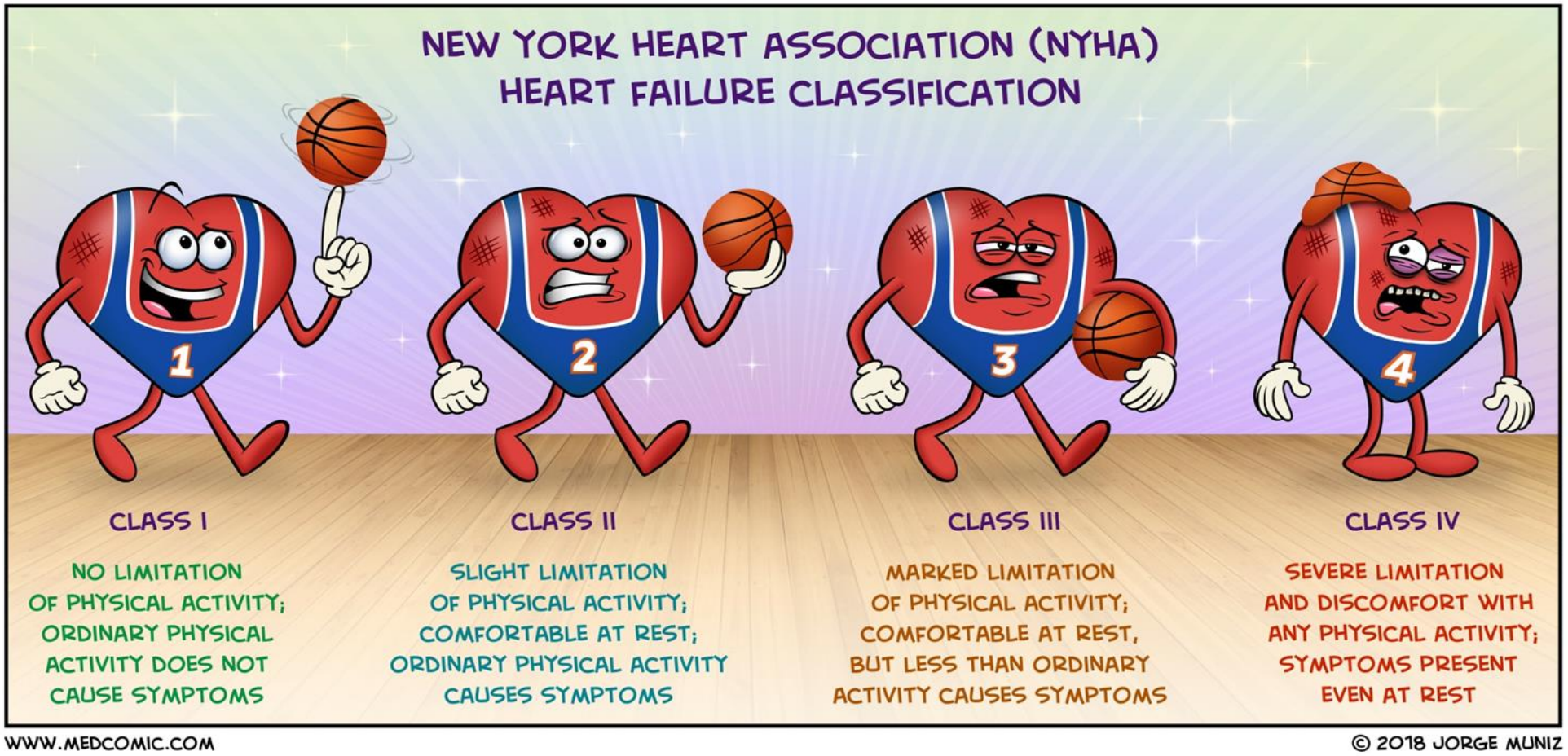
- Fatigue
- Dyspnoea
- Orthopnoea
- Paroxysmal nocturnal dysponea
- Peripheral oedema
- Chest pain and palpitations
- Abdominal distension/ascites
- Mild jaundice
- Weight gain

- Multi-system effects:
  - Reduced urine output
  - Confusion, delirium
  - Gout, cramps
  - Depression

Symptom Classification: NYHA

NYHA Class	Functional Capacity	Pathophysiology
Class I	No limitations. Ordinary physical activity does not cause fatigue, dysponea , etc	Asymptomatic/quiescen t cardiac abnormality
Class II	Slight limitation of physical activity. Ordinary activity results in symptoms	Compensated heart failure
Class III	Marked limitation of physical activity. Less than ordinary physical activity leads to symptoms	Decompensated heart failure
Class IV	Unable to carry out any physical activity without symptoms. May be present at rest	Advanced/end-stage heart failure

Subjective classification: NYHA class



Signs

- Hyper- or hypotension
- Tachycardia
- Tachypnoea, hypoxia
- Cyanosis
- Raised JVP
- Laterally displaced apex
- Gallop rhythm
- Cachexia
- Peripheral oedema
- Anasacra
- Hepatomegaly
- Ascites

If the patient is well compensated, there may be no signs

Always examine for signs of the underlying cause, eg: murmurs, CABG scars, AF

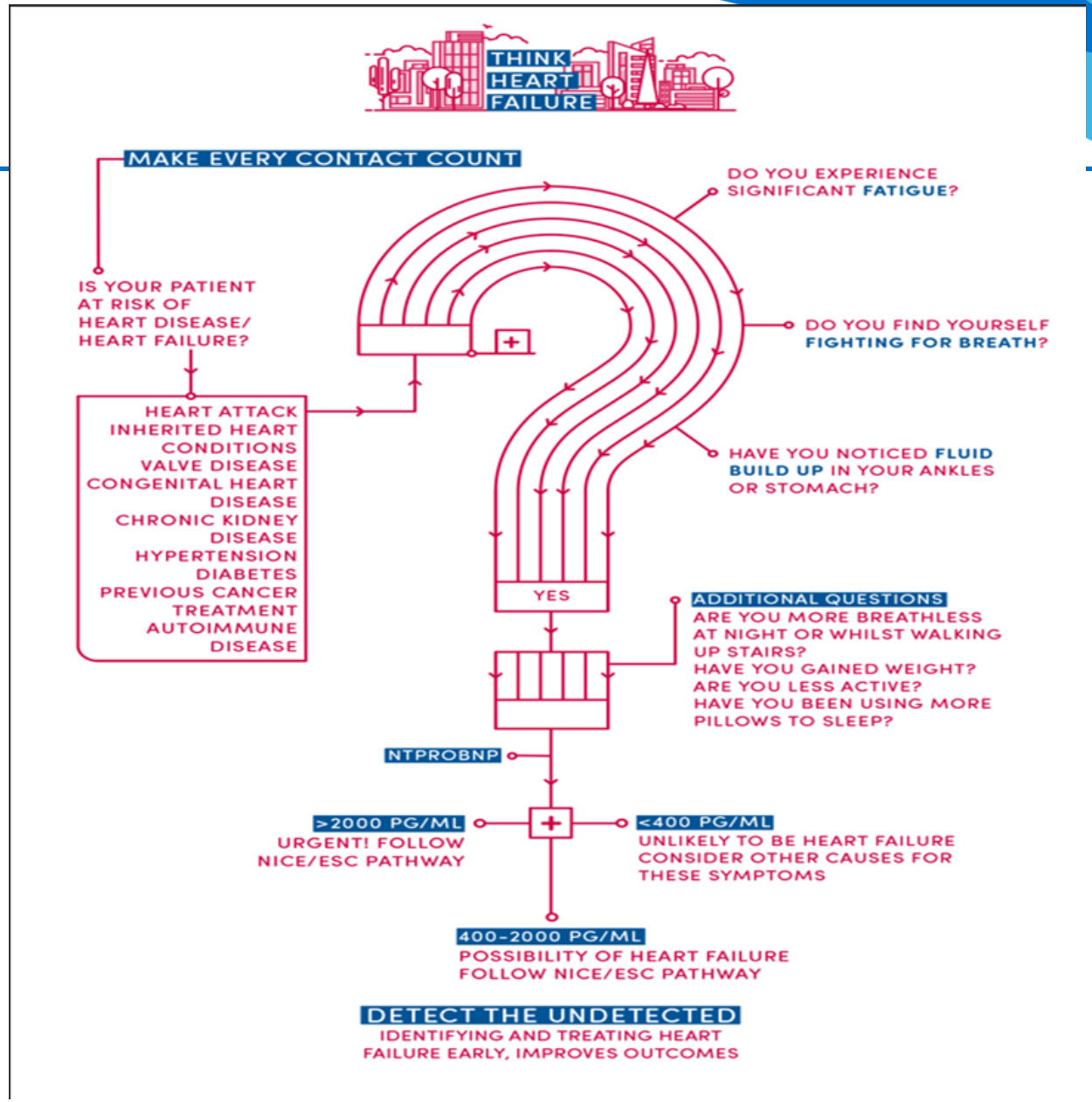
Think Heart Failure

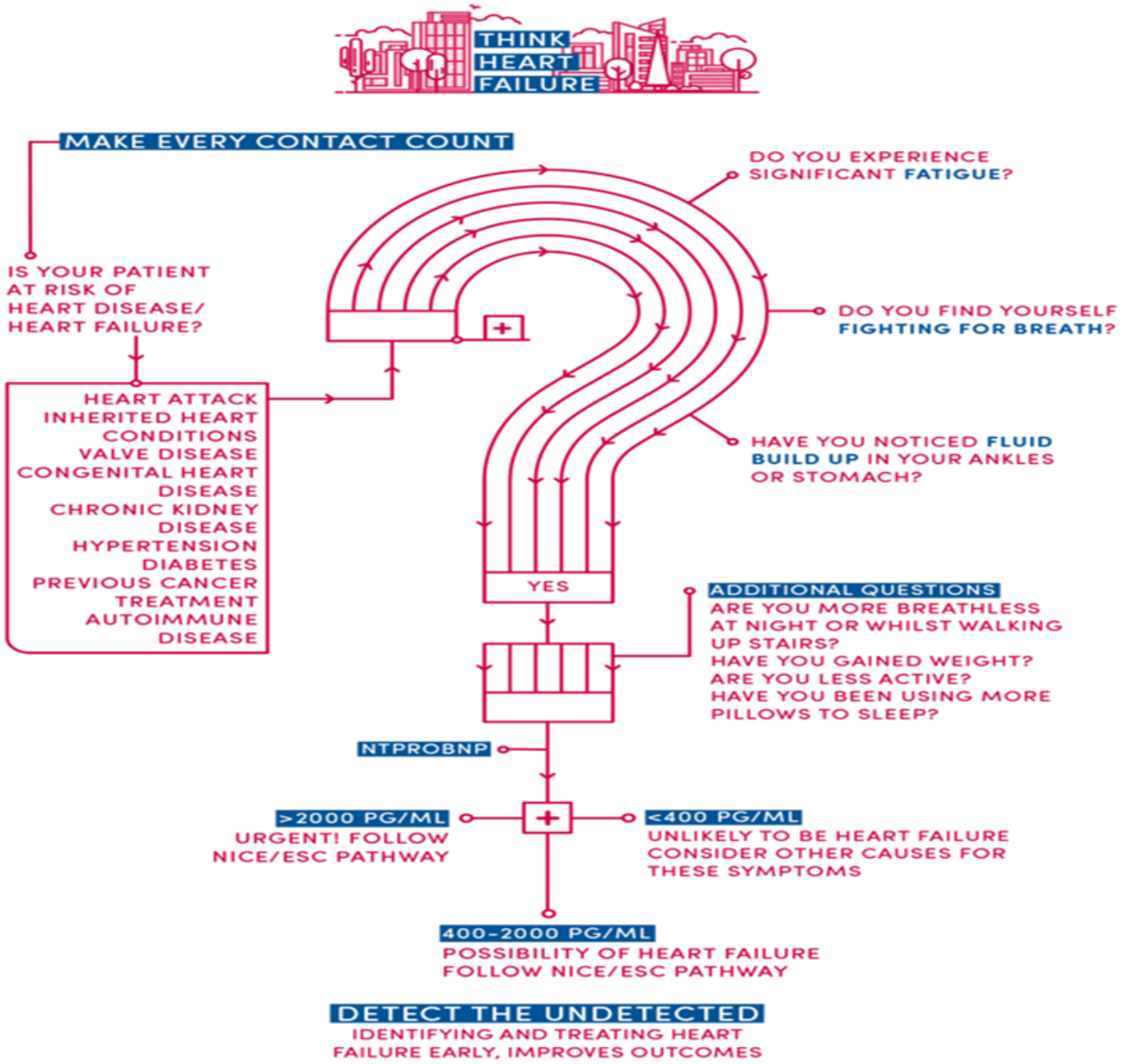
80% diagnosed in hospital

40% cases symptoms in primary care in months leading up to this

Aiming for earlier diagnosis

- Start treatment early
- Delay disease progression
- Prevent hospital admissions
- Improve quality of life





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Investigations

- **ECG: very rarely normal**
  - Arrhythmias, LVH, ischaemia, conduction defects (LBBB)
  - Heart failure is unlikely in patients with a completely normal ECG (sensitivity 89%)
- **Chest x-ray**
  - Assesses for pulmonary congestion
- **Natriuretic peptides**
  - Peptides released by stress on the ventricle
  - Have a high negative predictive value, ie: normal BNP makes heart failure very unlikely
- **Blood tests**
  - FBC, U+E's, LFT's, TFT's, troponin,
  - glucose, urate, iron studies
- **Echocardiogram: the key investigation**
  - Confirms systolic or diastolic dysfunction
  - Can identify causes

Investigations

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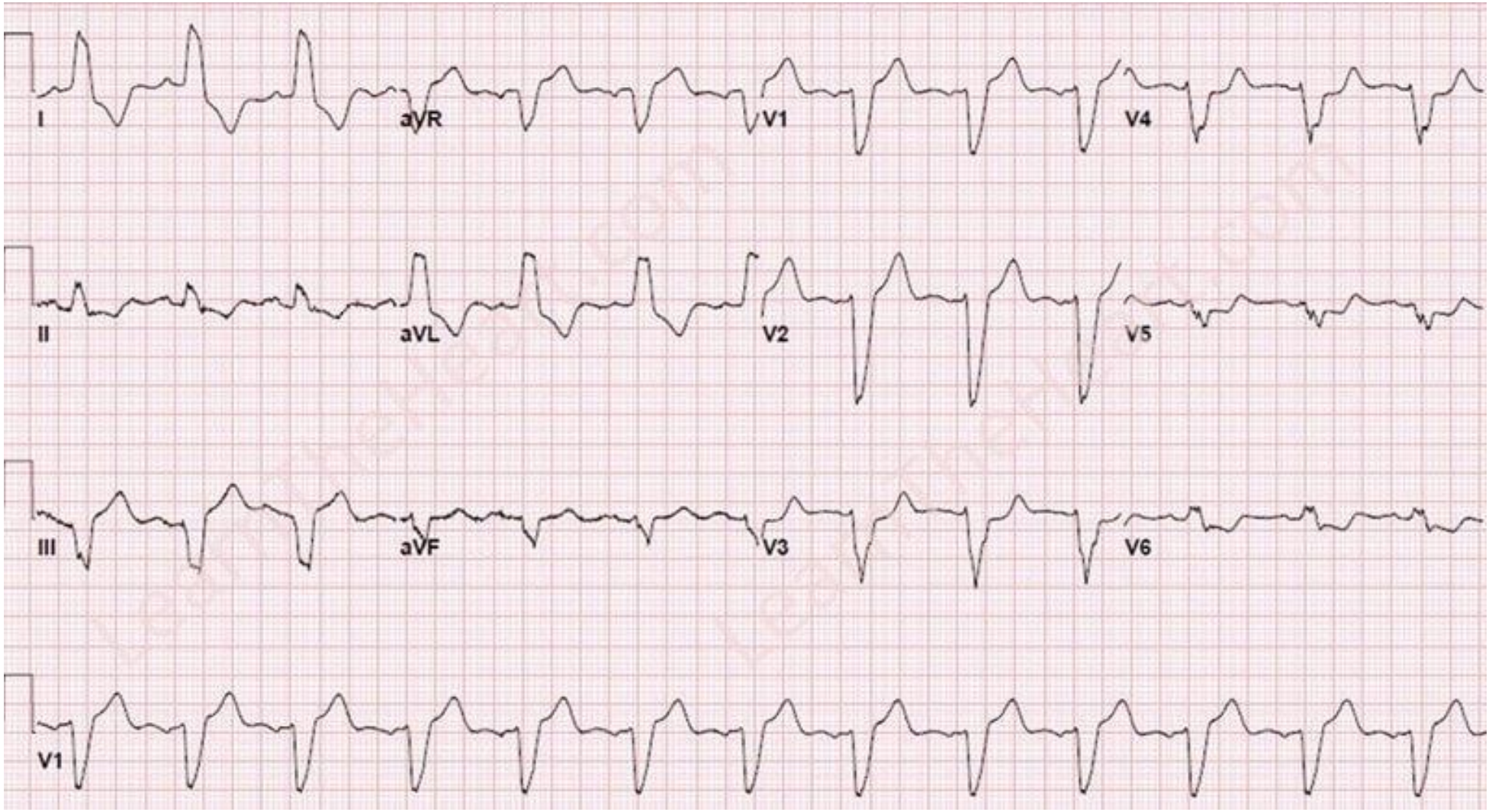
  - Arrhythmias, LVH, ischaemia, conduction defects
  - Heart failure is unlikely in patients with a completely normal ECG (sensitivity 89%)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aVL
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III
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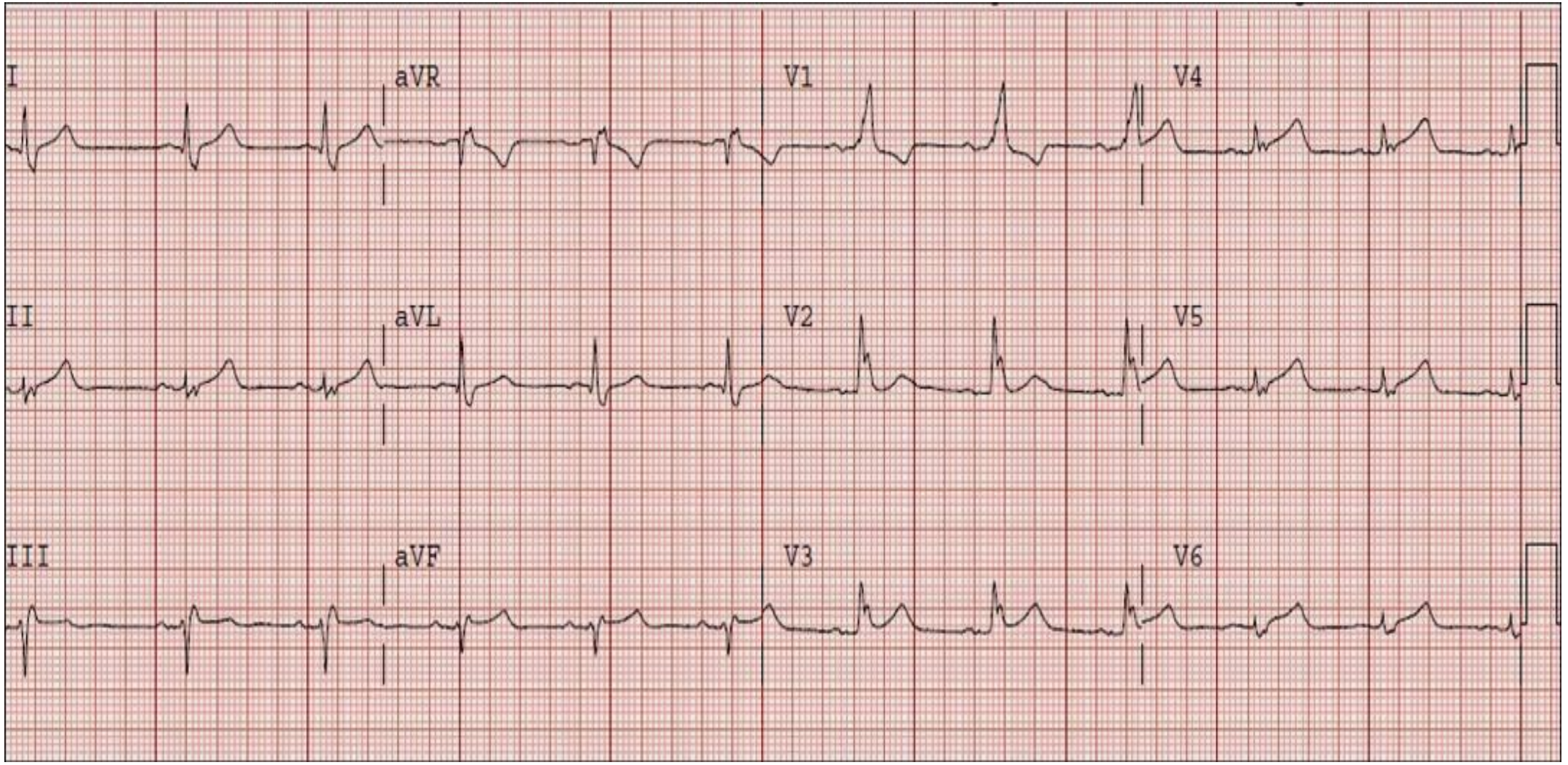
V3
V6
V1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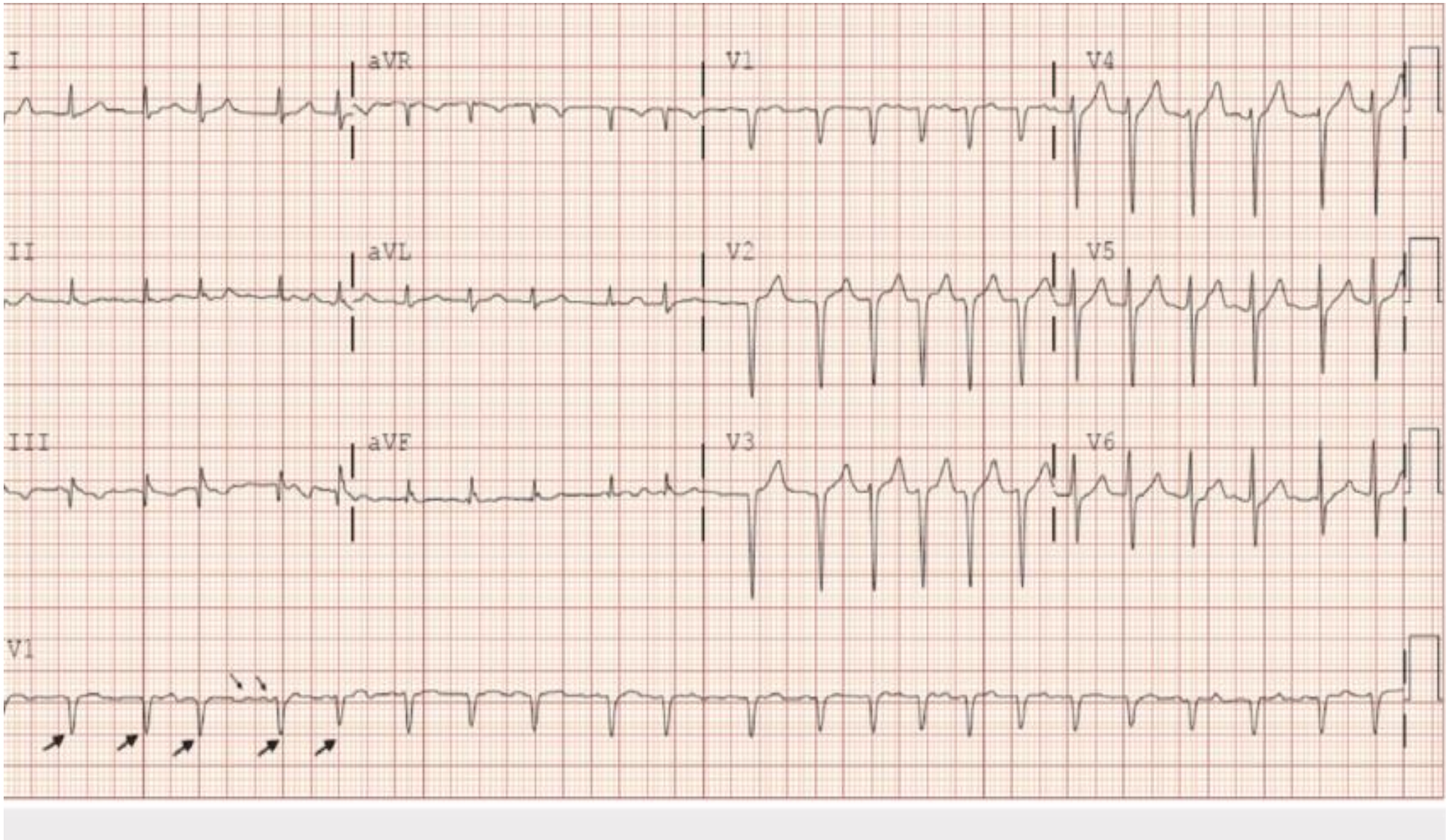
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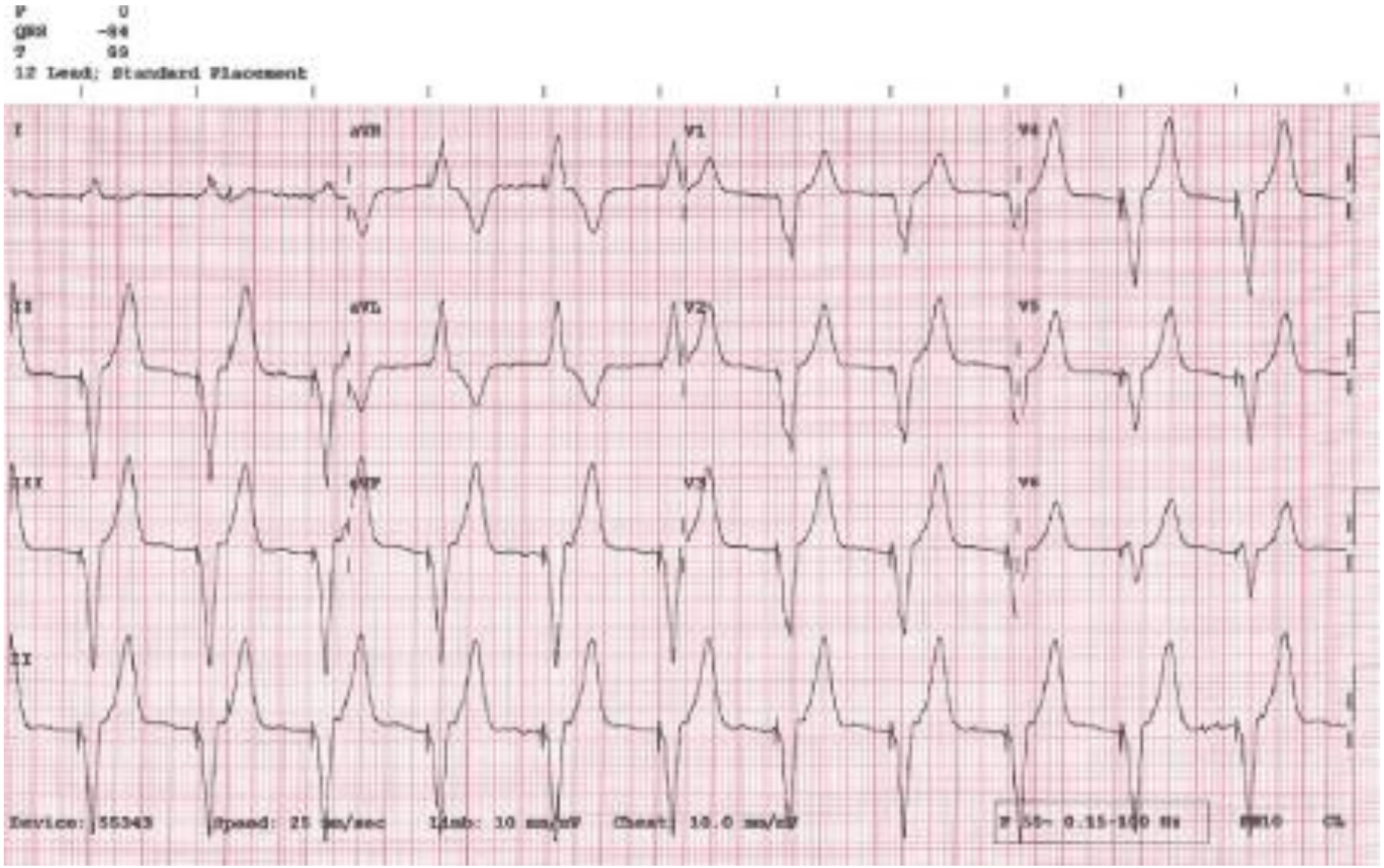
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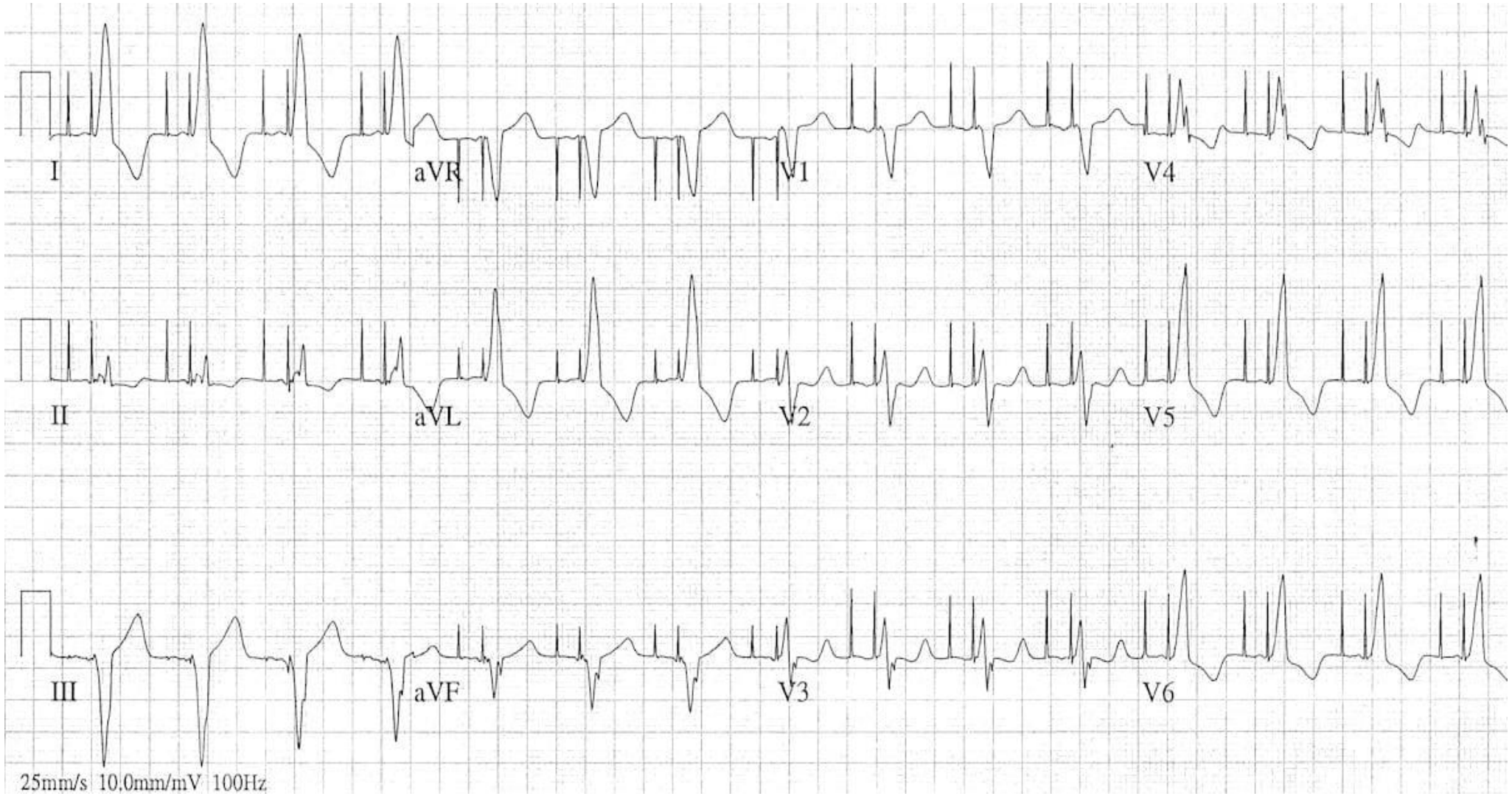
Chest: 10.0 mm/mV


I
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aVF
V3
V6
25mm/s 10.0mm/mV 100Hz

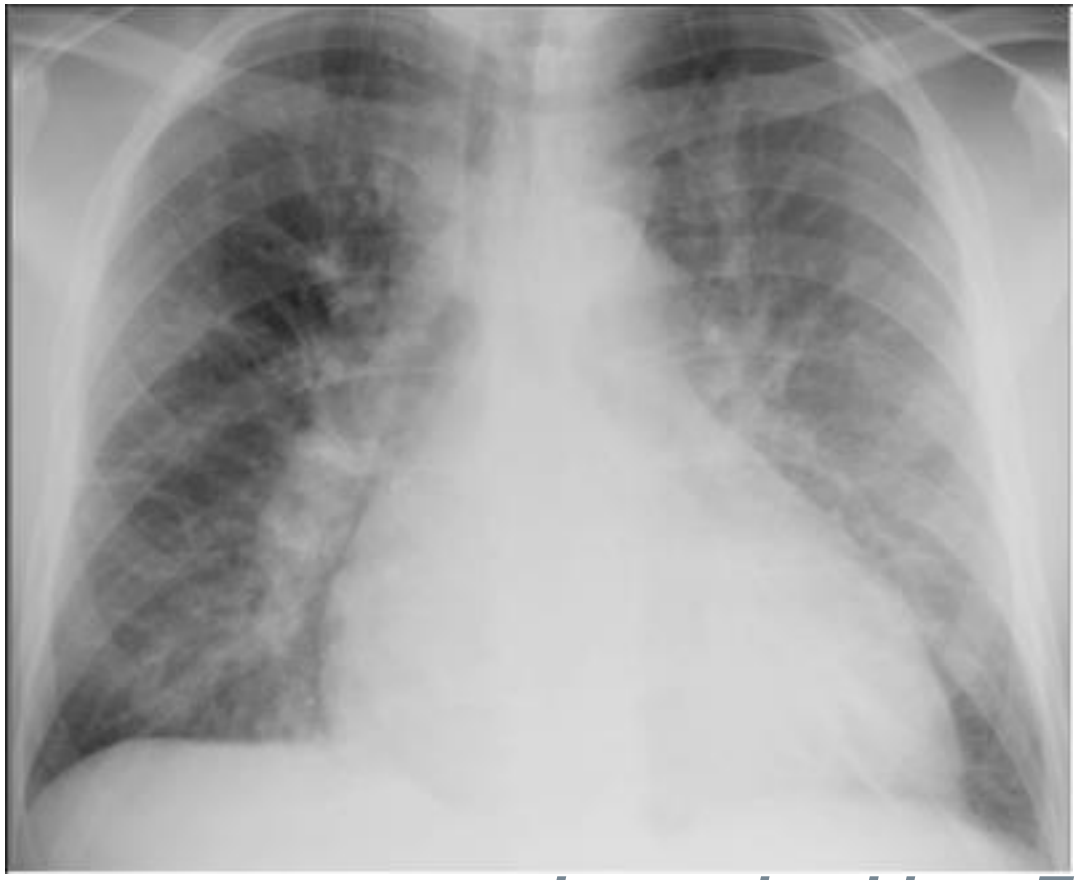
Investigations

- **Chest x-ray**
  - Assesses for pulmonary congestion

Features of heart failure on a chest x-ray

A B C D E F

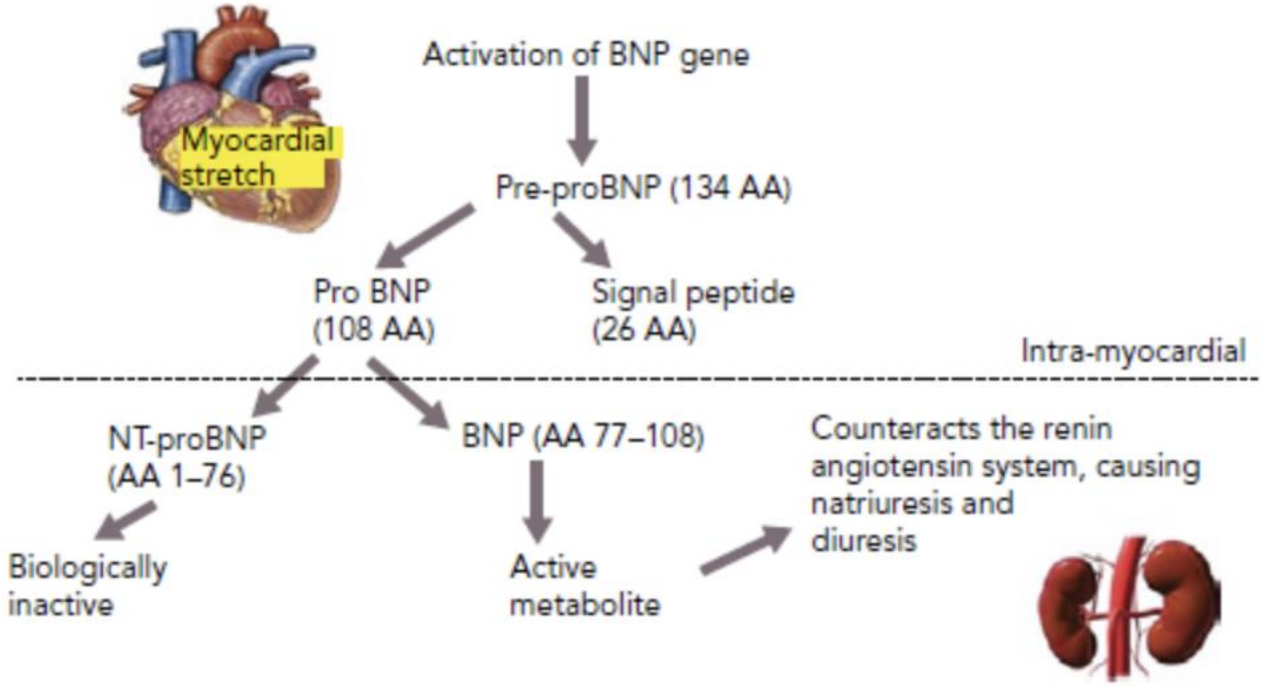
- **A**lveolar interstitial oedema
- **B**at winging / Kerley **B**-lines
- **C**ardiomegaly
- **D**iversions / **D**ilated pulmonary vasculature
- **E**ffusions
- **F**luid in horizontal Fissure



Investigations

- **Natriuretic peptides (BNP & NT-proBNP)**
  - Peptides released by stress on the ventricle
  - Have a high negative predictive value, ie: normal BNP makes heart failure very unlikely

NT-proBNP



A peptide released in response to myocardial stretch

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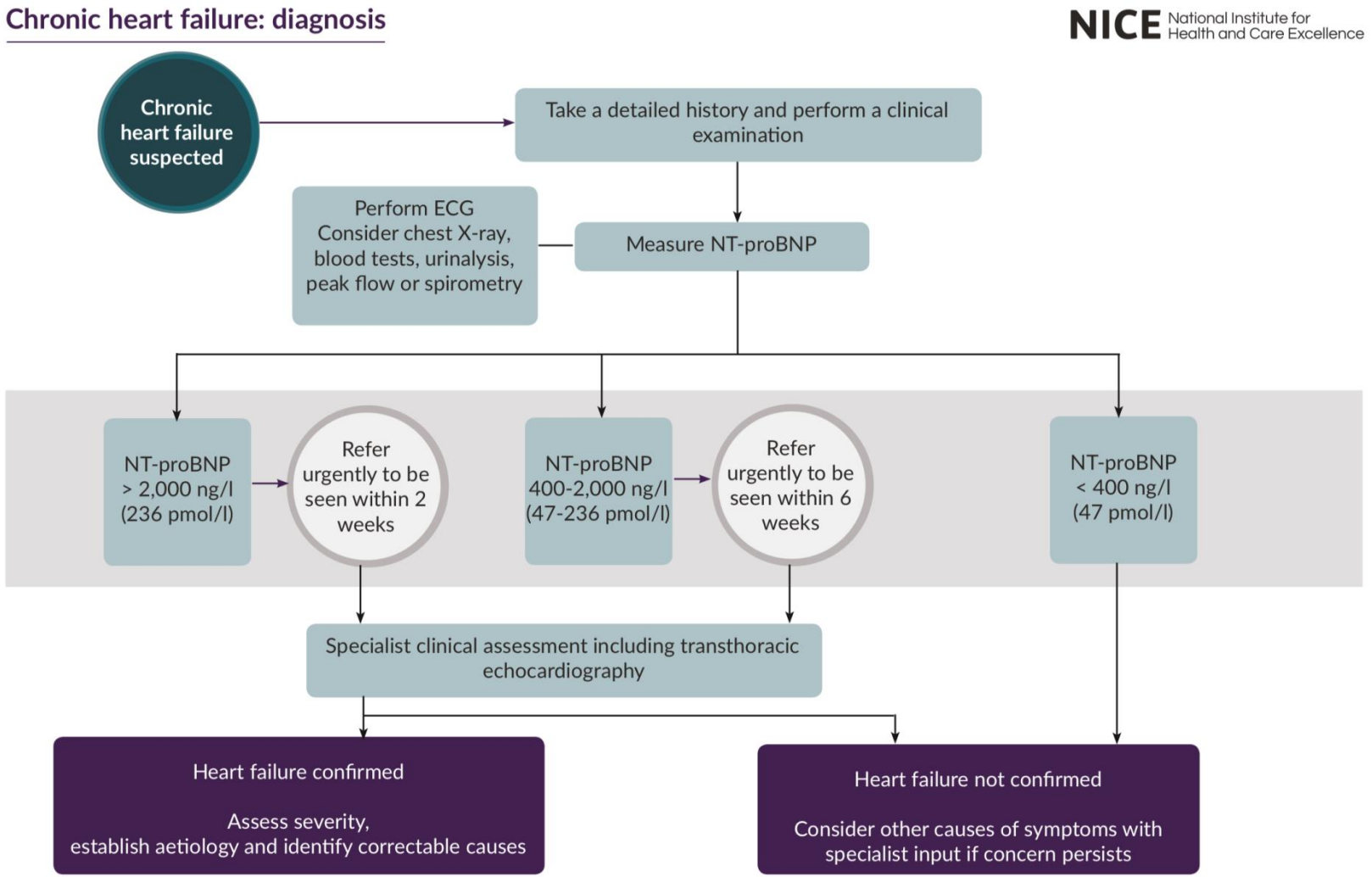
N-Terminal pro-B-type Natriuretic Peptide



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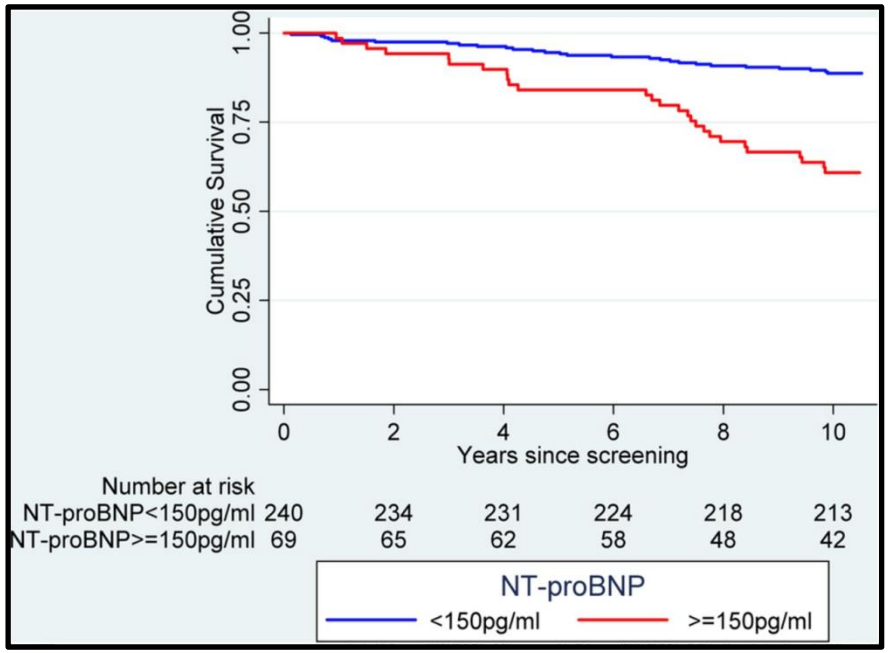
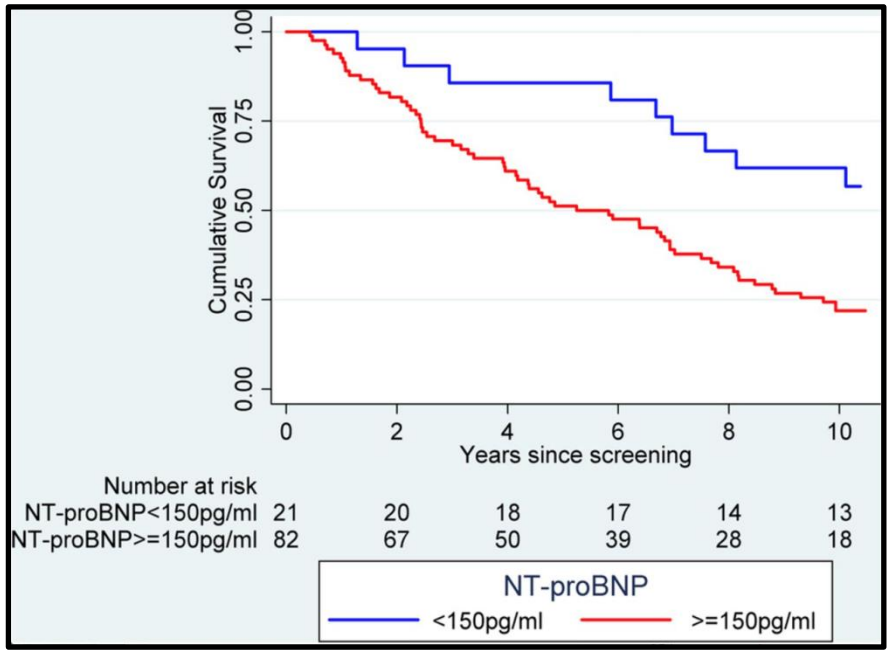
NT-proBNP

- Particularly useful in non-acute setting, e.g. primary care
- High negative predictive value (94-98%) for heart failure – good for exclusion
- But low positive predictive value (44-57%) – not good for diagnosis
- Very high BNP (>2000) carries a poor prognosis, so these patients need urgent specialist assessment within 2 weeks
- Levels do not differentiate between HFrEF, HFmrEF or HFpEF, although tend to be lower in HFpEF/HFmrEF
- Other causes of a raised BNP:

  LVH, ischaemia, tachycardia, RV overload,
  hypoxia, PE, renal dysfunction, sepsis,
  COPD, Diabetes, Age>70, Liver cirrhosis, AF
- Factors reducing BNP levels:

  Obesity, Diuretics, Beta-blockers, ACEIs, ARBs,
  MRAs, Afro-Caribbean ethnicity





Normal population

Heart failure population

RR = 17.7 for NT-proBNP > 150

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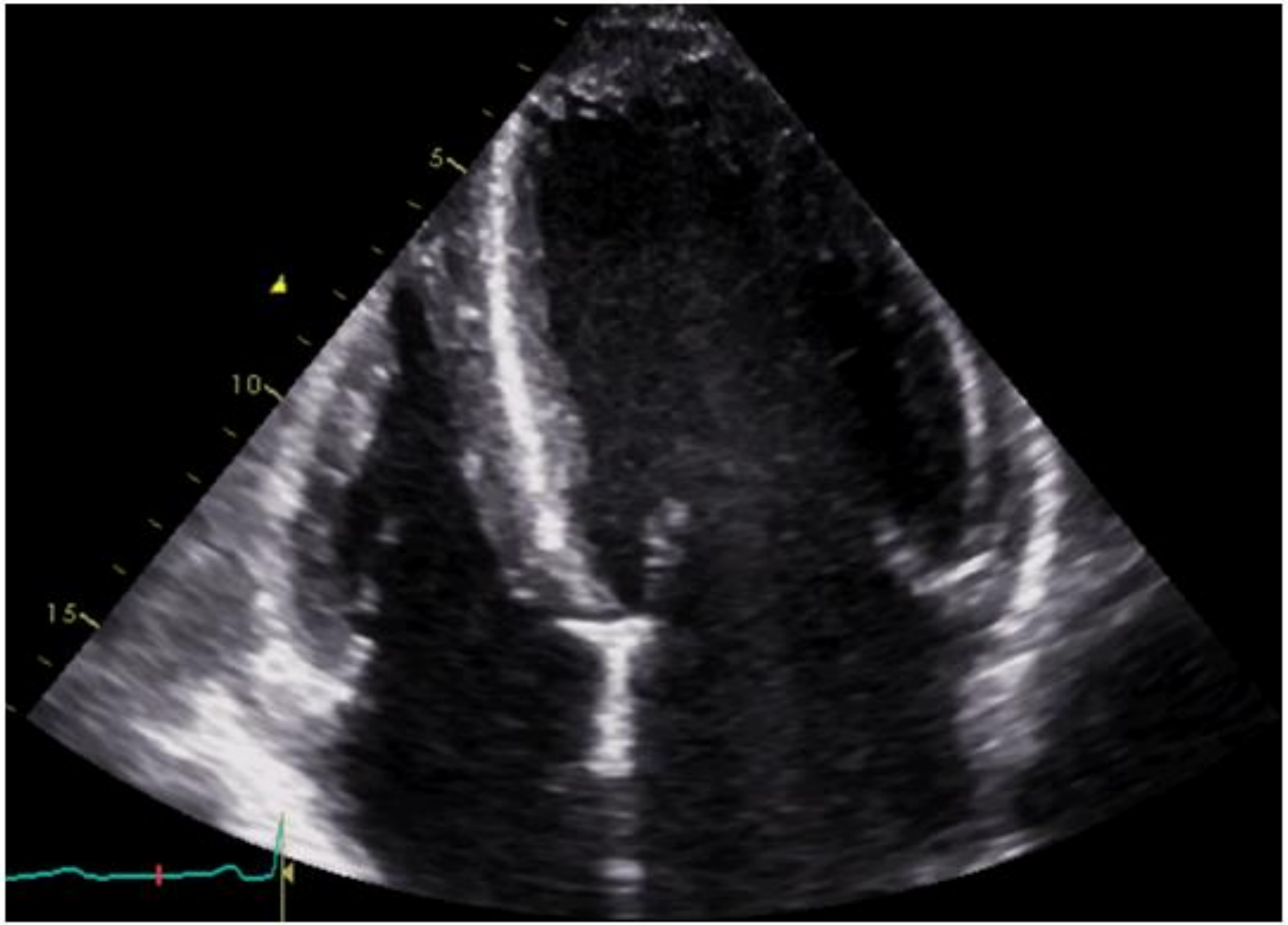
Taylor CJ et al, The potential role of NT-pro-BNP in screening for and predicting prognosis in heart failure: a survival analysis, BMJ Open, 2014; 4:e004675. doi: 10.1136/bmjopen-2013-004675

Investigations

- **Echocardiogram: the key investigation**
  - Confirms systolic or diastolic dysfunction
  - Can identify causes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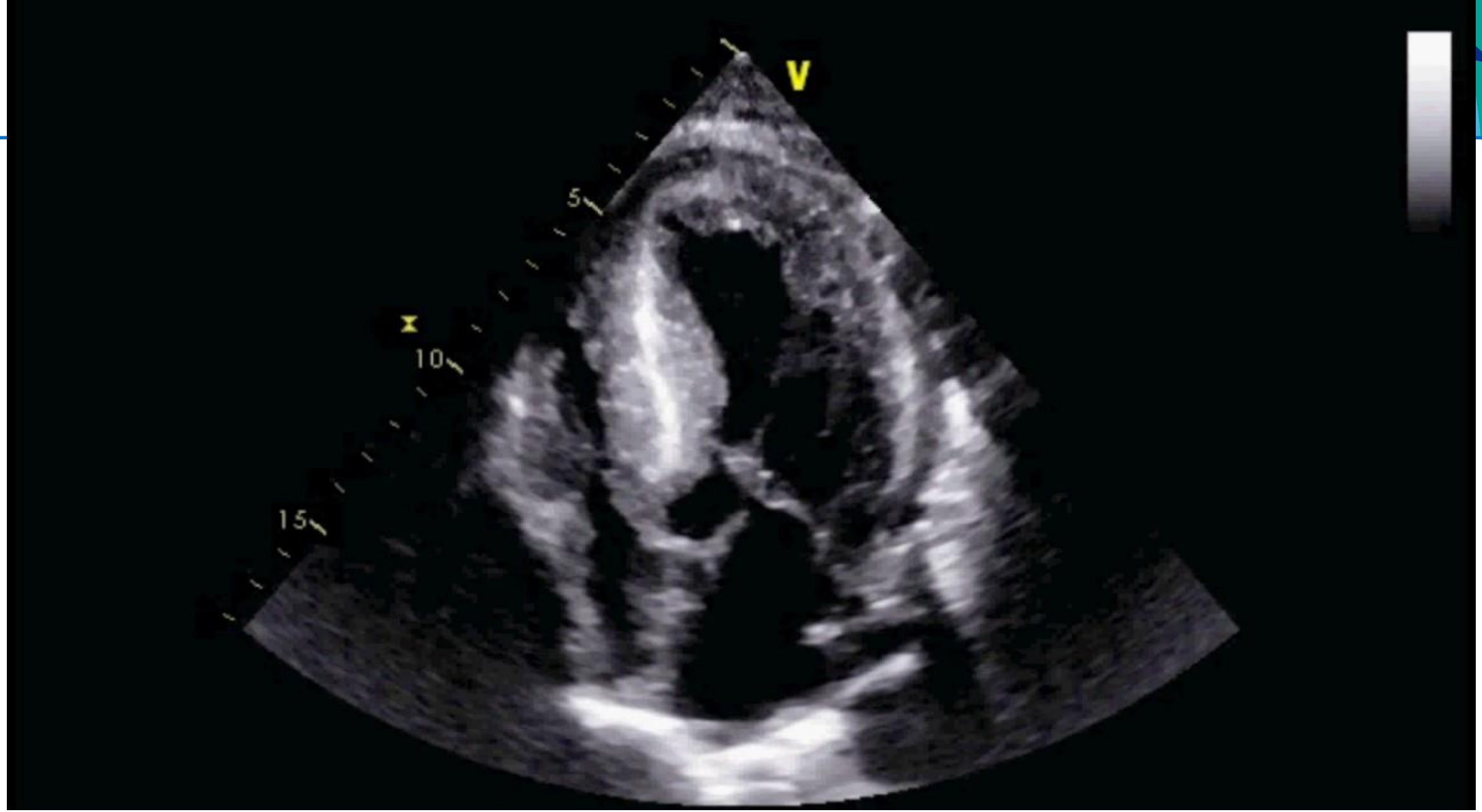
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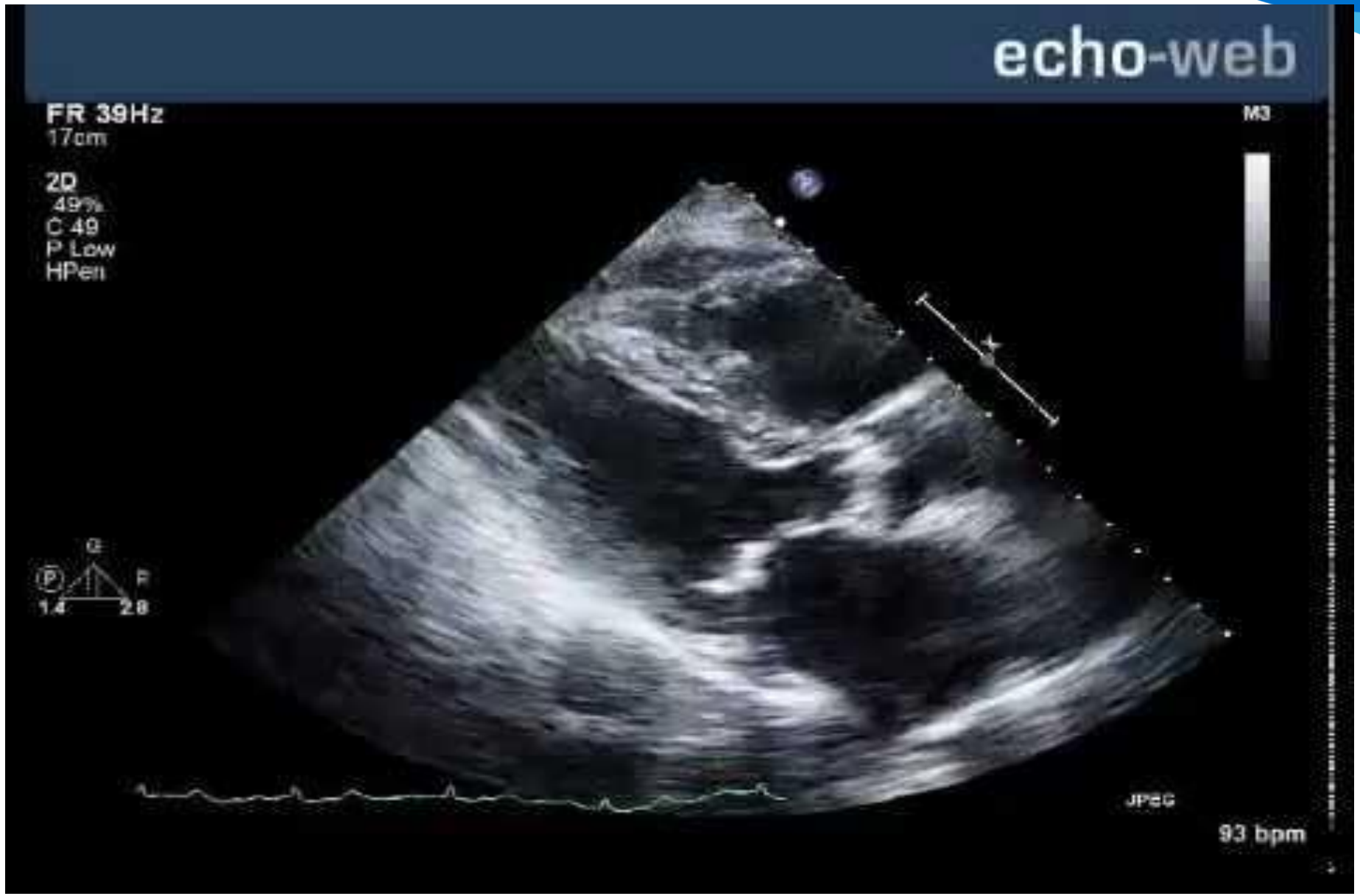

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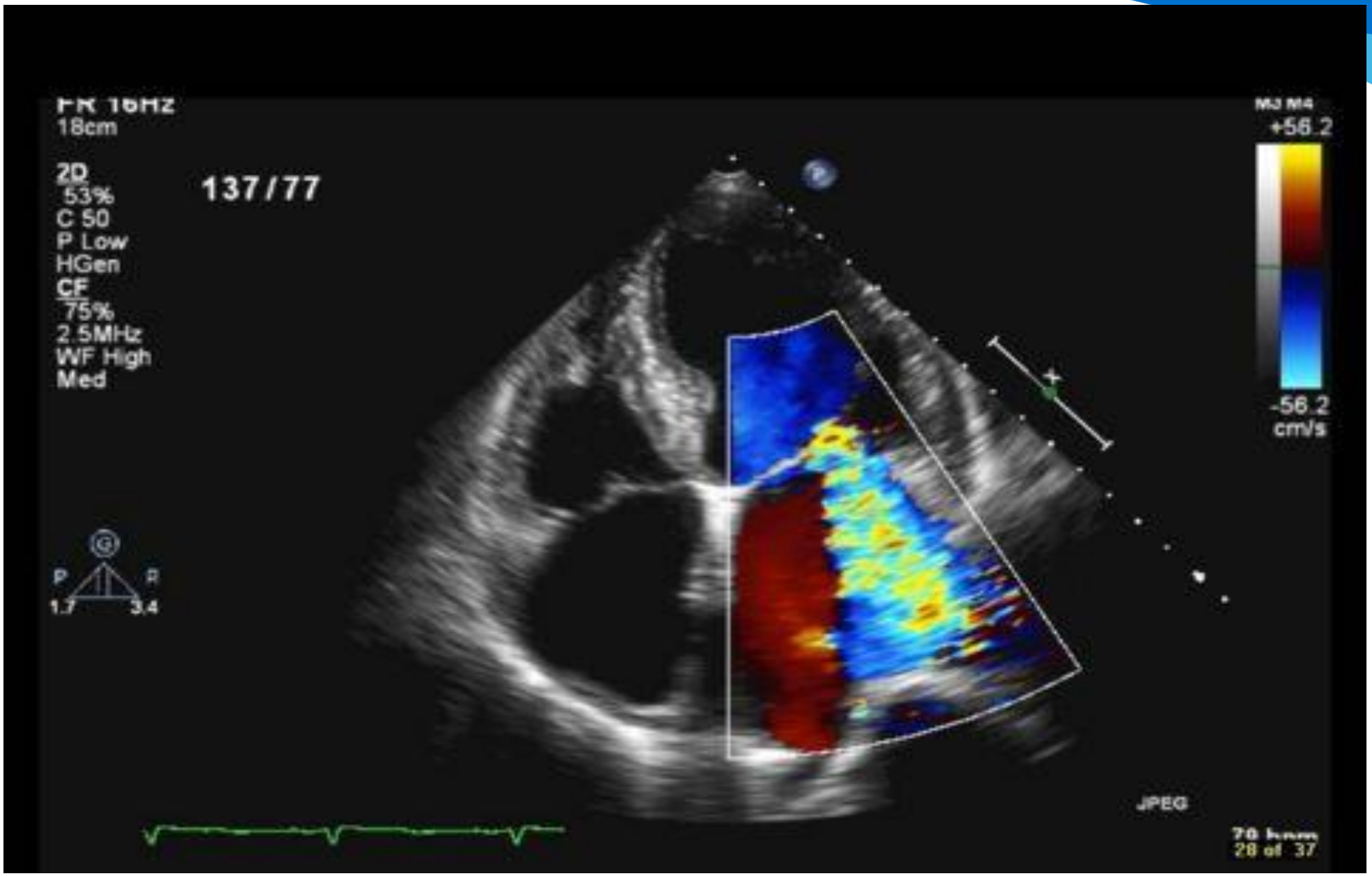

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Coding!

Check date the problem was coded and cross check in communication & letters: Is there a letter or an ECHO result?

If Echo or letter, check ejection fraction (EF) % and other information from HF team

Code the patient appropriately

1.	HFrEF (HF with EF≤40%)*	Snomed: 703272007
	AND Echo shows LVSD	Snomed: 407596008
2.	HFmrEF (HF with EF 41-49%)	Snomed: 788950000
3.	HFpEF (HF with EF≥50%)	Snomed: 446221000

*Patients with an original HFrEF diagnosis with an improved ejection fraction - i.e more recent ECHO with EF>40% due to optimisation should still be considered HFrEF as per original diagnosis and must remain on their prognostic medications

UCL Framework for HF
https://s42140.pcdn.co/wp-content/uploads/HF-pathway-NOV23-v2.pdf

Pharmacological Treatment

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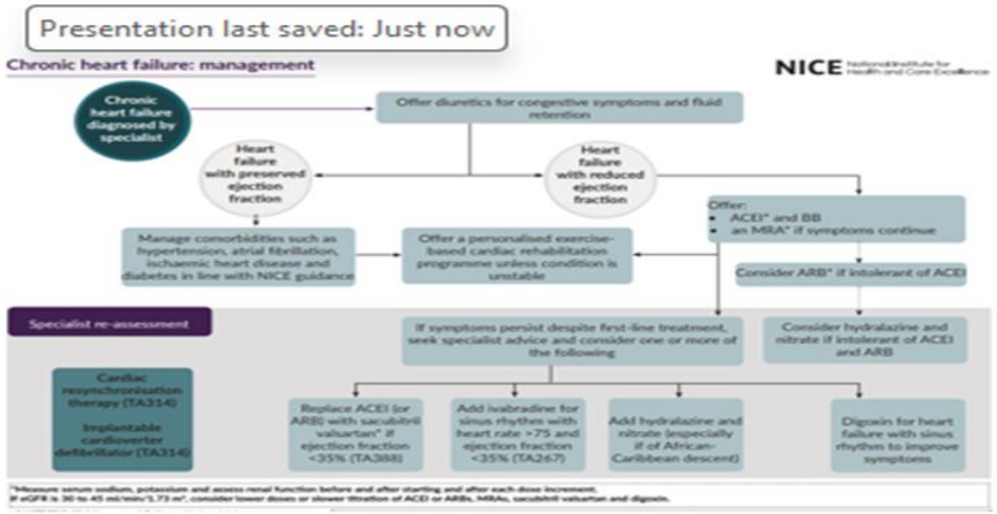
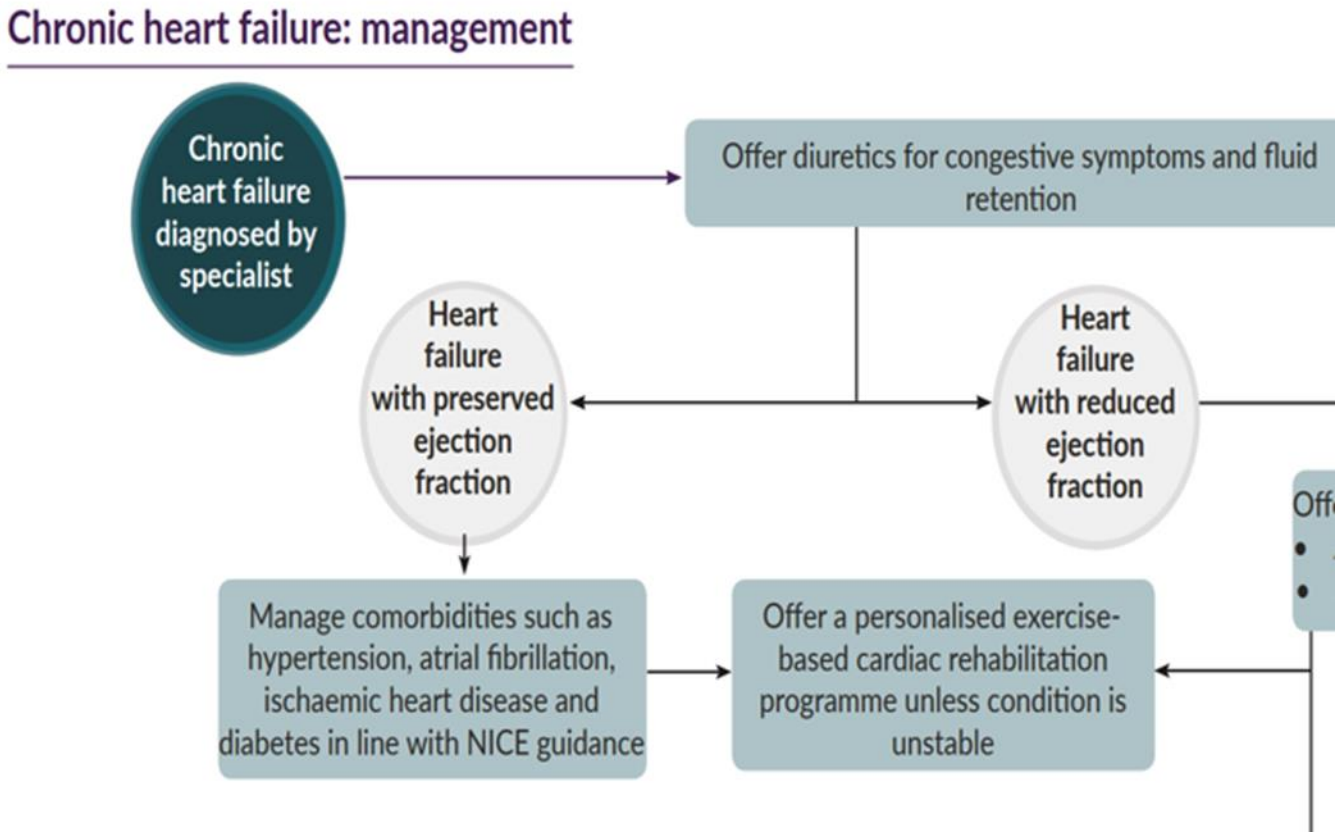
NICE Guidelines are out of date!

NICE Statement April 2023



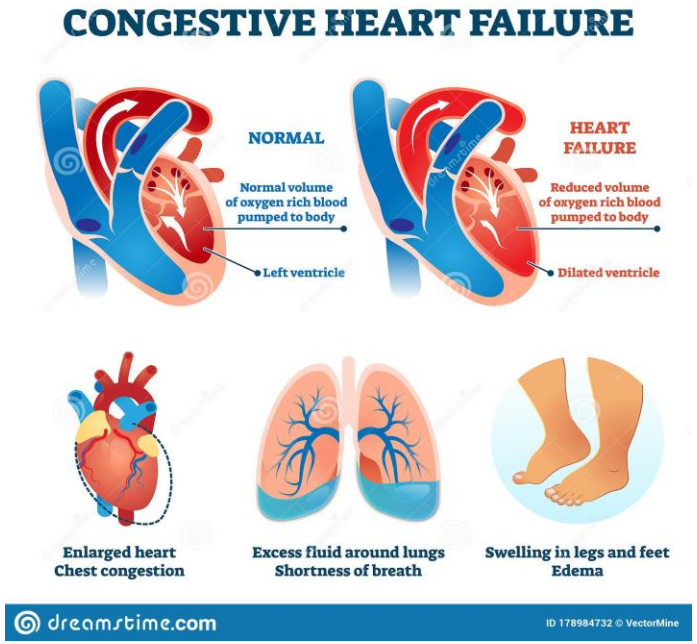
After considering the evidence and other intelligence, we will update the recommendations on pharmacological management for people with chronic heart failure

Step 1 still stands: diuretic for congestion



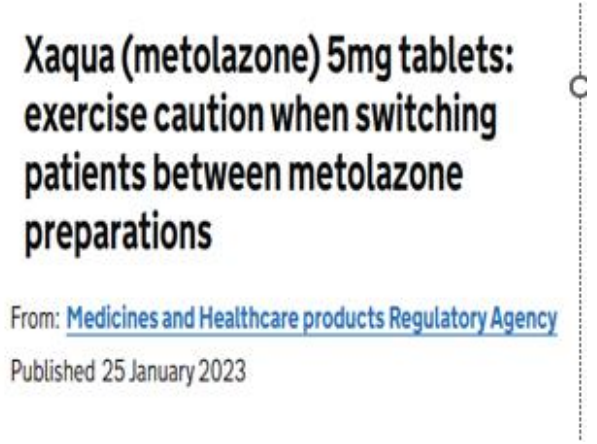
Loop Diuretics

- Control symptoms of fluid retention
- No mortality benefit proven
- Titrate dose to symptoms: increase or decrease
- Important to check what the patient takes
  - not what has been prescribed
- Monitor carefully: renal function, weight (same scales), electrolytes (K+, Na+, Mg++)



Treatment strategies if diuretics ‘not working’ ?

- May need to increase dose (remember to advise on timings of doses)
- Check concordance
- Add thiazide diuretic (e.g., bendroflumethazide or metolazone)
- Add MRA = mineralocorticoid receptor antagonist
  - e.g., spironolactone
- Refer to specialist HF service
  - community / day case / virtual ward / hospital admission for IV therapy



Prognostic Treatment HFrEF

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2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

European Heart Journal (2021) **42**, 3599–3726
doi:10.1093/eurheartj/ehab368

5.3 Drugs recommended in all patients with heart failure with reduced ejection fraction

Pharmacological treatments indicated in patients with (NYHA class II–IV) heart failure with reduced ejection fraction (LVEF ≤40%)

Recommendations	Class[a]	Level[b]
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[110–113]	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.[114–120]	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[121,122]	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[108,109]	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.[105]	I	B

ACE-I = angiotensin-converting enzyme inhibitor; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association.
[a]Class of recommendation.
[b]Level of evidence.

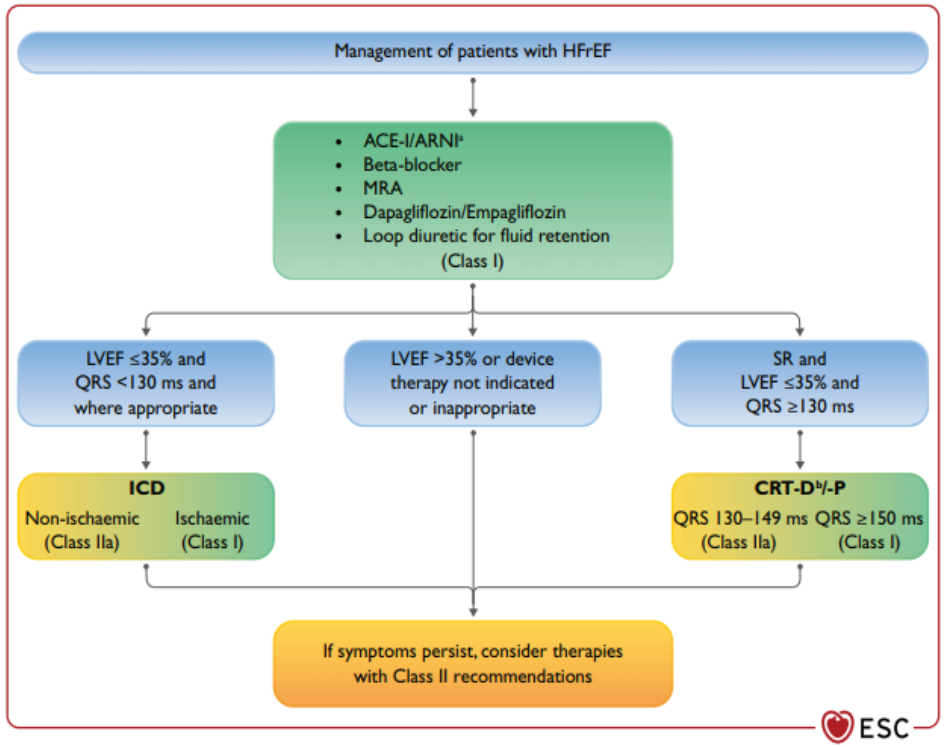
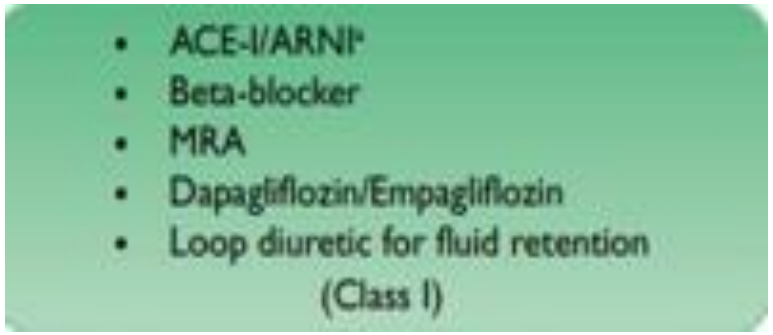


Figure 2 Therapeutic algorithm of Class I Therapy Indications for a patient with heart failure with reduced ejection fraction. ACE-I = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor-neprilysin inhibitor; CRT-D = cardiac resynchronization therapy with defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; ICD = implantable cardioverter-defibrillator; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; QRS = Q, R, and S waves of an ECG; SR = sinus rhythm. [a]As a replacement for ACE-I. [b]Where appropriate. Class I = green. Class IIa = Yellow.

Current thinking

- Traditional step wise approach considered outdated
- Much more rapid initiation and optimisation of treatment
- Personalised with respect to order
- Looking to introduce ‘4 pillar treatment’



Pillar 1

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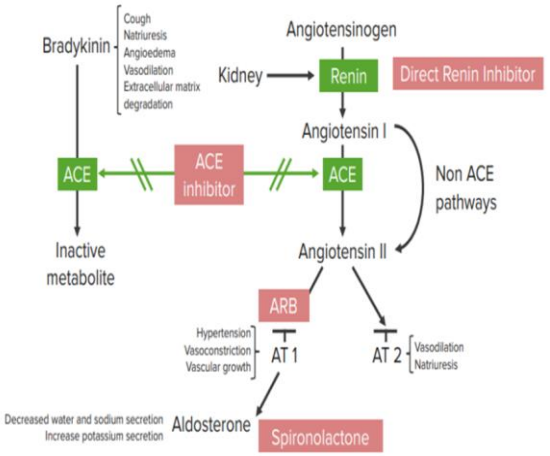
ACEi (or ARB)

- Start at low dose and titrate aiming for maximum dose (maximum tolerated dose)
- Re-check renal function and potassium 1-2 weeks after any dose change.
- Re-assess BP
  - Asymptomatic hypotension does not usually warrant decrease dose
  - Symptomatic hypotension
    - are there any other medicnes that can be stopped
    - euvolemic ? – can the diuretic be decreased
    - check for postural hypotension
- ARB should only be used if intolerant of ACEi – usual reason is ACEI cough
  - Candesartan, losartan or valsartan



RAAS inhibitors: renal function

Change in renal function associated with drug treatment in heart failure: national guidance

To cite: Clark AL, Kalra PR, Petrie MC, *et al*. *Heart* 2019;**105**:904–910.

Table 1 Management of RAAS inhibitors in response to change in renal function

Clinical assessment:

- Compare with baseline renal function (review series of results).
- Assess fluid status: if intravascularly depleted (jugular venous pulse not visible, postural drop in BP and no oedema), consider cautious intravenous fluids.
- Interpret BP in the context of usual values (low BP does not necessarily mean patient needs fluid).
- Reduce/withdraw RAASI if symptomatic hypotension.
- Repeated clinical and biochemical assessment is vital.
- Presence of moderate or severe hyperkalaemia may override recommendations based on change in renal function.
- In severe renal dysfunction assess for symptoms or uraemia.

	Recommendations for RAAS inhibitors	
Change in renal function compared with baseline	**HFpEF (assuming no other prognostic indication).**	**HFREF.**
Increase in serum creatinine by <30%	Consider stop ACEI/ARB/ARNI Review MRA according to fluid status.	Continue unless symptomatic hypotension.
Increase in serum creatinine 30%–50%	Stop RAAS inhibitor.	Consider reducing dose or temporary withdrawal.*
Increase in serum creatinine >50%	Stop RAAS inhibitor.	Temporarily stop RAAS inhibitor.*
Severe renal dysfunction, for example, eGFR <20	Stop RAAS inhibitor.	Stop RAAS inhibitor if symptomatic uraemia irrespective of baseline function.

*Reinitiate and/or retitrate when renal function improved in patients with HFrEF.

ACEI, ACE inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced left ventricular ejection fraction; HFpEF, heart failure with preserved left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonists; RAAS, renin–angiotensin–aldosterone.

RAAS inhibitors : potassium

Change in renal function associated with drug treatment in heart failure: national guidance

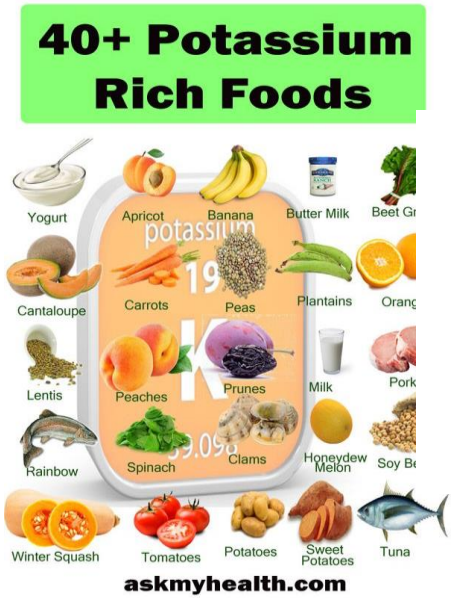
To cite: Clark AL, Kalra PR, Petrie MC, *et al*. *Heart* 2019;**105**:904–910.

Table 2 Considerations when managing a patient with heart failure who develops hyperkalaemia

Serum K^+ >5.4	All patients		
Check for overdiuresis/hypovolaemia. Non-selective beta-blockers can increase potassium. Review indication (prognostic benefit in HFrEF but not HFpEF) – try to continue in HFrEF. Stop K supplements. Stop amiloride and triamterene. Stop non-steroidal anti-inflammatory drugs. Stop trimethoprim. Stop sodium substitutes. Check for digoxin toxicity. Provide low K diet advice.			
Serum K^+	**Mild hyperkalaemia 5.5–5.9 mmol/L**	**Moderate hyperkalaemia 6.0–6.4 mmol/L**	**Severe hyperkalaemia >6.5 mmol/L**
Patient clinically well, no AKI	Increase frequency of biochemical monitoring but do not stop RAAS inhibitors. Consider reducing dose.	Stop RAAS inhibitor(s), repeat test Re-start at lower dose once K^+<5.5 Re-start one drug at a time, with biochemical monitoring, if the patient was previously on a combination of ACEI/ARB/ARNI plus MRA.	Admit to hospital for immediate K^+-lowering treatment. Stop RAAS inhibitor(s). Repeat blood test 24 hours later. Restart at lower dose once K^+ <5.5 Restart one drug at a time, with biochemical monitoring, if the patient was previously on a combination of ACEI/ARB/ARNI plus MRA.
Patient clinically unwell with sepsis or hypovolaemia and/or AKI.	Withhold RAAS inhibitors until sepsis/hypovolaemia corrected, then restart.	Withhold RAAS inhibitor(s) until sepsis/hypovolaemia corrected, then restart once K^+ <5.5.	Withhold RAAS inhibitor(s) until sepsis/hypovolaemia corrected, then restart once K^+ <5.5. Restart one drug at a time, with biochemical monitoring, if the patient was previously on a combination of ACEI/ARB/ARNI plus MRA.
Patient clinically unwell with decompensated heart failure with/without AKI	Do not withhold RAAS inhibitors. Consider reduce dose. Treat congestion with loop diuretics or combination of loop and thiazide diuretics.	Reduce dose of RAAS inhibitor(s) and monitor frequently. Treat congestion with loop diuretics or combination of loop and thiazide diuretics.	Withhold RAAS inhibitor(s) and restart at lower dose when serum K^+ <6.0. Restart one drug at a time, with biochemical monitoring, if the patient was previously on a combination of ACEI/ARB/ARNI plus MRA.

ACEI, ACE inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blocker; ARNI angiotensin receptor-neprilysin inhibitor; RAAS, renin–angiotensin–aldosterone; MRA, mineralocorticoid receptor antagonist.

NB Hyperkalaemia may be artefactual in samples sent from primary care: this can be caused by fist clenching during phlebotomy, use of small-gauge needles causing low-grade haemolysis, prolonged tourniquet use, and most importantly, delays in sample processing, particularly in cold weather.



Improving Lives Together

Specialist team initiate: sacubitril+ valsartan (Entresto®)

- Particularly if patient remains symptomatic on good treatment or younger patients or very low ejection fraction

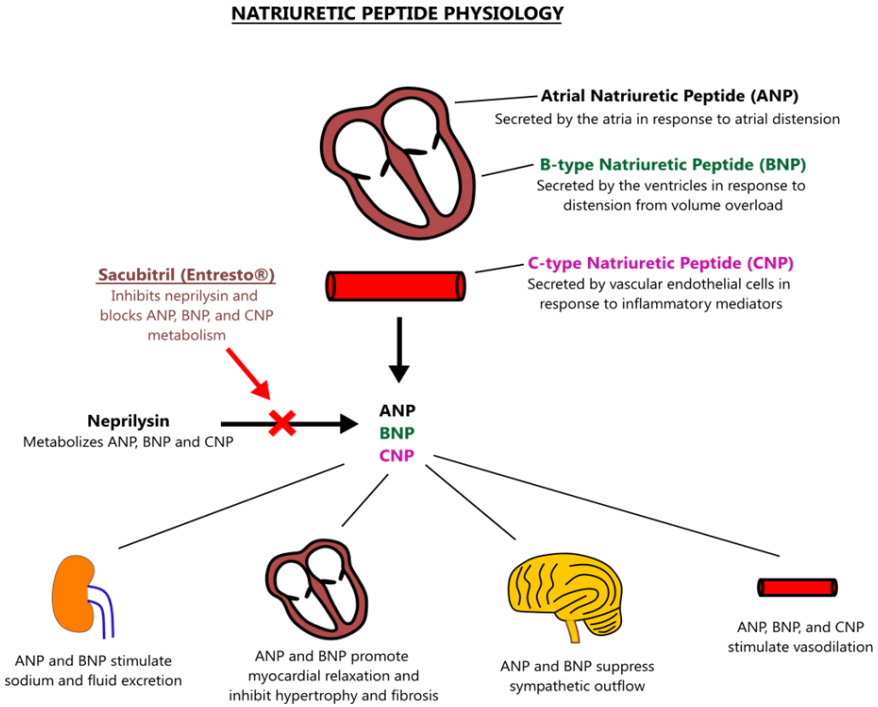
1 Recommendations

NICE
National Institute for Health and Care Excellence

1.1 Sacubitril valsartan is recommended as an option for treating symptomatic chronic heart failure with reduced ejection fraction, only in people:

- with New York Heart Association (NYHA) class II to IV symptoms and
- with a left ventricular ejection fraction of 35% or less and
- who are already taking a stable dose of angiotensin–converting enzyme (ACE) inhibitors or angiotensin II receptor–blockers (ARBs).

https://www.nice.org.uk/Guidance/TA388 **April 2016**



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Switching to ARNI

Do not have to be on maximum dose ACE/ARB before switching to ARNI

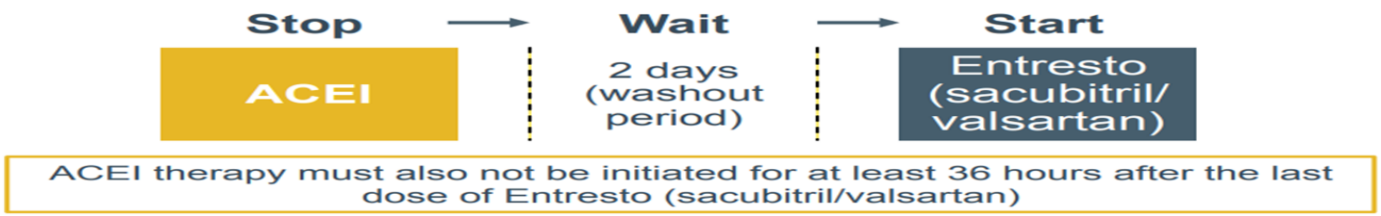
More hypotension
Naturesis: may need to reduce dose of diuretic
Start at low or middle dose and titrate
Monitor RF and potassium (as you would with ACEi/ARB)

IMPORTANT

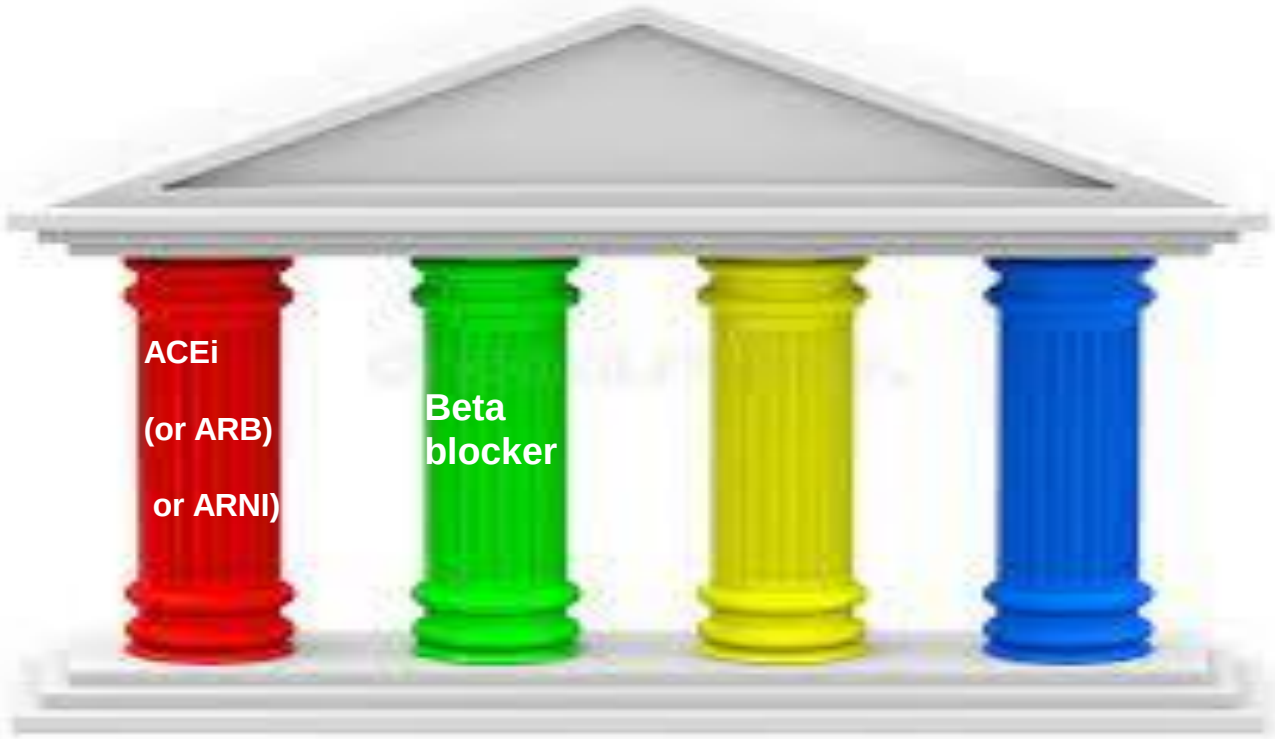
A washout period is required when switching from an ACEI[1]

The combination of Entresto (sacubitril/valsartan) with an ACEI is contraindicated due to the increased risk of angioedema

- Entresto (sacubitril/valsartan) must not be initiated for at least 36 hours after the last dose of ACEI therapy



Pillar 2



Improving Lives Together

Beta-blocker – licensed for HFrEF

- Clear evidence that beta-blockers reduce mortality in addition to RAS inhibitor

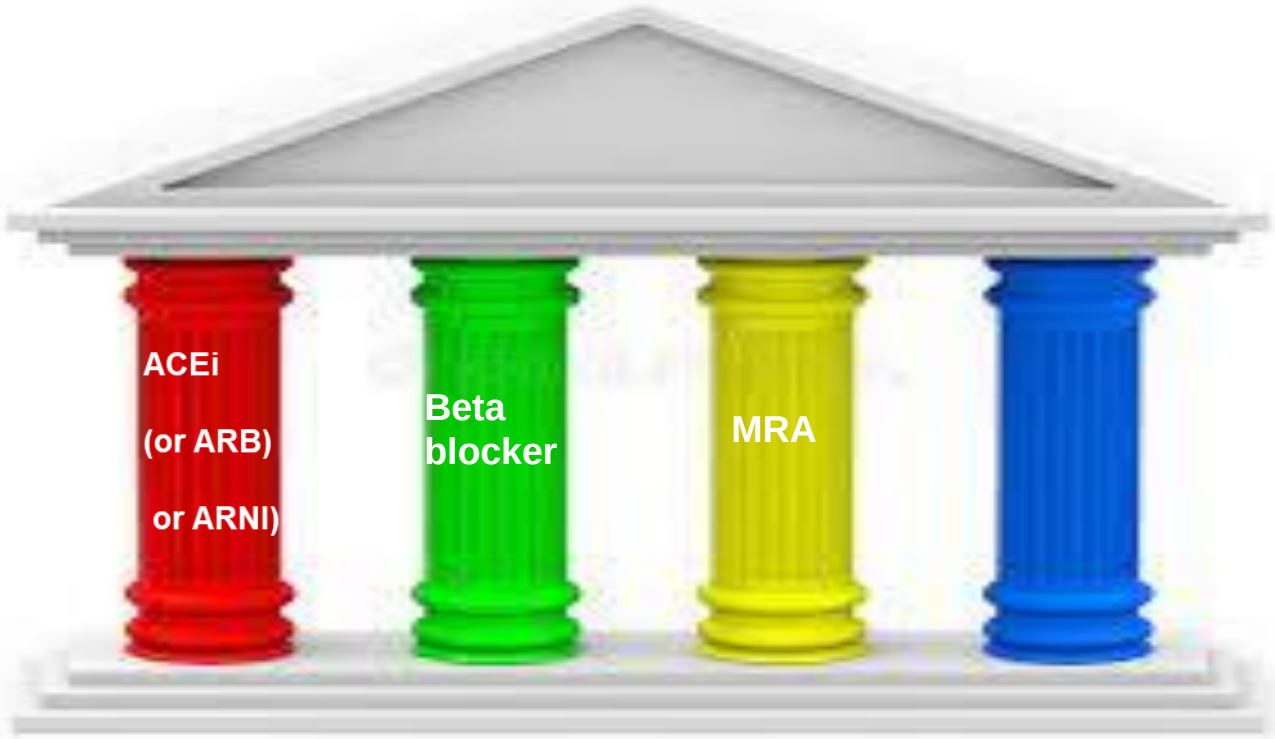
- Only prescribe beta-blocker licensed for HFrEF.
  In UK = **bisoprolol or carvedilol** or nebivolol

- Start at low dose and titrate: monitor blood pressure and heart rate
  - In sinus rhythm - aim for resting heart rate (60 bpm)
  - In AF benefits less clear - aim for good AF rate control (HR 80bpm)

- Target doses

  bisoprolol = 10mg/day carvedilol = 25mg bd (50mg bd if > 85kg) nebivolol = 10mg od

Pillar 3



Improving Lives Together

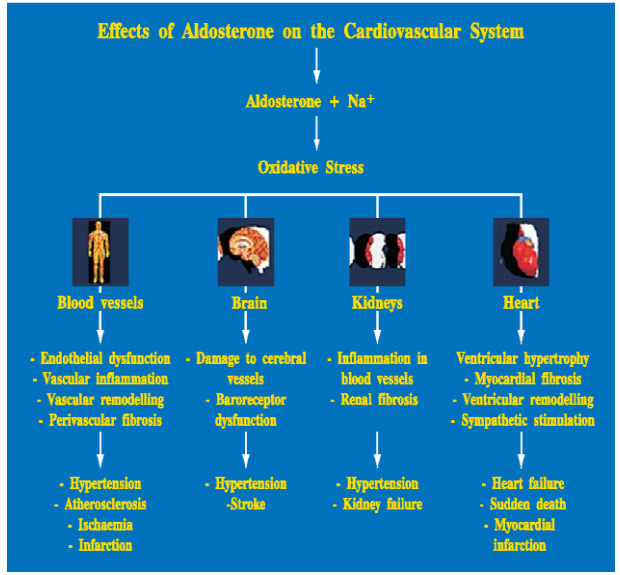
Mineralocorticoid Receptor Antagonist (MRA): Spironolactone or Eplerenone

- **Not being prescribed simply as a diuretic**

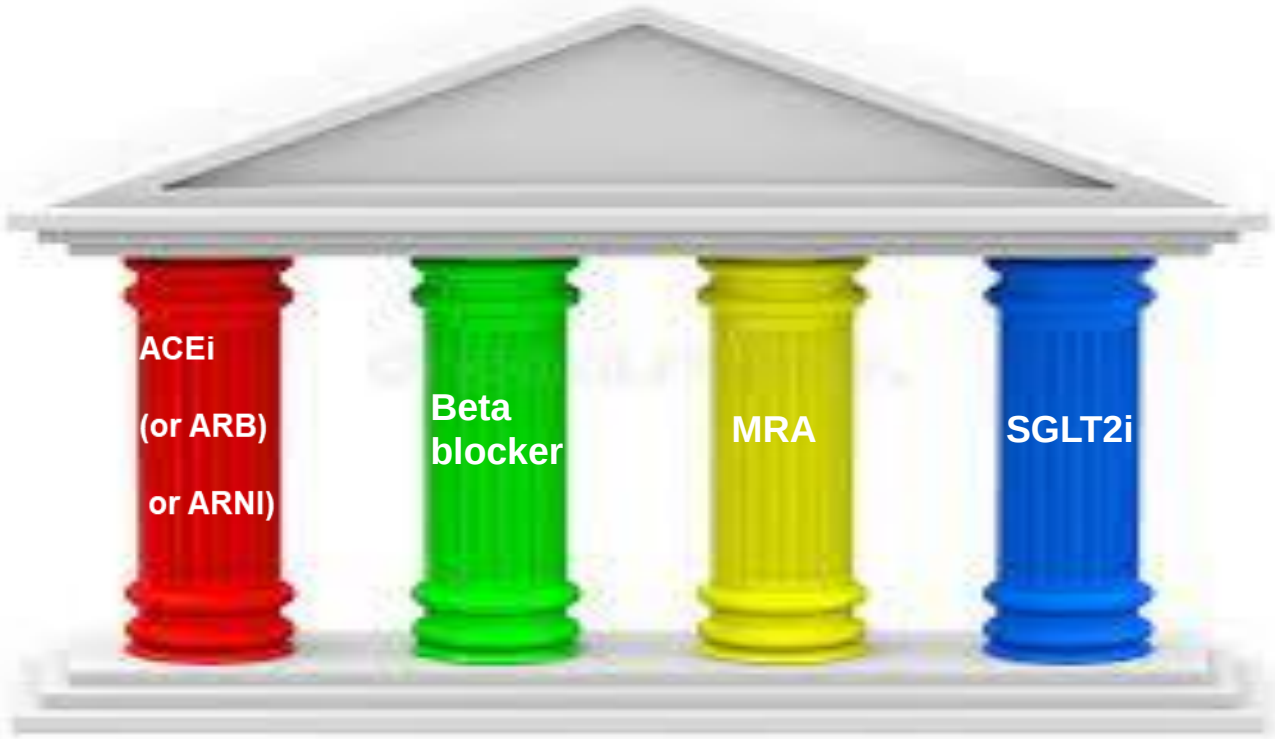
- Prognostic treatment in
  - HFrEF
  - Post ACS with EF< 40% and symptoms or diabetes: eplerenone

- Risk of renal impairment and hyperkalemia
  - Check at 1 week, 1 month, 2 months, 3 months, 6 months
  - If normal RF and stable check 6 monthly
  - If CKD may need to check more frequently
- **Do not exceed dose of 50mg once a day**

- Gynecomastia with spironolactone



Pillar 4



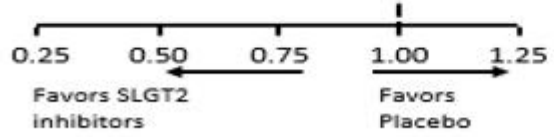
Sodium glucose cotransporter 2 inhibitor (SGLT2i)

- Developed as treatment for diabetes
  - Increase urinary excretion of glucose
- Cardio-vascular outcome trial (CVOT) required
  - Need to demonstrate neutral for CV outcomes
  - Showed benefits – particularly in HF outcomes
- Two studies undertaken in HFrEF +/- type 2 diabetes
  - **DAPA-HF trial** N Engl J Med 2019; 381:1995-2008
  - **EMPEROR Reduced trial** N Engl J Med 2020; 383:1413-1424

Outcomes DAPA-HF and EMPEROR-REDUCED

EMPEROR-Reduced and DAPA-HF: Reduction in HF Hospitalization or CV Death With SGLT2 Inhibitors in HFrEF

	No. With Event/No. of Patients (%)		HR (95% CI)
	SGLT2 Inhibitor	Placebo	
With diabetes			
EMPEROR-Reduced	200/927 (21.6)	265/929 (28.5)	0.72 (0.60-0.87)
DAPA-HF	215/1075 (20.0)	271/1064 (25.5)	0.75 (0.63-0.90)
Subtotal			**0.74 (0.65-0.84)**
Test for overall treatment effect, P <.0001 Test for heterogeneity of effect, P = .76			
Without diabetes			
EMPEROR-Reduced	161/936 (17.2)	197/938 (21.0)	0.78 (0.64-0.97)
DAPA-HF	171/1298 (13.2)	231/1307 (17.7)	0.73 (0.60-0.88)
Subtotal			**0.75 (0.65-0.87)**
Test for overall treatment effect, P <.0001 Test for heterogeneity of effect, P = .65 Test for treatment by subgroup interaction, P = .81			



Zannad. Lancet. 2020;396:819.

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SGLT2i outcomes: evidence into practice

- Safety outcomes from HFrEF trials with SGLT2i
  - No new safety concerns raised

- Benefits seen in non–diabetics and type 2 DM (do not Rx 1DM)
  - May need downward adjustment of dose of insulin and /or sulphonlyurea (e.g gliclazide)

- Benefits appeared early – improvement in quality of life as soon as 4/52

- Small reduction in blood pressure (more if BP raised)
- Small reduction in potassium
- Initial small rise in Cr / dip in eGFR but over time renal protective
- May have to reduce diuretic dose

Potential ADRs

Common side effects include: dizziness, rash, back pain, UTI, vulvovaginitis/balanitis, dysuria or polyuria, initial dip in CrCl, hypoglycaemia (with insulin or sulphonylureas)

Risk of diabetic ketoacidosis (DKA)
Inform patients of the signs and symptoms of DKA, (including rapid weight loss, nausea or vomiting, abdominal pain, fast and deep breathing, sleepiness, a sweet smell to the breath, a sweet or metallic taste in the mouth, or a different odour to urine or sweat), and advise them to seek immediate medical advice if they develop any of these.
GP/hospital to test for raised ketones in patients with signs and symptoms of DKA, even if plasma glucose levels are near-normal or normal.

Rare or very rare - Angioedema; Fournier's gangrene (Rare but potentially life threatening infection – discontinue. Urgent medical attention needed)

With Intercurrent illness:

Temporarily withhold dapagliflozin (or any other SGLT2 inhibitor) in patients who

- are hospitalised for major surgery or acute serious illnesses (MRHA 2020): blood ketone levels should be monitored (and be normal before restarting)
- also consider stopping in any other hospital admission until patient well/stable -if unsure withhold and seek advice from senior member of the team
- are not eating or drinking
- with inter-current conditions that may lead to volume depletion (e.g. vomiting /diarrhoea)
- have major infection

Treatment may be restarted once the patient's condition has stabilised and they are eating normally for at least 24 hours (providing no new contra-indications exist -see above)

https://int.sussex.ics.nhs.uk/clinical_documents/sglt2i-guideline-for-the-safe-and-appropriate-use-of-sodium-glucose-co-transporter-2-inhibitors-sglt2-inhibitors-in-adults/

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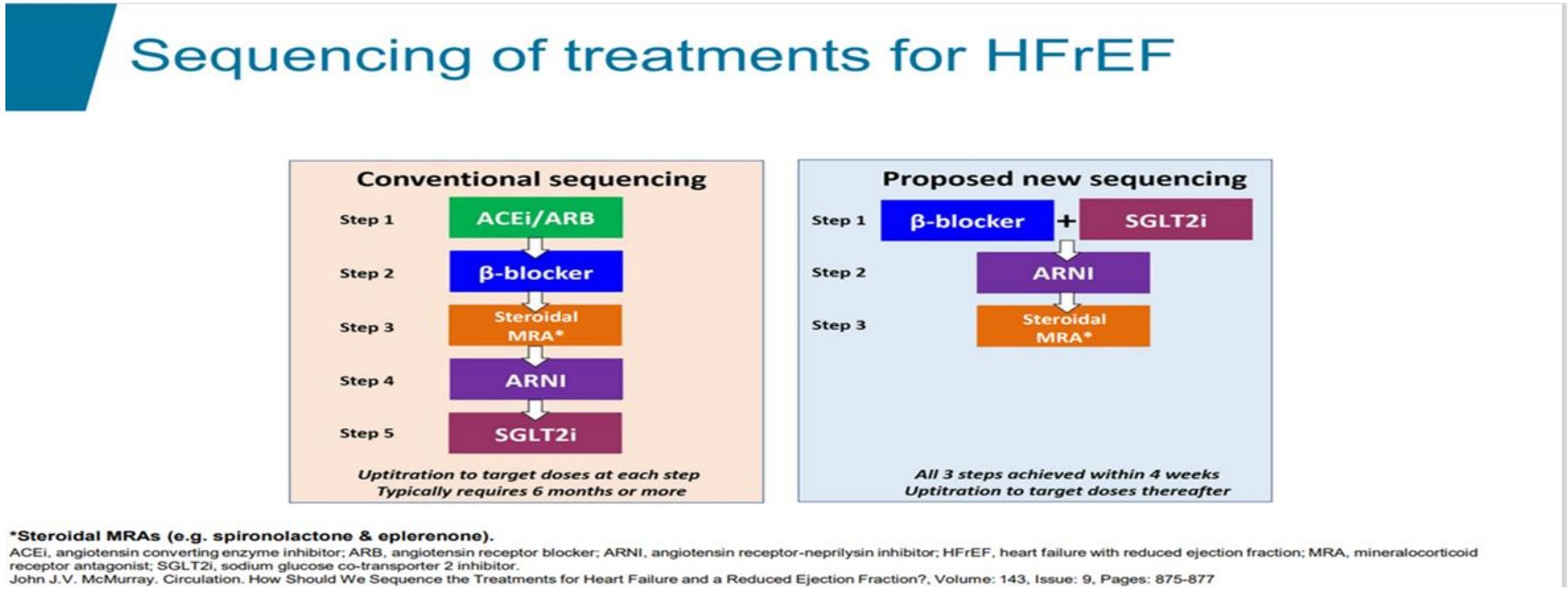
Modelling – ? Change of sequencing



- Order to be personalised
- Initiate early x 4 and then titrate
- Safe for hospitalised patients (STRONG-HF trial)

The Lancet 2022 400 10367 1938-1952

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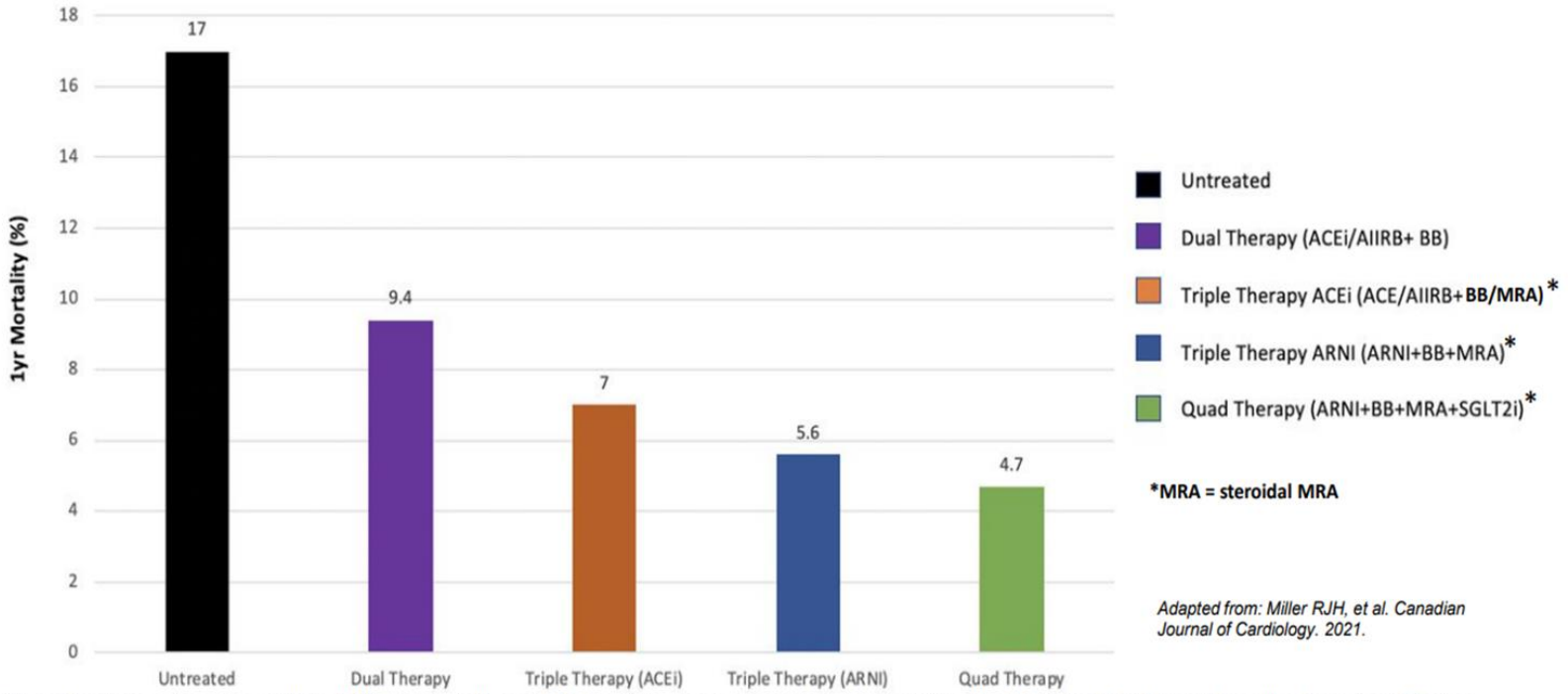
Four pillar benefits…….

Mortality rate at 1 year for additive therapies for HFrEF



Adapted from: Miller RJH, et al. Canadian Journal of Cardiology. 2021.

ACEi, angiotensin converting enzyme inhibitor; AIIRB, angiotensin II receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BB, beta blocker; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium glucose co-transporter 2 inhibitor.

Miller RJH, Howlett JG, Fine NM. A Novel Approach to Medical Management of Heart Failure with Reduced Ejection Fraction. Canadian Journal of Cardiology. 2021 Apr;37(4):632–43.

Other treatments you might see for HFrEF

Ivabradine : If additional rate control needed

- In HFrEF if HR >75bpm + symptomatic + in sinus rhythm + on maximum tolerated dose BB

Digoxin

- Useful for rate control in AF
- In sinus rhythm symptomatic relief but no mortality benefit

Hydralazine and nitrates

- Alternative in ACEI/ARB intolerant patients
- Addition of hydralazine and nitrate (especially if of African Caribbean descent)

Intravenous Iron infusion : low iron stores

- Improves quality of life measures (delivered via secondary care)

Potassium binders

- Patiromer (Veltassa®) or sodium zirconium cyclosilicate (Lokelma®)
- May allow prescription of RAAS inhibitors +/- MRA if high potassium levels are dose limiting.

Non-Pharmacological Treatments for Heart Failure

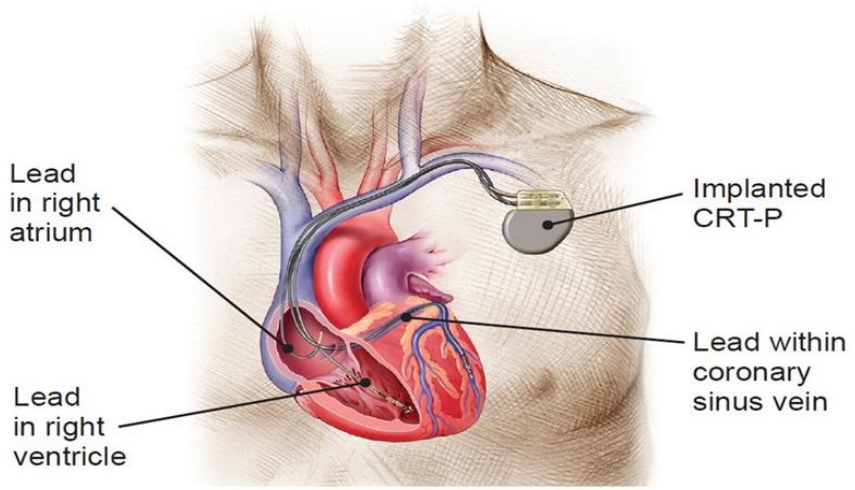
- **Cardiac resynchronisation therapy (CRT)**
  - Paces both ventricles simultaneously in patients with LV dys-synchrony (LBBB), to improve co-ordination of LV contractility
- **Implantable cardiac defibrillator (ICD)**
  - In heart failure, risk of ventricular arrhythmias and SCD can be higher
  - ICD's can recognize and treat life-threatening arrhythmias
- **Dialysis & ultrafiltration**
- **Left ventricular assist device (LVAD)**
  - Bridge to transplant or to transplant assessment
- **Cardiac transplantation**

Treatment options with ICD or CRT for patients with heart failure and HFrEF with an EF of 35% or less

	NYHA class			
QRS interval	**I**	**II**	**III**	**IV**
<120 milliseconds	**ICD if there is a high risk of sudden cardiac death**			**ICD and CRT not clinically indicated**
120–149 milliseconds without LBBB	ICD	ICD	ICD	CRT-P
120–149 milliseconds with LBBB	ICD	CRT-D	CRT-P or CRT-D	CRT-P
≥150 milliseconds with or without LBBB	CRT-D	CRT-D	CRT-P or CRT-D	CRT-P

LBBB, left bundle branch block; NYHA, New York Heart Association

Cardiac Devices



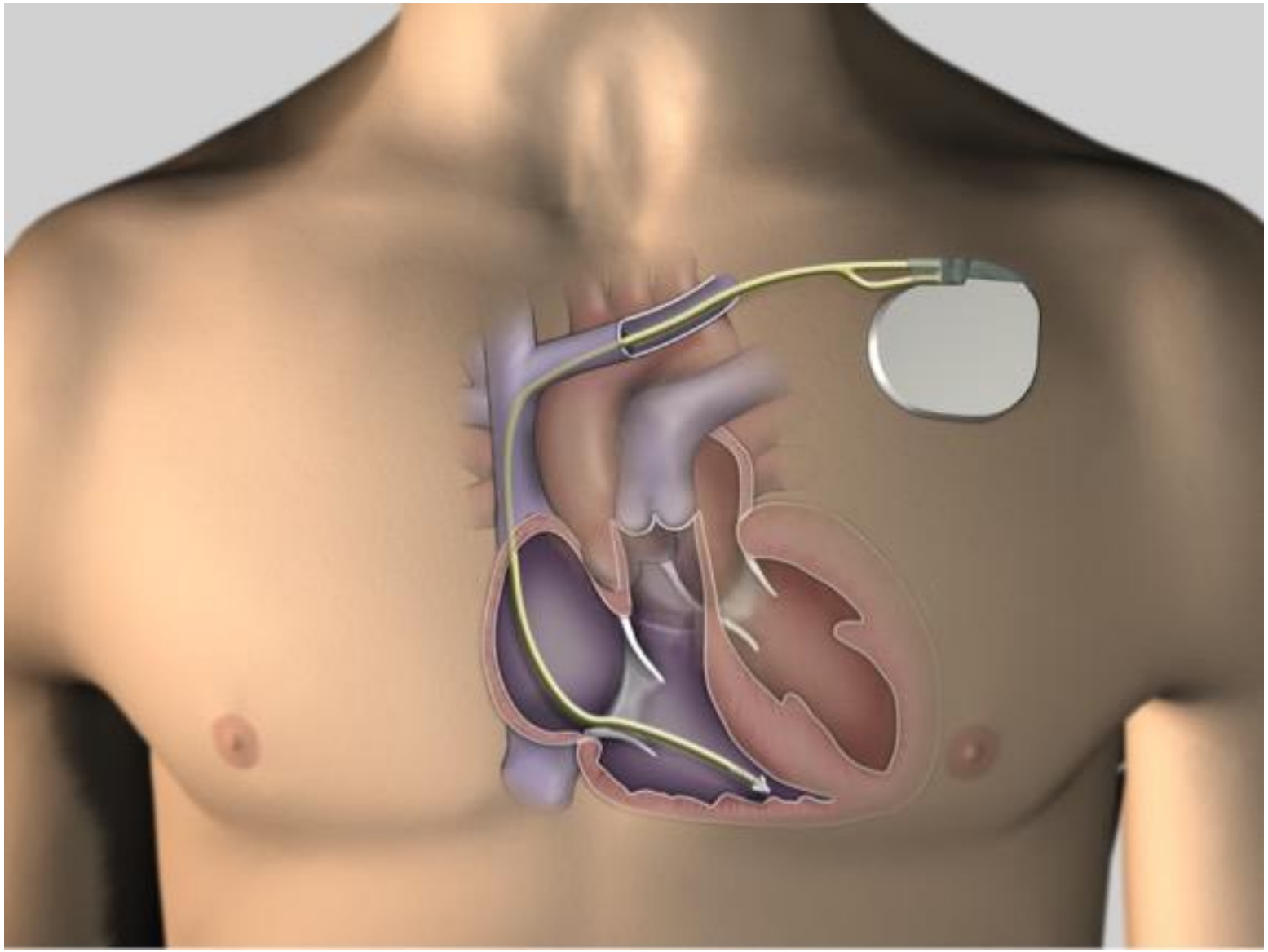
ICD
(implantable cardioverter defibrillator)

- ICDs prevent bradycardia and can identify and stop ventricular arrhythmias to reduce the risk of **sudden death** and **all-cause mortality** in patients with heart failure[1,2]

CRT-P and CRT-D
(cardiac resynchronisation therapy pacemaker / defibrillator)

- CRT devices improve the heart's pumping efficiency and blood flow, which can lead to **improved symptoms** and **quality of life**[1,2]
- Compared with optimal medical treatment alone, CRT devices **reduce mortality** in patients with heart failure[3]

Single Chamber ICD



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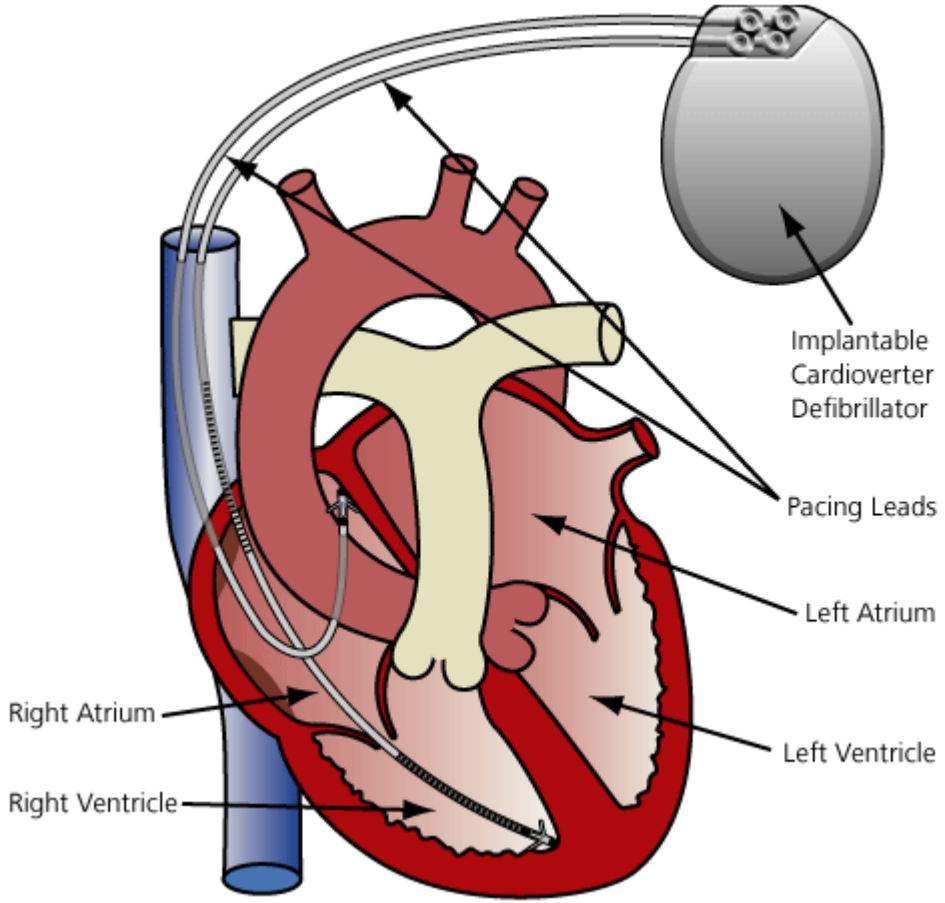
Dual Chamber ICD



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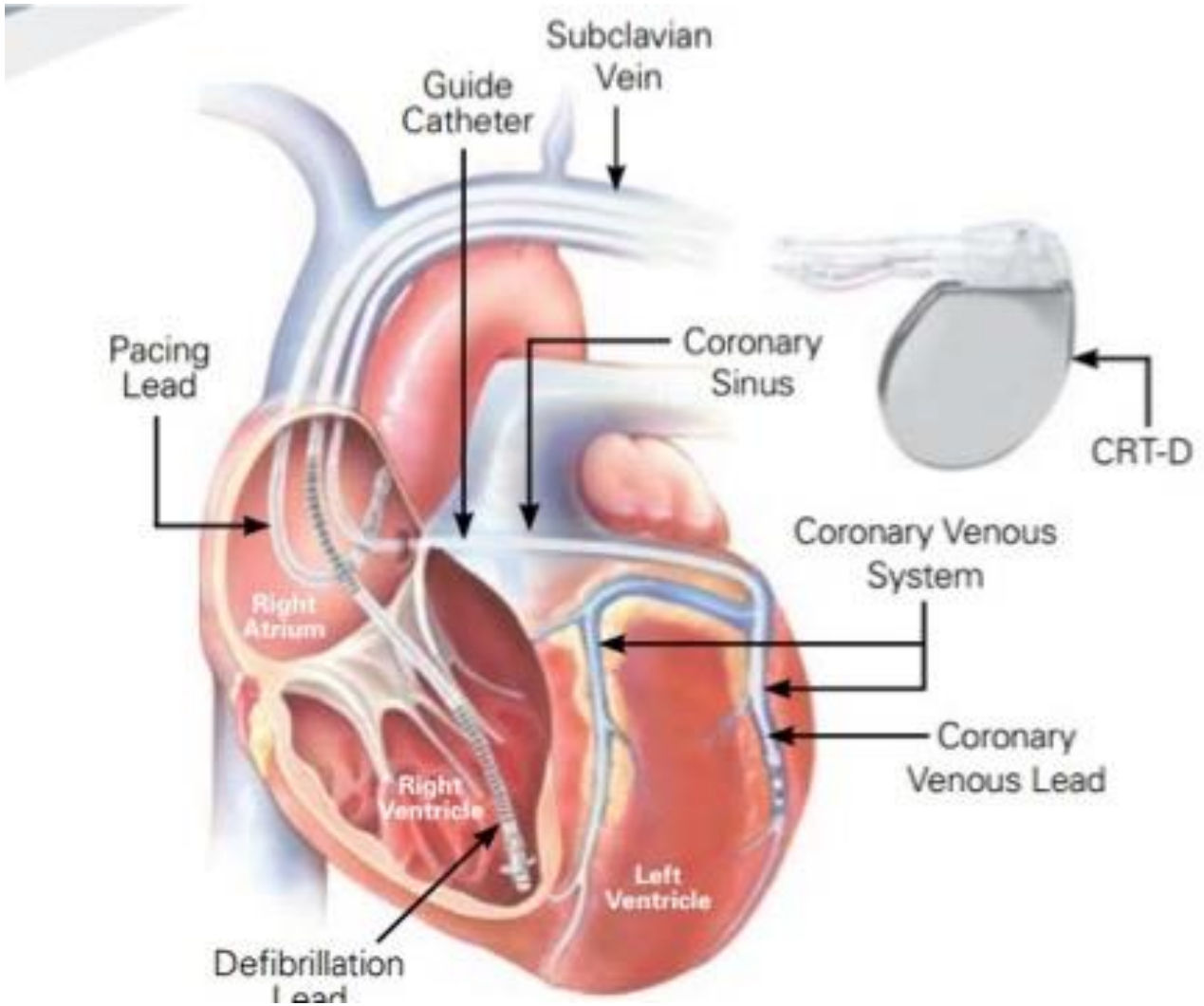
CRT-D



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S-ICD