The Prince Charles Hospital
Heart and Lung Institute
innovation and collaboration
Queensland Government

Tips and Tricks
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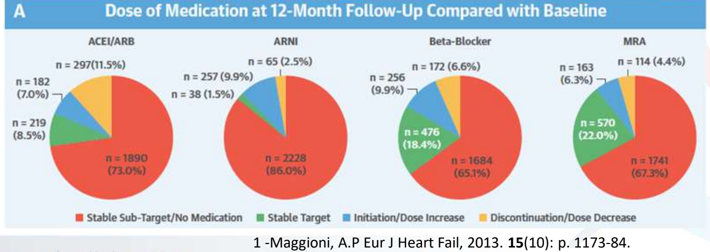
CARDIO-VASCULAR
MOLECULAR & THERAPEUTICS
Translation Research Group

Learning Objectives

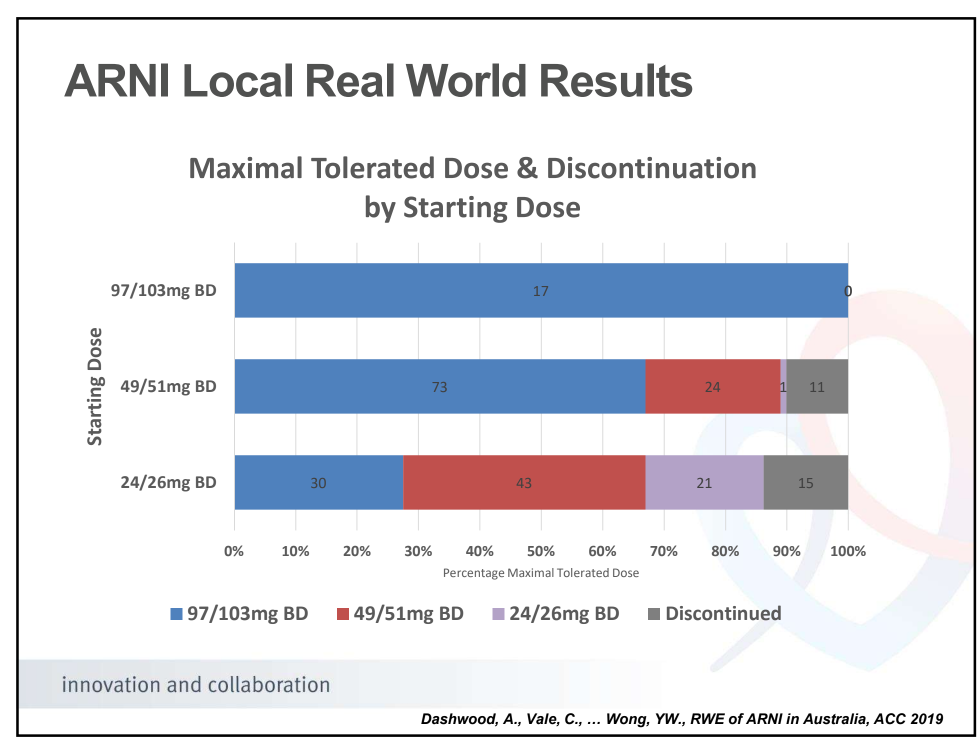
- Background
- Interactive with Questions
- Tips and tricks we use in clinical practice
  - Assessing HF
  - Titration
  - Recognising comorbidities
  - Getting patients to take control of their illness

Background

- Guideline directed medical therapy (GDMT) = Target dose.
- Registry data - Globally we are poor .
  - Europe - 29% achieved target doses ACEI/ARB, 18% Achieved BB[1]
  - America - <1% simultaneous target doses of BB/MRA/ACEI/ARB/ARNI[2]
- Respect differences in Clinical trials and real world clinical practice.
  - Trials consistently achieve target dose in 50-60% of patients enrolled[3]
- We are highly dependent on primary physicians and Nurse practitioners in achieving GDMT and target doses.



1 -Maggioni, A.P Eur J Heart Fail, 2013. **15**(10): p. 1173-84.
2 - Greene, S.J., et al., J Am Coll Cardiol, 2019. **73**(19): p. 2365-2383.
3 - Packer, M., et al., N Engl J Med, 2001. **344**(22): p. 1651-8.


ARNI Local Real World Results
Maximal Tolerated Dose & Discontinuation
by Starting Dose
Starting Dose
97/103mg BD
49/51mg BD
24/26mg BD
17
0
73
24
1
11
30
43
21
15
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Percentage Maximal Tolerated Dose
97/103mg BD
49/51mg BD
24/26mg BD
Discontinued
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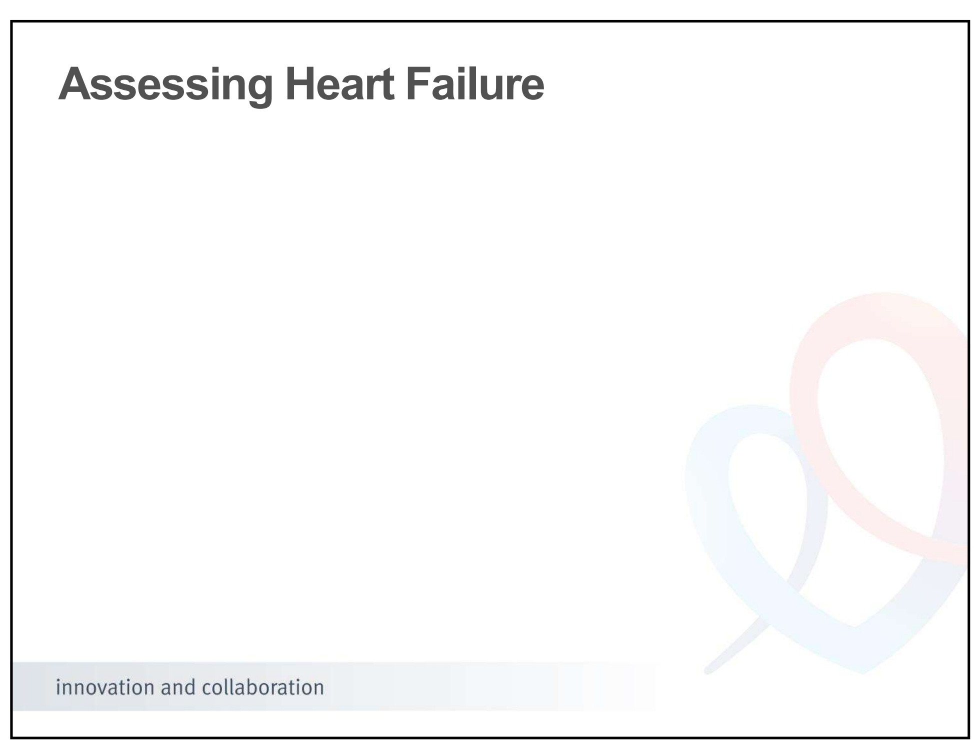
Dashwood, A., Vale, C., … Wong, YW., RWE of ARNI in Australia, ACC 2019


Assessing Heart Failure
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Question

- 54 year old female with EF of 40% has recently moved to QLD. Not had check up for many years. Stable with slight limitation when doing the shopping. Finds it hard to complete flight of 10 steps. Euvolemic, HR 78 BPM and BP 118/70 no postural symptoms. What NYHA class is she?
  - NYHA 1
  - NYHA 2
  - NYHA 3
  - NYHA 4

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Question

- 54 year old female with EF of 40% has recently moved to QLD. NYHA Class II. Stable with slight limitation when doing the shopping. Ramipril 5mg, Bisoprolol 5mg and spironolactone 12.5mg. Euvolemic, HR 78 BPM and BP 118/70 no postural symptoms. How would you manage?
  - Continue current Meds
  - Aim to increase Ramipril to 10mg
  - Aim to increase Bisoprolol to 10mg
  - Aim to increase both Rampiril and Bisoprolol

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Importance of NYHA Class

- EF is a number
- Symptoms define Quality of Life
- NYHA Class II
  - Easily overlooked
  - Inclusion criteria to many studies
  - PBS criteria

One-year Mortality
100
90
80
70
60
50
40
30
20
10
0
I
II
III
IV
Clinical Class
SAVE
SOLVD
VHeFT
CONSENSUS
Hy-C
GESICA

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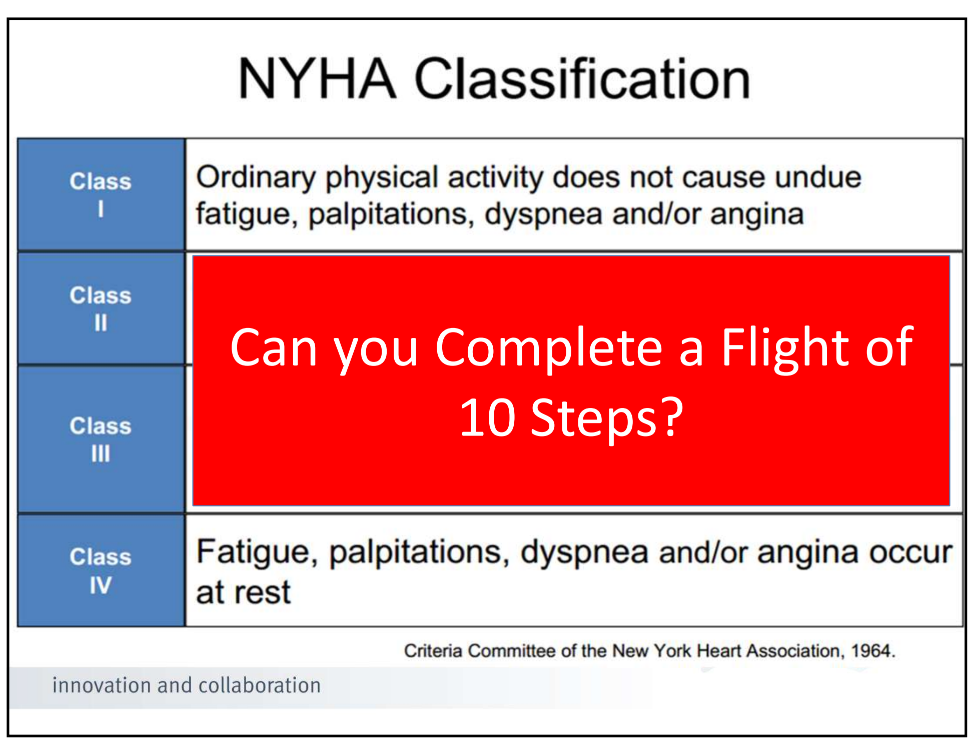

Question

- When echo results come back how confident are you with interpreting them?
  - I find it difficult
  - Different centers report differently
  - Easy to interpret

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TTE: Compare with previous

Report:

Normal LV size by volume (indexed LVEDV = 59 ml/m²) but mildly dilated by dimension (indexed LVEDD = 3.3 cm/m²) with moderate global LV systolic dysfunction. No obvious resting regional wall motion abnormalities. The ejection fraction is 42 % by Simpson's biplane method. Normal LV wall thickness. Grade 1 diastolic dysfunction (impaired relaxation with low to normal LV filling pressures). LV GLS is reduced at 16 % (abnormal <20%).

Normal right ventricular size and systolic function. TAPSE is measured at 25 mm (normal >= 17 mm), Doppler tissue imaging s' velocity is 14 cm/s (normal >= 9.5 cm/s).

Normal sized atria. The interatrial septum appears intact on the 2D and colour Doppler examination.

The mitral valve leaflets are mildly thickened. There is grade 0-1/4 mitral regurgitation.

The aortic valve appears trileaflet and functionally normal. No aortic regurgitation detected. Aortic root dimensions are within the normal limits for patient size. The ascending aorta was not able to be imaged on this study.

Structurally normal pulmonary and tricuspid valves. Unable to estimate the RVSP due to insufficient tricuspid regurgitation. Grade 1-2/4 pulmonary regurgitation.

There is an echodense soft tissue layer attached to the epicardial surface of the heart which is consistent with epicardial fat.

NEDA Consent: Not available

Conclusions:

1. Normal LV size with moderately impaired LV systolic function, EF = 42 %. Avg GLS = 16%.
2. Normal RV size and systolic function. Unable to accurately estimate RVSP.
3. Normal atrial size.
4. Grade 0-1/4 MR.
5. Grade 1-2/4 PR.

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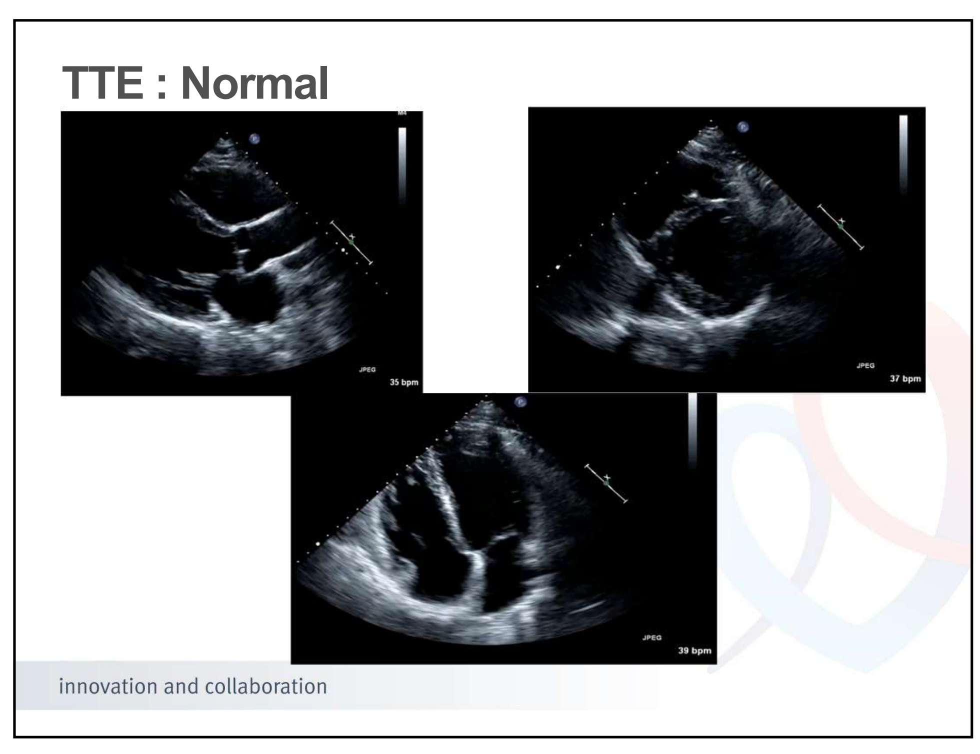
TTE : Normal
35 bpm
37 bpm
39 bpm
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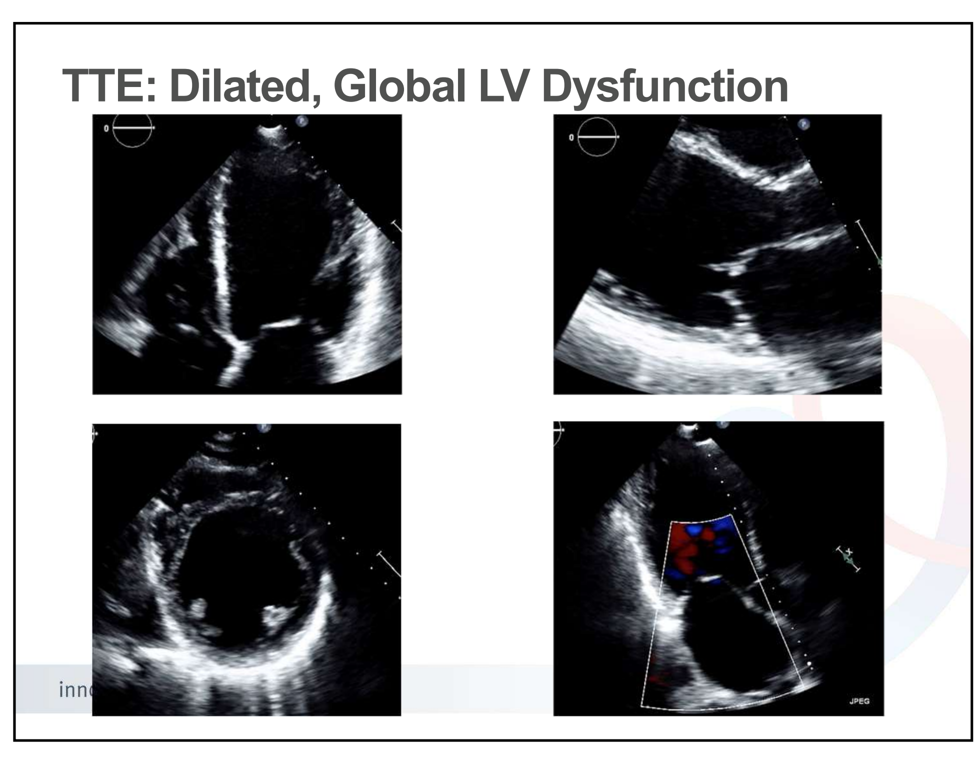
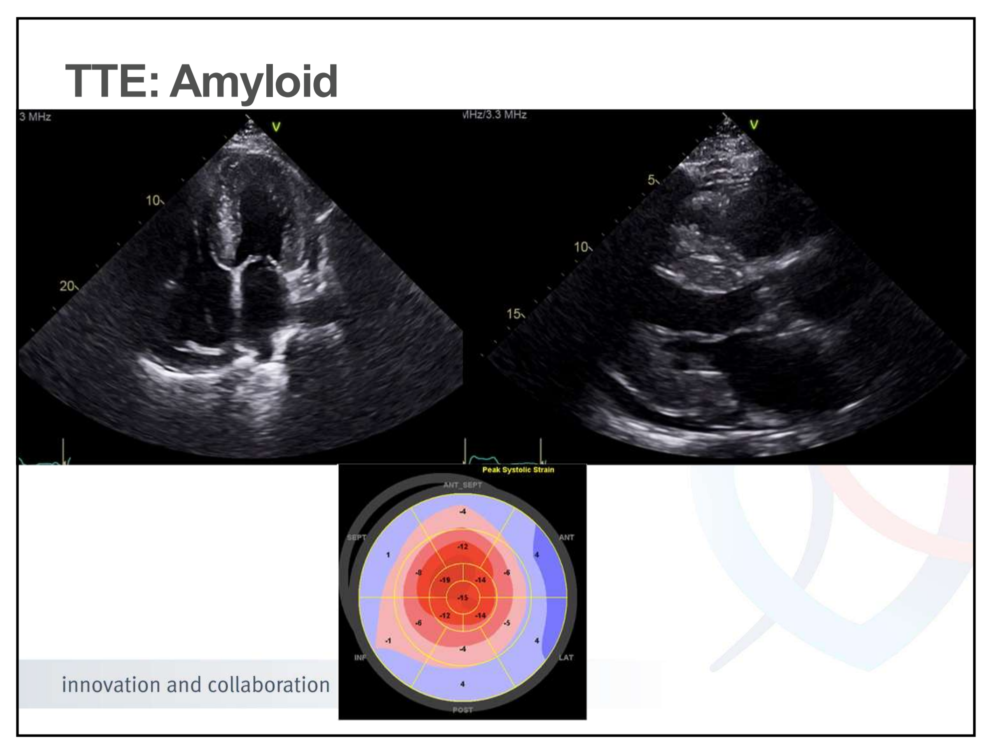

TTE: Dilated, Global LV Dysfunction


TTE: Amyloid
Peak Systolic Strain
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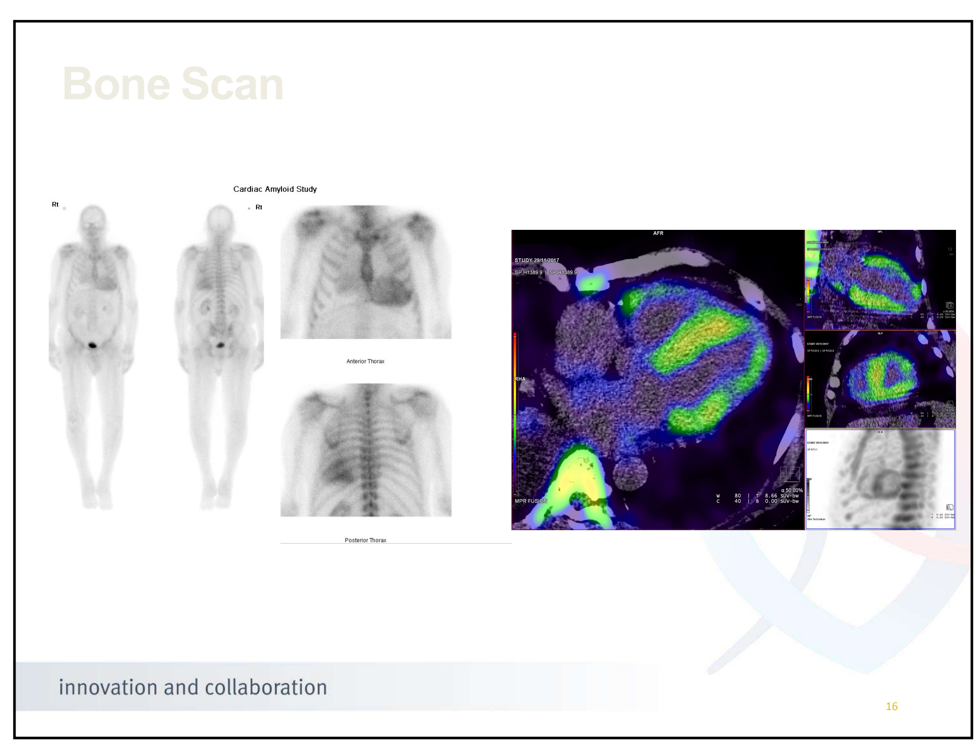
Bone Scan
Cardiac Amyloid Study
Anterior Thorax
Posterior Thorax
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Titration

Question

- Are all ARBs shown to have beneficial effects in HF with reduced ejection fraction.
  - Yes
  - No

ACEI or ARB

- ARB
  - Candasartan, Losartan, Valsartan
- ACEi – class effect
  - Cough - Increase dose!!!
- Start with ACEI first

Drug	Initial Daily Dose(s)	Maximum Dose(s)
ACE inhibitors		
Captopril	6.25 mg 3 times	50 mg 3 times
Enalapril	2.5 mg twice	10 to 20 mg twice
Fosinopril	5 to 10 mg once	40 mg once
Lisinopril	2.5 to 5 mg once	20 to 40 mg once
Perindopril	2 mg once	8 to 16 mg once
Quinapril	5 mg twice	20 mg twice
Ramipril	1.25 to 2.5 mg once	10 mg once
Trandolapril	1 mg once	4 mg once
Angiotensin receptor blockers		
Candesartan	4 to 8 mg once	32 mg once
Losartan	25 to 50 mg once	50 to 100 mg once
Valsartan	20 to 40 mg twice	160 mg twice

Question

- Following assessment and classified as NYHA class 2 you increase Ramipril to 10mg and arrange to see her in 2 weeks time. Stable with slight limitation when doing the shopping. Euvolemic, HR 60 BPM and BP 118/70 but states in the morning after meds feels light headed?
  - Continue current Meds
  - Reduce ramipril
  - Split dose to 5mg BD
  - Stop Spironolactone

Tips and Tricks

- Split dose
- Go slow
- Educate what to expect and how much does it limit QofL
- Life style
  - Sit up for two minutes
  - Stand for two minutes before walking
  - Remain Euvolemic

Question

- Ischemic DCM with scar, no chest pain for many years, Stable with slight limitation when doing the shopping. Ramipril 10mg, Bisoprolol 7.5mg and spironolactone 12.5mg, ISMN 120mg mane. Euvolemic, HR 60 BPM and BP 118/70 but states in the morning after meds feels light headed?
  - Continue current Meds
  - Reduce ramipril
  - Split dose to 5mg BD
  - Reduce ISMN

Tips and Tricks

- Rationalize meds
- Reduce non GDMT meds with no outcome on mortality.
  - ISMN
  - Nicorandil
  - Hydralazine
  - Amlodipine (neutral in HF patients)

Question

- 54 year old with EF 25%. Sacubitril/valsartan 49/51mg BD, Bisoprolol 7.5mg and spironolactone 12.5mg. Euvolemic, HR 60 BPM and Lying BP 98/70 and Standing BP 95/70. Normal renal function. No postural symptoms?
  - Continue current Meds
  - Reduce Sacubitril/valsartan
  - Increase Sacubitril/valsartan to 73/77mg BD with r/v
  - Increase Sacubitril/valsartan to 49/51mg mane and 73/77mg nocte with r/v
  - Increase Sacubitril/valsartan to 73/77mg mane and 49/51mg nocte with r/v

Tips and Tricks

- BP is a number
- Lying and standing BPs
- Be inventive
  - Spit the increase
  - Beta blocker in morning and ACEi/ARB at night
  - BB – carvedilol has BP effect

Question 4

- 54 year old with EF 35%, slightly overweight. Ramipril 10mg, Bisoprolol 7.5mg and spironolactone 12.5mg. Euvolemic, HR 60 BPM and BP 145/70. 24 hr BP monitor and BP does not dip at night. Also higher in morning
  - Add Amlodipine
  - Add hydralazine
  - Check for sleep apnoea
  - Loose weight

OSA

- Common co-morbidity
- Hard to correct BP with medications if other issues not treated.
- No nocturnal dipping is bad.

Hypotension

- Number one barrier to initiation and titration
- Blood Pressure for perfusion
  - Think, Wee and Stand
- Clinic is a single finding
  - Lying and standing
- Number and Symptoms – Temporal relationship
- Low BP = HF Severity[1]
- If tolerate – derive equal benefit[2]

Ambrosy, A.P., et al. Am Heart J, 2013. **165**(2): p. 216-25
Bohm Et al. European Heart Journal (2017) 38, 1132–1143

Question

- 54 year old with EF 35%, NYHA class II, stable for past year. Ramipril 10mg, Bisoprolol 7.5mg and spironolactone 12.5mg. Euvolemic, HR 60 BPM and BP 115/70. Normal renal function. No postural symptoms?
  - Continue current Meds
  - Stop Rampiril, Start Sacubitril/valsartan 24/26mg Bd this evening
  - Stop Rampiril, Start Sacubitril/valsartan 49/51mg BD this evening
  - Stop Rampiril, Start Sacubitril/valsartan 24/26mg in 48 hours
  - Stop Rampiril, Start Sacubitril/valsartan 49/51mg in 48 hours

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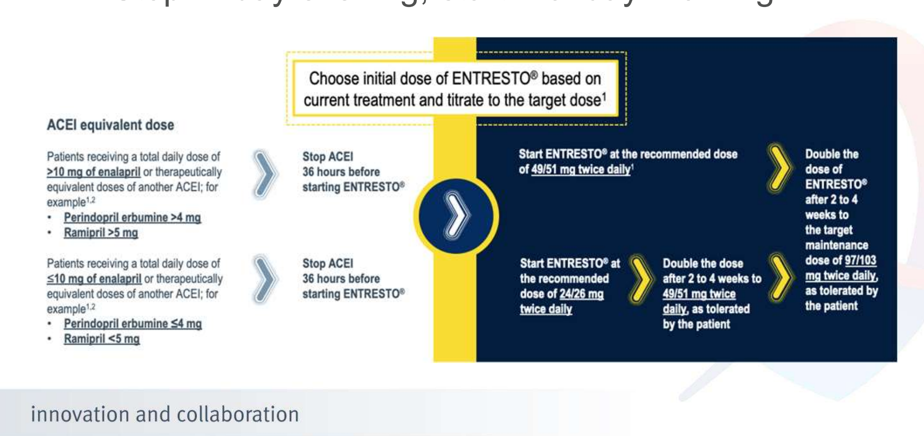
Tips and Tricks

- NYHA class II
- Need at least 36 hr wash out from ACEi
  - – Stop Friday evening, start Monday morning.



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Question

- Within limits, accepting slight loose in renal function is better than running a patients slightly Wet.
  - – Yes
  - – No

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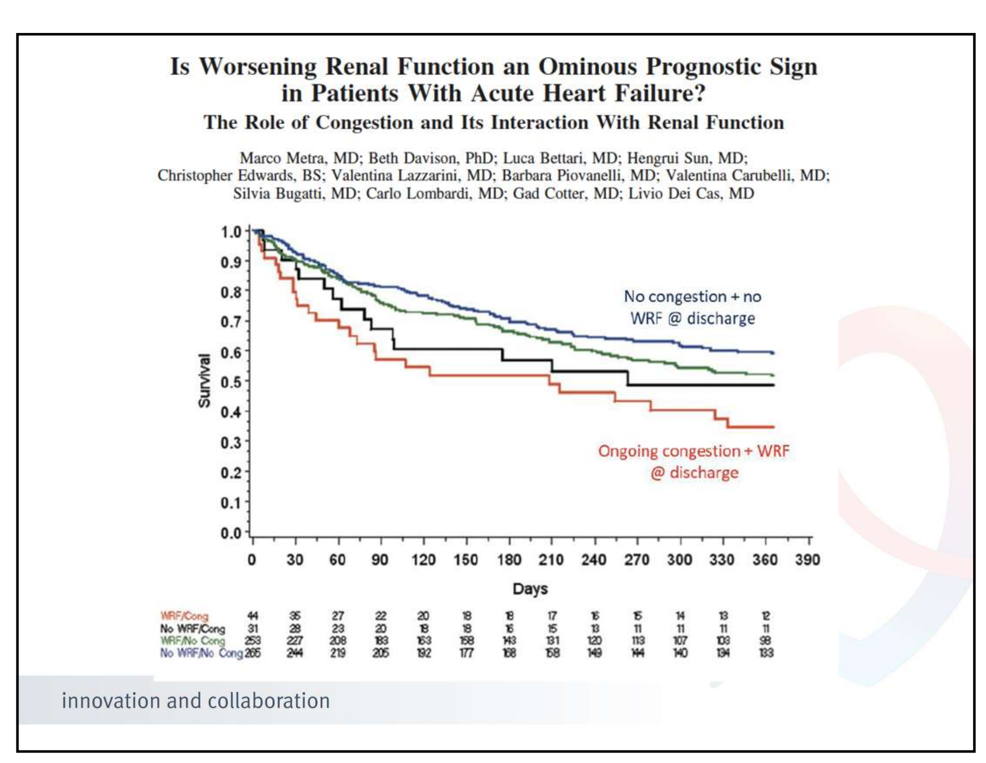

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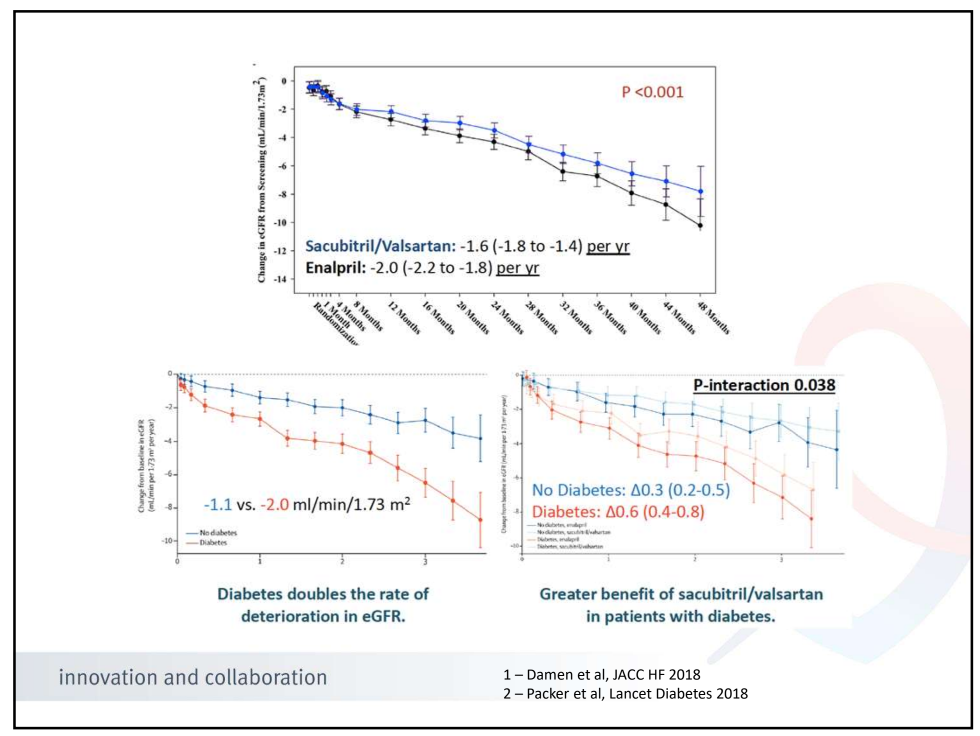

Renal function

- Important to measure
- With change, check after 1 week
- Medications are protective on renal function over all.
- >20 - 25% worsening – Ix for Renal artery stenosis.

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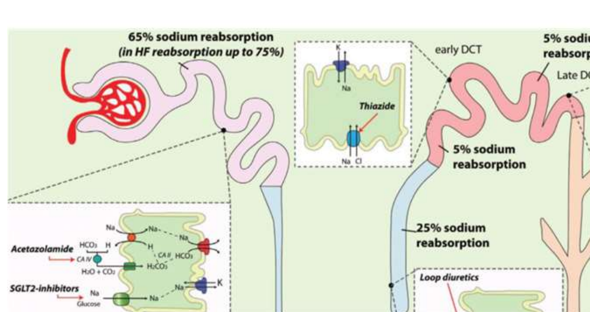
Failure of Diuretic therapy

- Repeated reviews for fluid overload despite escalation of frusemide. Now on 80mg BD.
  - Increase Frusemide to 120mg BD
  - Add in Hydrocholorthiazide 12.5mg
  - Change to Bumetanide 2mg BD
  - Ensure no Salt

Tips and Tricks



- Weight diary
- Fluid restriction
- Bumetanide
- SALT restriction
  - Asian/Frozen/Tinned
- Sequential nephron blockade
  - Hydrochlorothiazide, azetazolomide
  - Repeat bloods
  - Watch potassium
- CKD – need higher amount of frusemide.

Question: How often do you do an echo

- Every review
- Once yearly
- Change of symptoms
- Never
- 3-6 months after GDMT and if change in symptoms

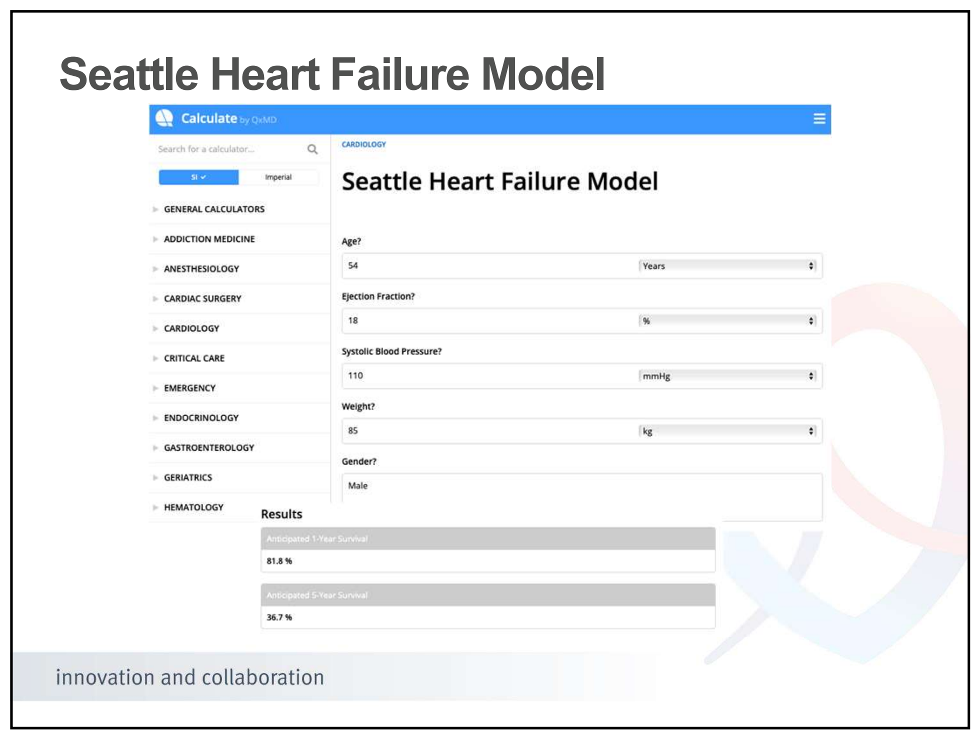
5.2.4. Diagnostic Tests to Guide Therapy in Heart Failure
Recommendation: Transthoracic echocardiography should be considered in patients with HFrEF 3–6 months after the start of optimal medical therapy, or if there has been a change in clinical status, to assess the appropriateness for other treatments, including device therapy (implantable cardioverter defibrillator (ICD) or cardiac resynchronisation therapy (CRT), or both).
(Weak recommendation FOR; low quality of evidence.)

Practice advice

Getting Patient to buy in to treatment

Nurse practioner titration clinic

- Invaluable resource
- Improve patients' health literacy
  - Tailored education
  - Medication adherence and safety
  - Development of self-management skills
  - Recognition of signs and symptoms of decompensation.



Summary of Talk

- Stable HF needs intervention
  - NYHA Class II
- Numbers are numbers
- Think, Wee and Stand
- Rationalize medications
- New medications: Clinical Inertia
- Split doses
- Get patient to buy into treatment

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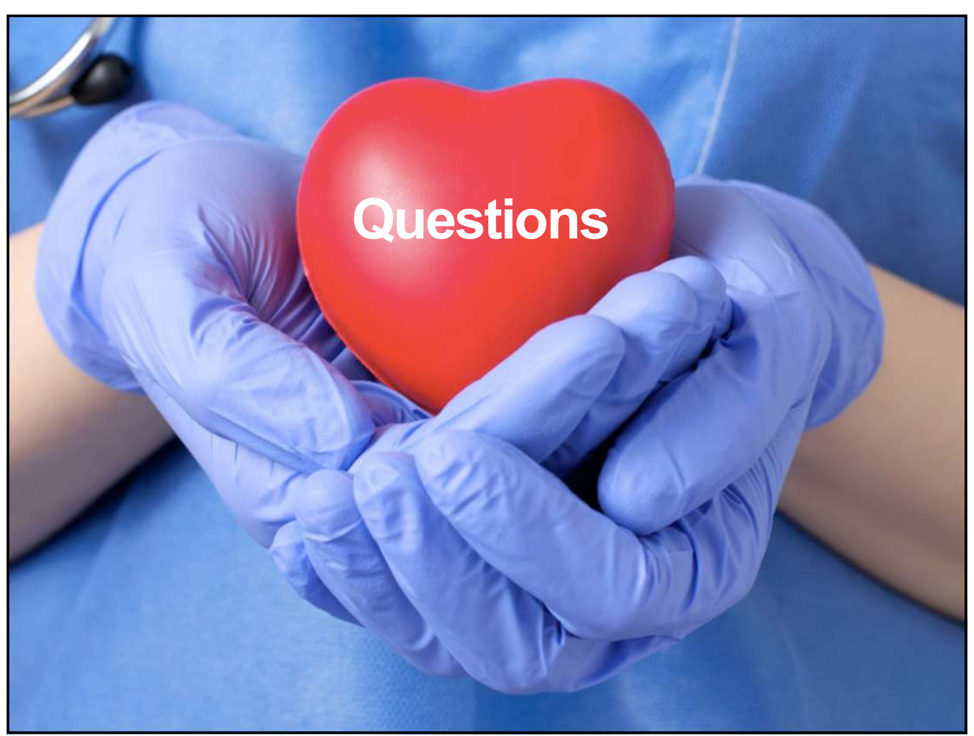
Questions