

The Prince Charles Hospital

Heart^{and} Lung Institute

innovation and collaboration



Queensland
Government



Case Studies

Dr Yee Weng Wong, Dr Alexander Dashwood &
Mrs Haunnah Rheault
Staff Specialist: Advanced Heart Failure &
Cardiac Transplantation

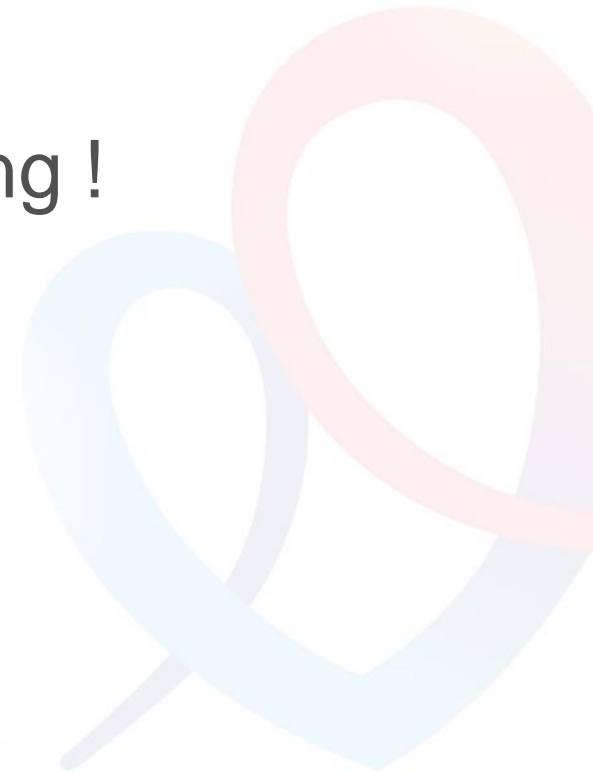


CARDIO-VASCULAR
MOLECULAR & THERAPEUTICS
Translation Research Group



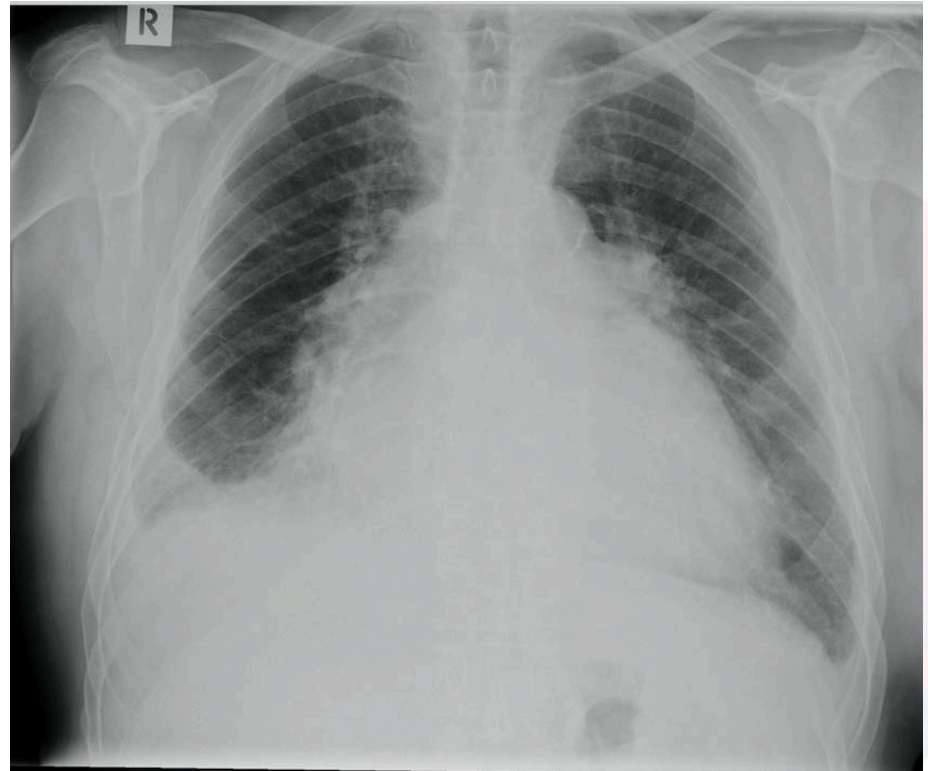
Learning Objectives

- Interactive with Questions
- Some will be admission and inpatient based
- Not always one right answer
- Encourage questions and heckling !



Patient A

- 44 year old gentleman referred to ED for SOB on exertion and peripheral edema. Episodes of palpitations. BMI 36
- PMHx – HTN - 300mg irbesartan
- SHx – Non smoker with two children.
- Hb 134, WCC 8.6,
- Na 144, K 4.6, Creat 70, eGFR >90
- ECG – sinus, narrow, 82 BPM
- Cant see JVP, crackles at bases



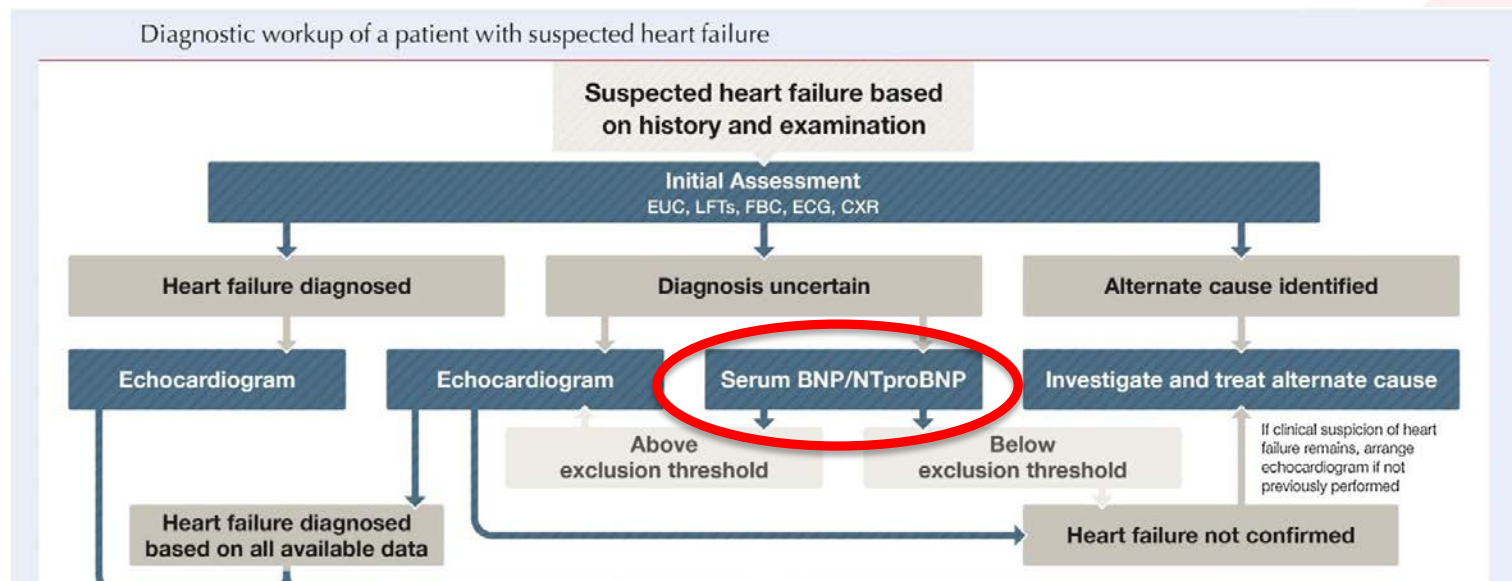
Question: What would you like to do next ?

- Sputum samples
- CT chest
- Transthoracic echo
- BNP
- Cardiac MRI
- Discharge home

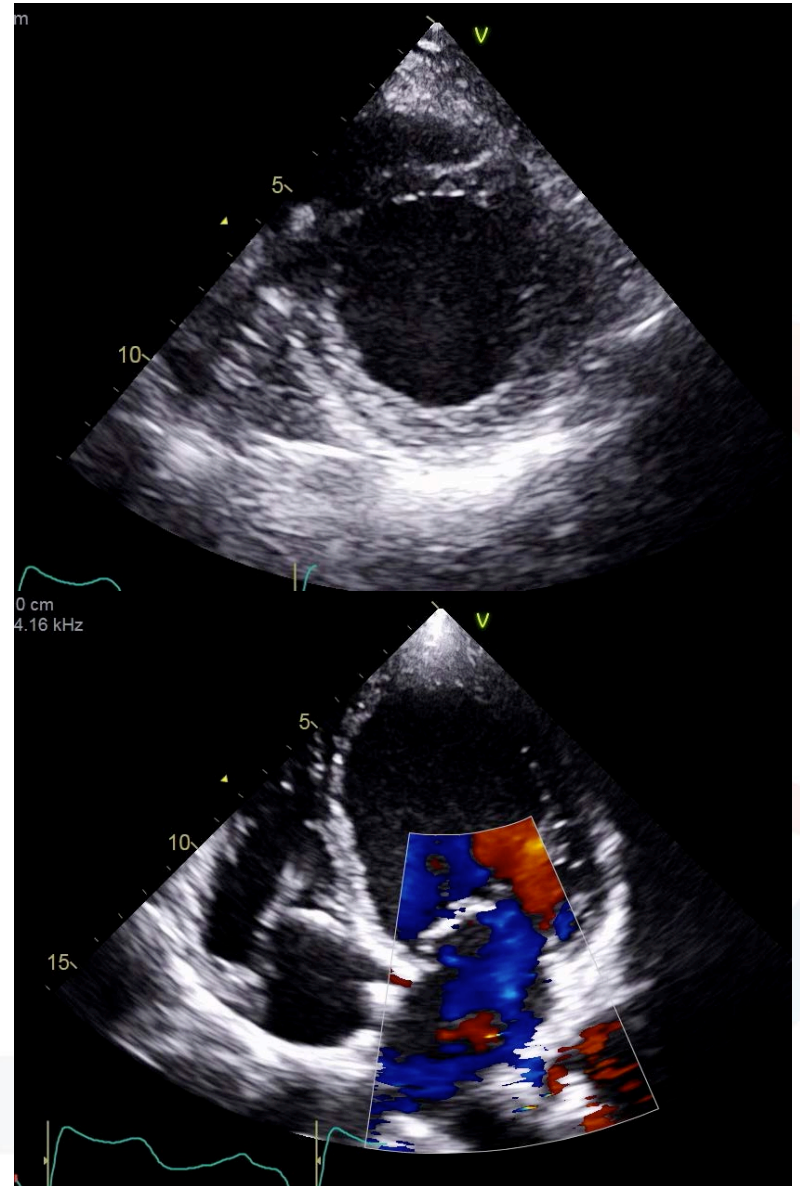
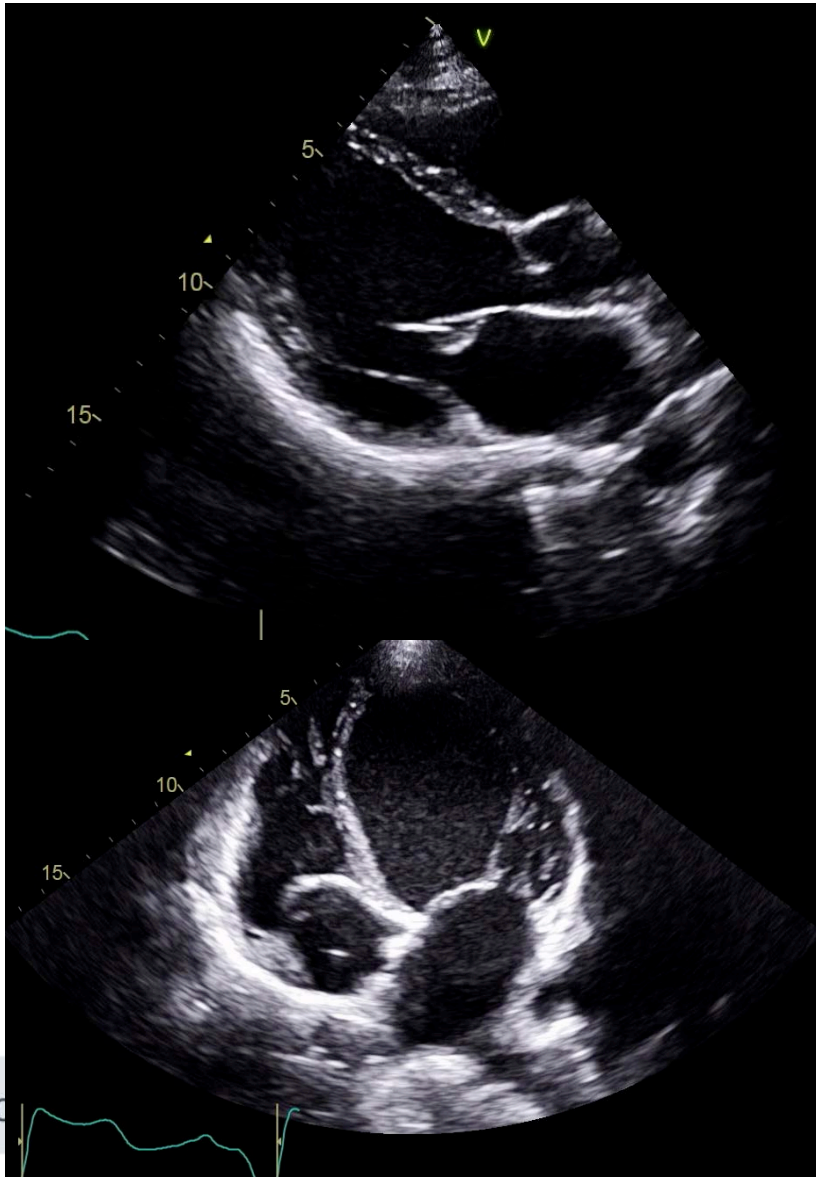


Views on BNP

- HF is a clinical diagnosis
- BNP < 100 ng/L and an NT proBNP < 300 ng/L for rule-out.
- Affected by individual patient characteristics.
- Levels can be elevated in PAH, AF, ACS, PE, CTEPH



TTE images



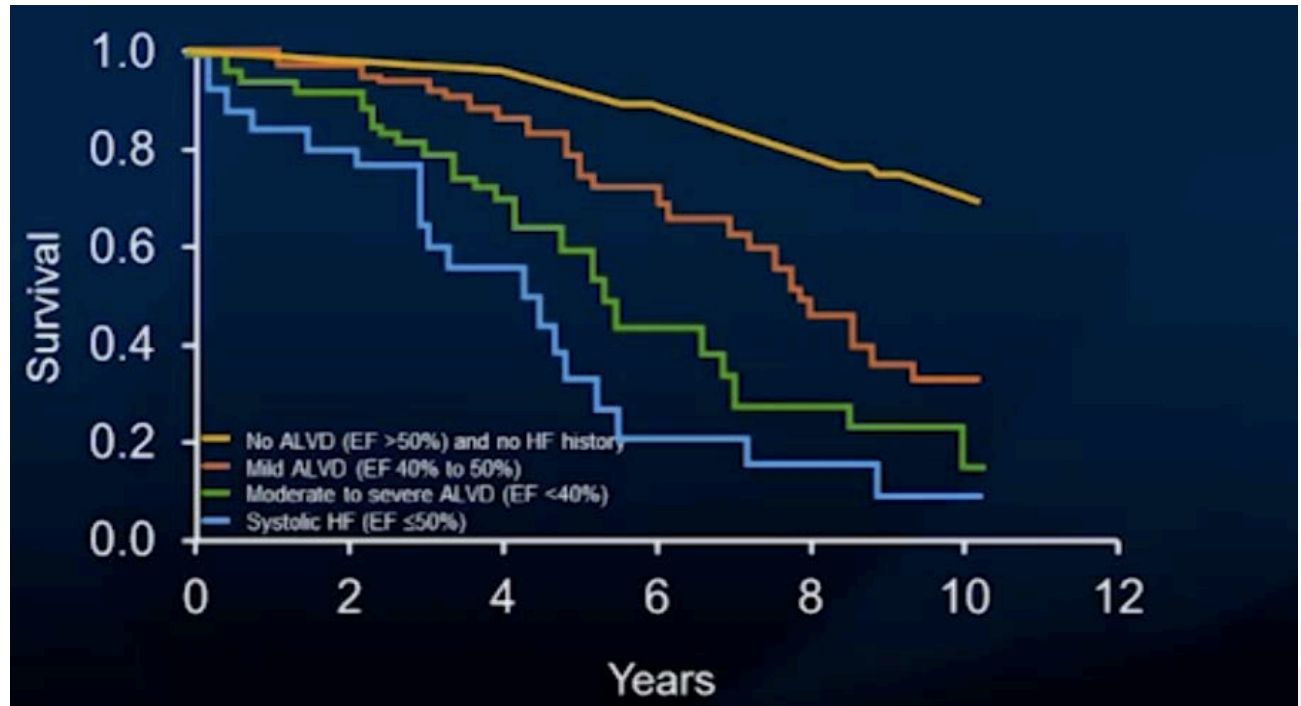
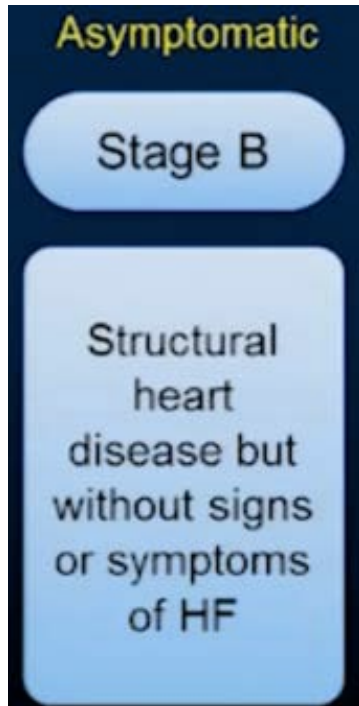
Question A: Treatment

- Patient admitted, echo shows EF 32%, iLVEDV 113ml/m². responding to IV frusemide 40mg BD with 2kg of weight loss a day. No documented issues with ACEi.
- HR 88, BP 110/74, JVP 8cm, improving peripheral edema. Hb 134, eGFR 86.
 - Bisoprolol 2.5mg and irbesartan 300mg
 - Bisoprolol 2.5mg and Ramipril 2.5mg BD
 - Bisoprolol 2.5mg
 - Ramipril 2.5mg BD

Question B: Treatment

- Asymptomatic left ventricular dysfunction with EF 45% and mildly dilated (iLVEDD 3.3cm/m²). All bloods and clinical exam normal. Would you start?
 - No Meds
 - Bisoprolol 2.5mg and Ramipril 2.5mg BD
 - Bisoprolol 2.5mg
 - Ramipril 2.5mg BD

Panel: Asymptomatic with structural abnormality



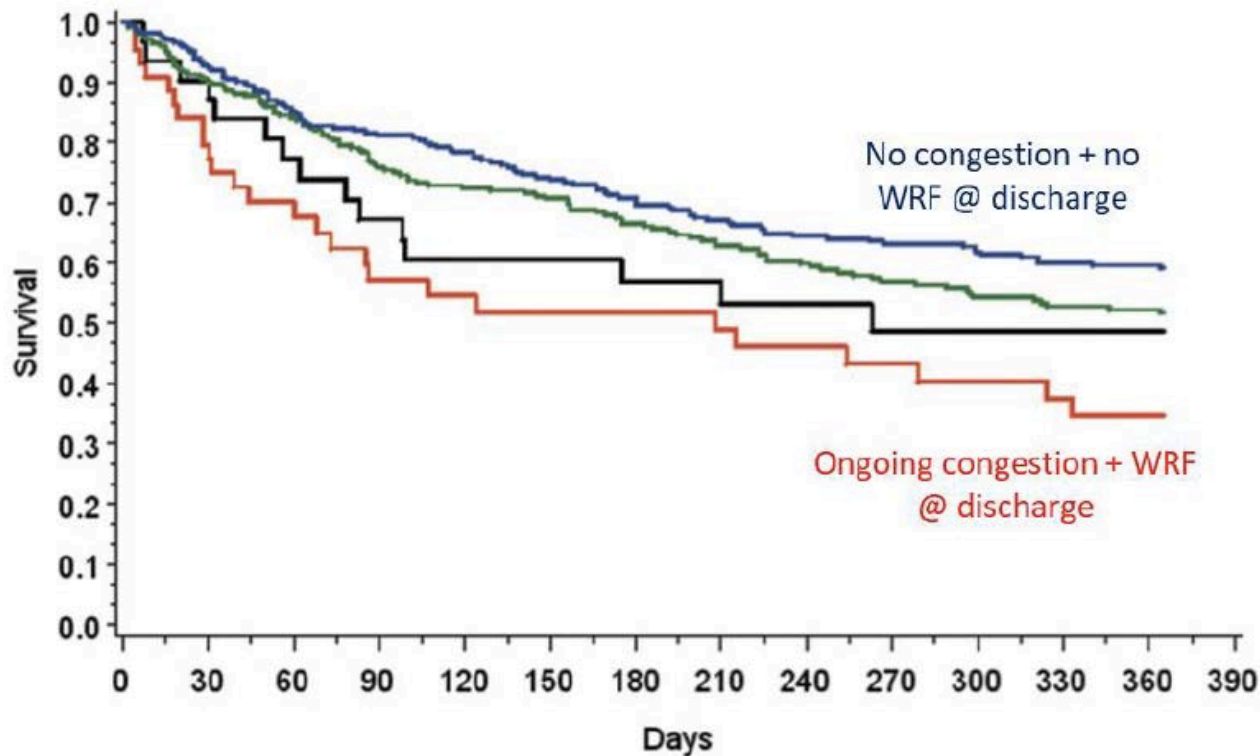
Question

- Stabilized on ward on 7.5mg Bisoprolol and Ramipril 5mg. PND and orthopnea have resolved. You have him on IV frusemide 40mg BD and happy to change him to PO.
 - Change to PO frusemide and discharge
 - Not sure he is euvolemic - do a BNP
 - Change to PO 40mg BD and observe for another 24hrs
 - Bumetanide 1mg BD

Is Worsening Renal Function an Ominous Prognostic Sign in Patients With Acute Heart Failure?

The Role of Congestion and Its Interaction With Renal Function

Marco Metra, MD; Beth Davison, PhD; Luca Bettari, MD; Hengrui Sun, MD; Christopher Edwards, BS; Valentina Lazzarini, MD; Barbara Piovaneli, MD; Valentina Carubelli, MD; Silvia Bugatti, MD; Carlo Lombardi, MD; Gad Cotter, MD; Livio Dei Cas, MD



WRF/Cong	44	35	27	22	20	18	18	17	16	15	14	13	12
No WRF/Cong	31	28	23	20	18	18	16	15	13	11	11	11	11
WRF/No Cong	253	227	208	183	163	158	143	131	120	113	107	103	98
No WRF/No Cong	265	244	219	205	192	177	168	158	149	144	140	134	133

Question: Pre Discharge

- Patient diagnosed with idiopathic DCM. Titrated on to ramipril 5mg , bisoprolol 7.5mg and frusemide 40mg daily with no issues for 24 hours. HR 68, BP 115/70 and ambulatory.
 - Discharge
 - Discharge with Life style – Na, ETOH, daily weights.
 - Discharge with Review by HF NP
 - All of above

Prior to Discharge

- Sodium restrict to < 2 grams per day
- Fluid restrict < 2 L a day
- Exercise - 30minutes 5 times a week
- ETOH – ideally abstain
- Diuretic plan
- Nurse practitioner education
- Work out goals and wishes including NFR

Question: You see in clinic 2 months later. NO follow up from discharge facility.

- Discharged on Ramipril 10mg, bisoprolol 10mg and frusemide 40mg daily, Finding it hard to walk up stairs.
- HR 78, LBBB 126ms, Lying 108/70, standing 102/70, eGFR 80, EF: 32%
 - Continue current meds
 - Spironolactone 12.5mg
 - Ivabradine 5mg BD
 - Spironolactone and ivabradine at above doses
 - Change bisoprolol to carvedilol

Aldosterone Antagonist

- NYHA class II-IV with EF < 40%
- Avoid in stage 4 or 5 CKD
 - eGFR < 30mL/min
- Potassium and creatinine
 - K⁺ - 3 days, 1 week, monthly for first 3.
 - Creatinine increase by 30% stop, or K >5.5
- Gynecomastia

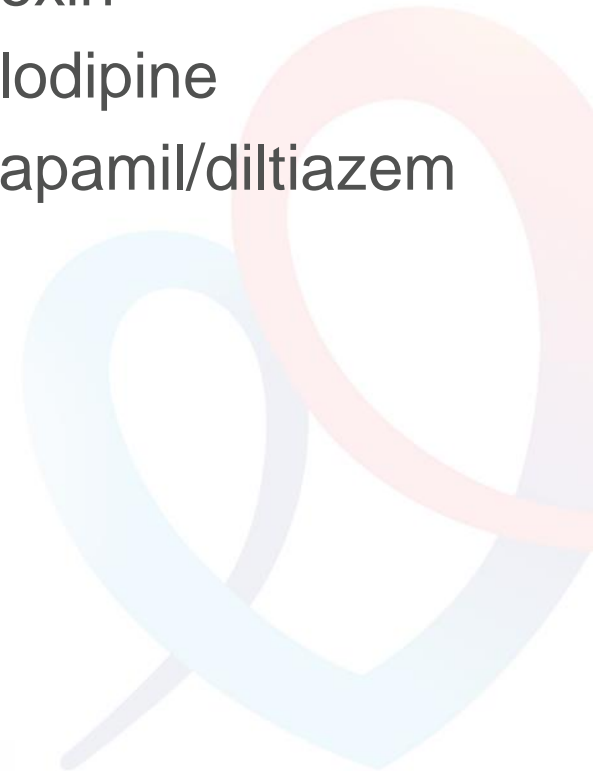
Ivabradine

- Shift trial
- Reduced hospitalization but no mortality
- EF <35%, NYHA II/IV, HR >70
- Ensure sinus rhythm
- Goal dose BB



Question: In HFrEF which drugs have:

- Mortality benefit
 - Reduced hospitalization
 - Neutral
 - Contraindicated.
- Hydralazine and Nitrates
 - Digoxin
 - Amlodipine
 - Verapamil/diltiazem

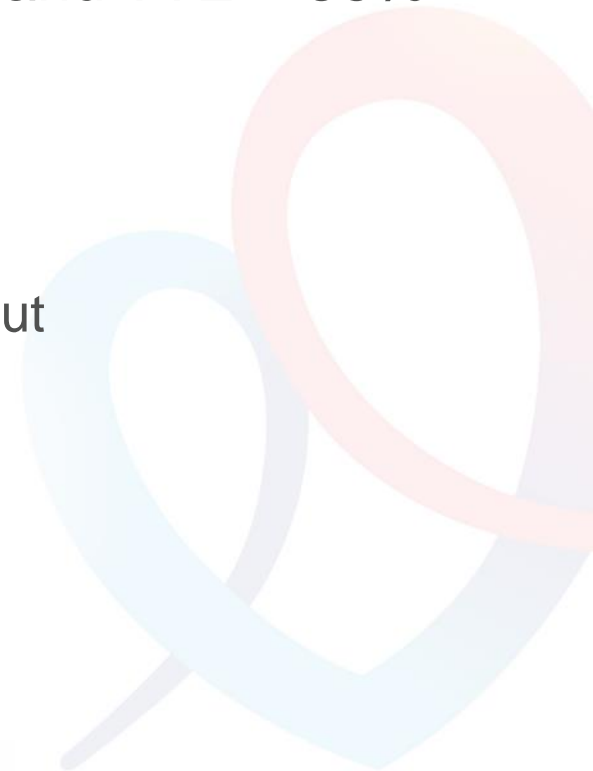


Other medications

- Hydralazine and Nitrates
 - Class 1 – symptomatic African-Americans despite ACEi/ARB intolerance
 - Class IIa for ACEi/ARB intolerance
 - [N Engl J Med.](#) 2004 Nov 11;351(20):2049-57
- Digoxin
 - Reduced HF hospitalization – NEJM 1997 The Digoxin Investigation Group
- Amlodipine
 - Safe but no outcome data
- Verapamil/diltiazem
 - Contraindicated if EF < 40%

Patient A

- Now 6 months since index admission. You are happy with patient. Stable on current meds for 2 months on ramipril 10mg, Spiro 12.5mg, Bisoprolol 10mg, frusemide 40mg mane. He is NYHA II, able to do shopping
- HR 62, LBBB 126ms, BP 110/70 eGFR 78 and TTE – 36%
 - Keep current meds the same
 - Spironalactone 25mg
 - Entresto 49/51 mg BD with 48 hr wash out
 - Entresto 49/51 mg BD with no required wash out



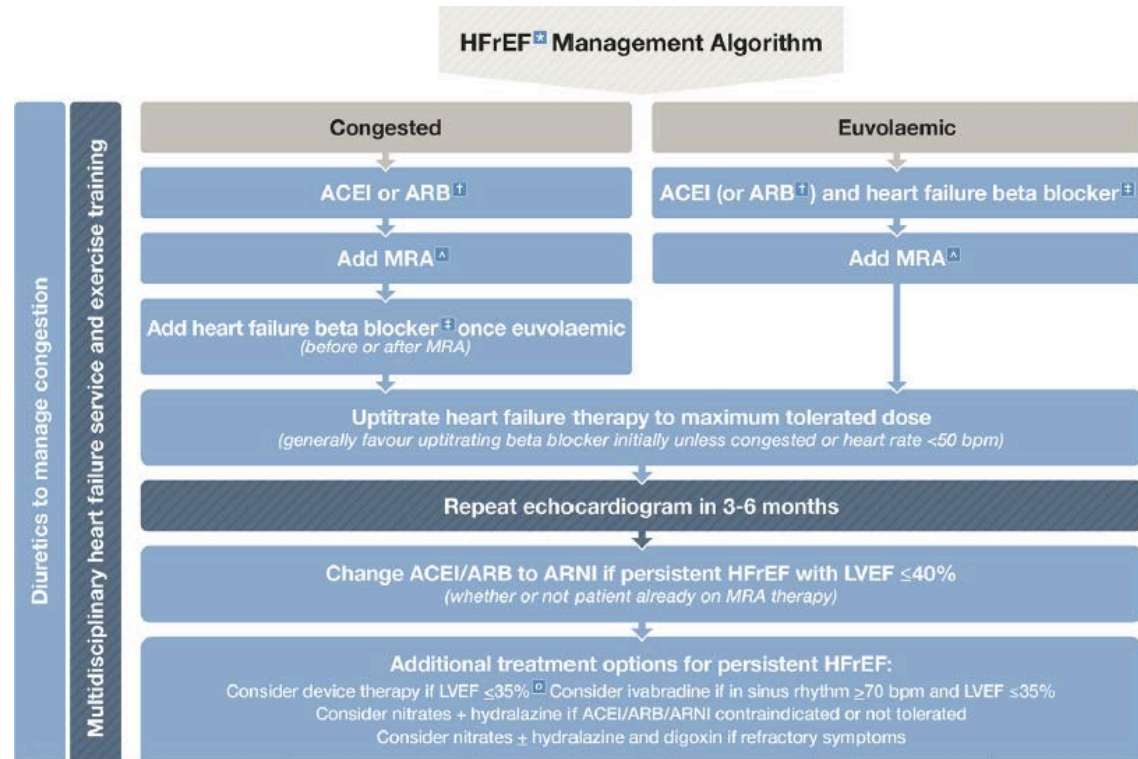
Search for the NYHA class II

Characteristic	LCZ696 (N = 4187)	Enalapril (N = 4212)
NYHA functional class — no. (%)¶		
I	180 (4.3)	209 (5.0)
II	2998 (71.6)	2921 (69.3)
III	969 (23.1)	1049 (24.9)
IV	33 (0.8)	27 (0.6)
Missing data	7 (0.2)	6 (0.1)

- Usually easier to start when hypervolemic
- Be wary of the diuretic effect – reduce frusemide
- Split the dose
- Renal sensitivity

Tips to Titration

- Go slow
- Tolerate asymptomatic hypotension
 - ‘Think, stand and Pee’ I am not worried about BP as long as symptomatic
- Do Lying and standing BP
- Treat patient not creatinine
 - Tolerate modest increase
- Share Seattle HF model
 - Life expectancy goes from 4 to 9 years they will buy in
- Daily weight diary
- Repeat TTE at end of last dose increase.



Question?

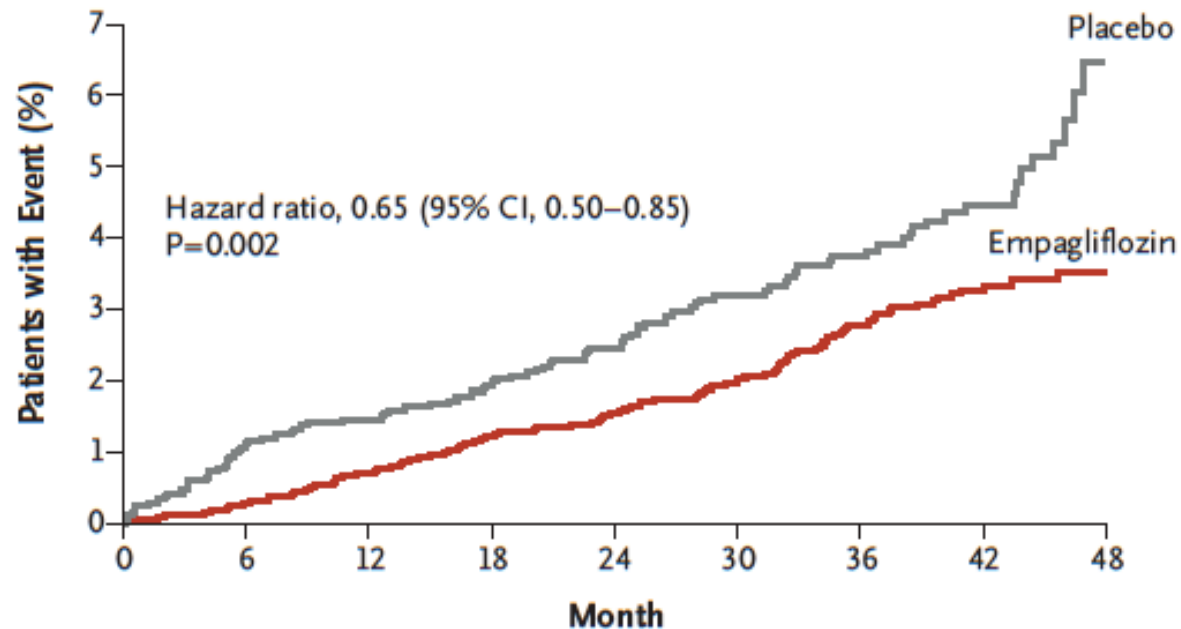
- Stable on sacubitril/valsartan 97/103mg BD, bisoprolol 10mg, spironolactone 12.5mg, bumetanide 2mg BD and metformin. EF 36%, BMI 38
- Organize bloods - eGFR 78, Hb 134, ferritin 114, T sats 10%, HbA1C 8.1%
 - Metformin
 - Oral iron
 - IV iron
 - Empagliflozin
 - First two – Metformin and oral iron
 - Last two – IV iron and empagliflozin



Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D., Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H., Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D., and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

D Hospitalization for Heart Failure



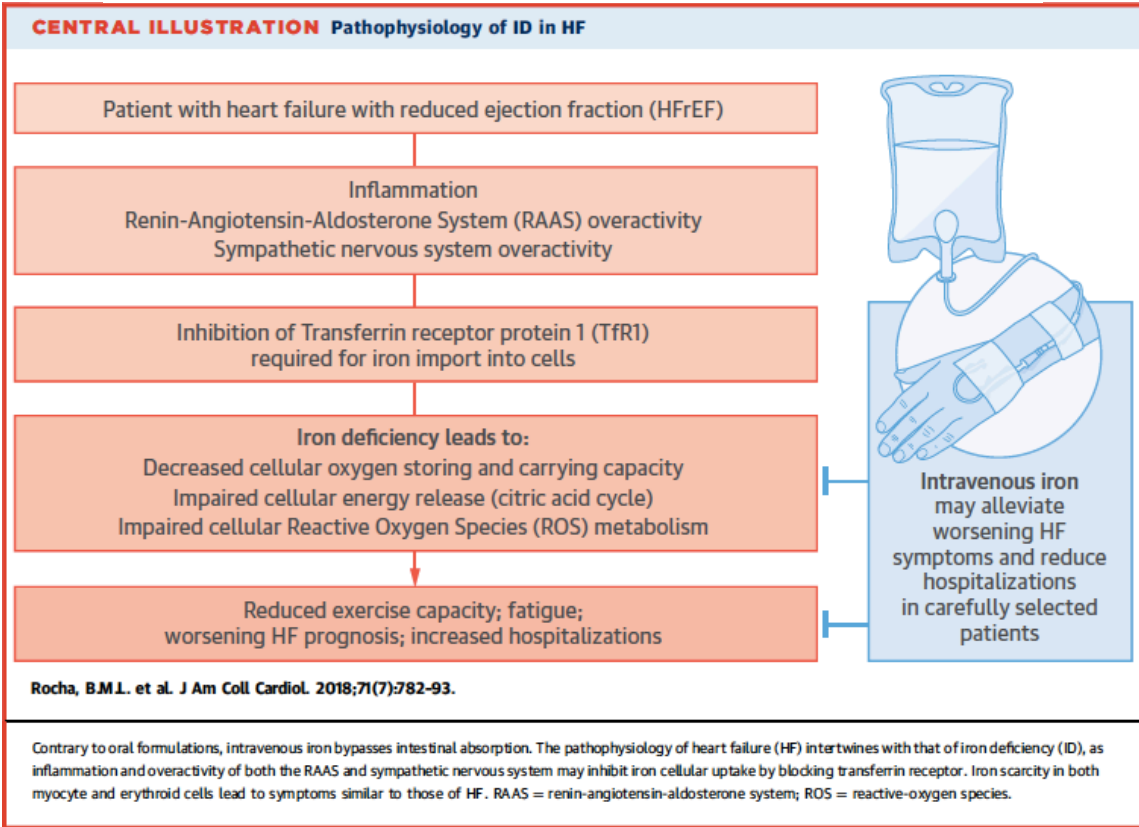
No. at Risk

Empagliflozin	4687	4614	4523	4427	3988	2950	2487	1634	395
Placebo	2333	2271	2226	2173	1932	1424	1202	775	168

Effect of Oral Iron Repletion on Exercise Capacity in Patients With Heart Failure With Reduced Ejection Fraction and Iron Deficiency

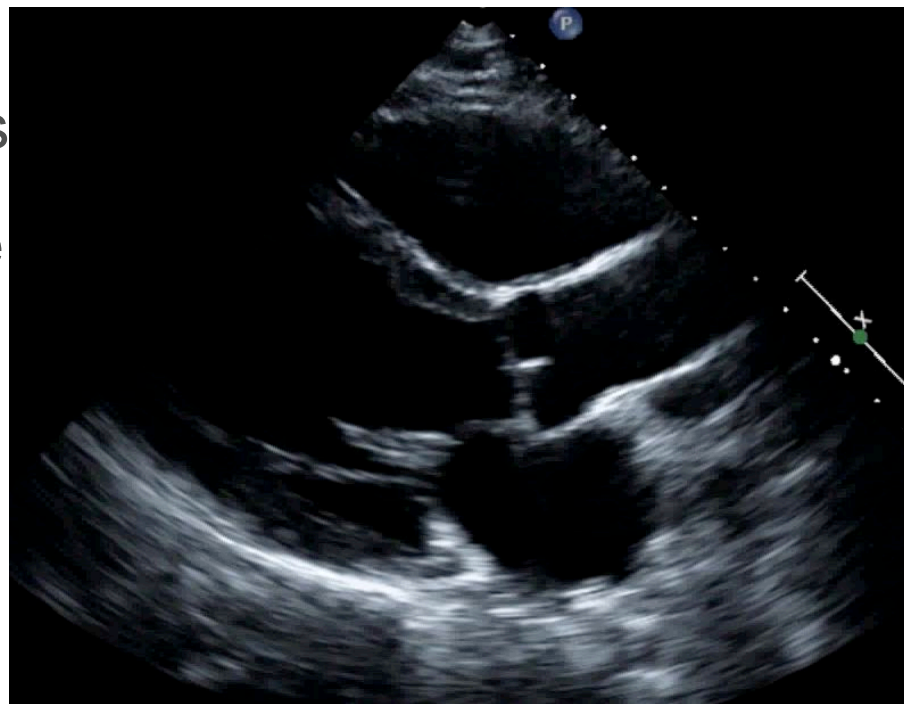
The IRONOUT HF Randomized Clinical Trial

Gregory D. Lewis, MD; Rajeev Malhotra, MD; Adrian F. Hernandez, MD, MHS; Steven E. McNulty, MS; Andrew Smith, MD; G. Michael Felker, MD, MHS; W. H. Wilson Tang, MD; Shane J. LaRue, MD; Margaret M. Redfield, MD; Marc J. Semigran, MD; Michael M. Givertz, MD; Peter Van Buren, MD; David Whellan, MD; Kevin J. Anstrom, PhD; Monica R. Shah, MD, MHS; Patrice Desvigne-Nickens, MD; Javed Butler, MD; Eugene Braunwald, MD; for the NHLBI Heart Failure Clinical Research Network



Question: How would you manage?

- Patient has been stable for many years with EF of 55%, Not dilated on five subsequent TTE. No admissions to hospital and NYHA class 1 for past 4 years. He is frustrated with taking Meds Entresto 73/77mg BD, Bisoprolol 10mg, Spironalactone 12.5mg and would like to stop.
 - Slowly reduce medications with interval TTE
 - Re-educate and preach continuation
 - Echo with strain and if normal stop meds
 - Refer for second opinion



Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial

Brian P Halliday, Rebecca Wassall, Amrit S Lata, Zohya Khaliq, John Gregson, Simon Newsome, Robert Jackson, Tsveta Rahneva, Rick Wage, Gillian Smith, Lucia Venneri, Upasana Tayal, Dominique Auger, William Midwinter, Nicola Whiffin, Ronak Rajani, Jason N Dungu, Antonis Pantazis, Stuart A Cook, James S Ware, A John Baksi, Dudley J Pennell, Stuart D Rosen, Martin R Cowie, John G F Cleland, Sanjay K Prasad

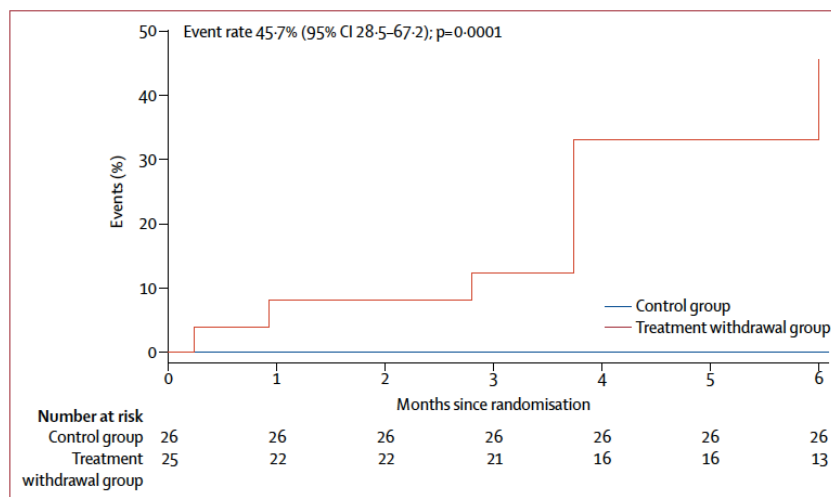


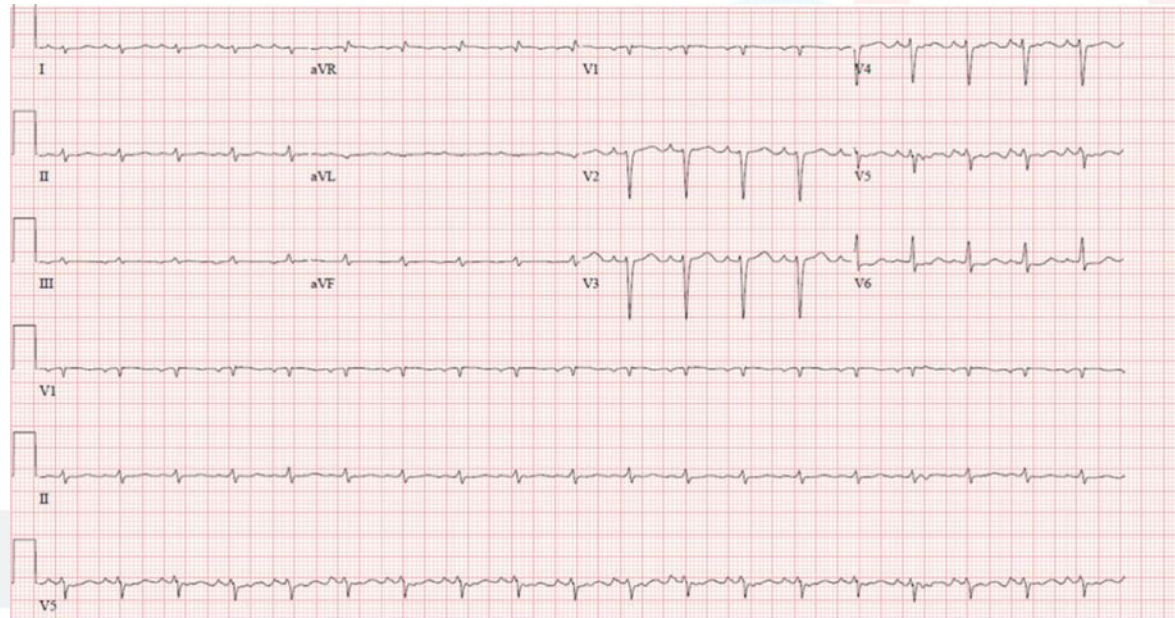
Figure 3: Kaplan-Meier curve of time to primary endpoint in randomised phase, according to treatment group. One patient dropped out at 7 days.

Findings Between April 21, 2016, and Aug 22, 2017, 51 patients were enrolled. 25 were randomly assigned to the treatment withdrawal group and 26 to continue treatment. Over the first 6 months, 11 (44%) patients randomly assigned to treatment withdrawal met the primary endpoint of relapse compared with none of those assigned to continue treatment (Kaplan-Meier estimate of event rate 45.7% [95% CI 28.5-67.2]; p=0.0001). After 6 months,

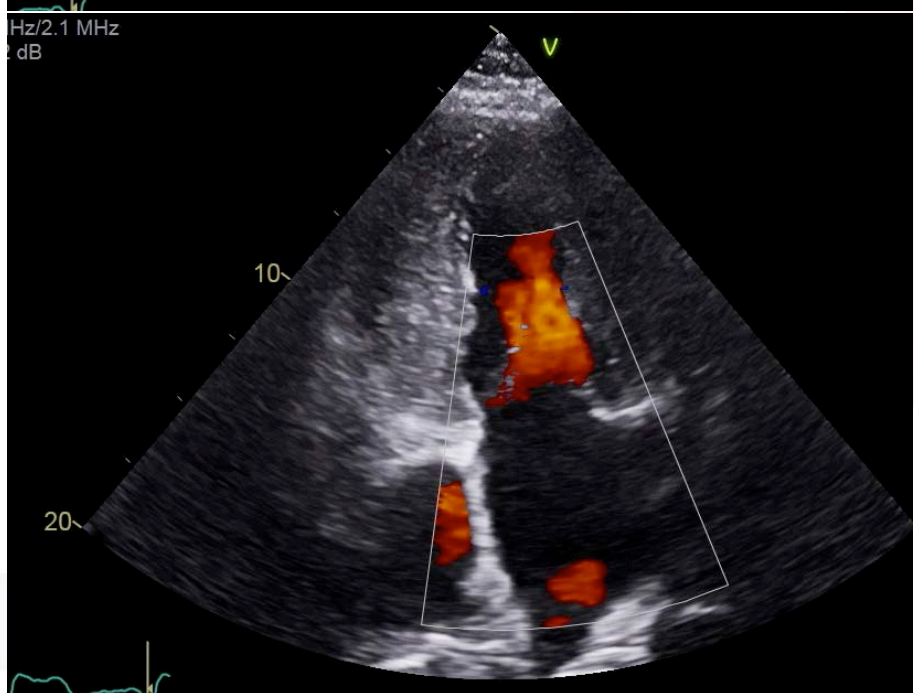
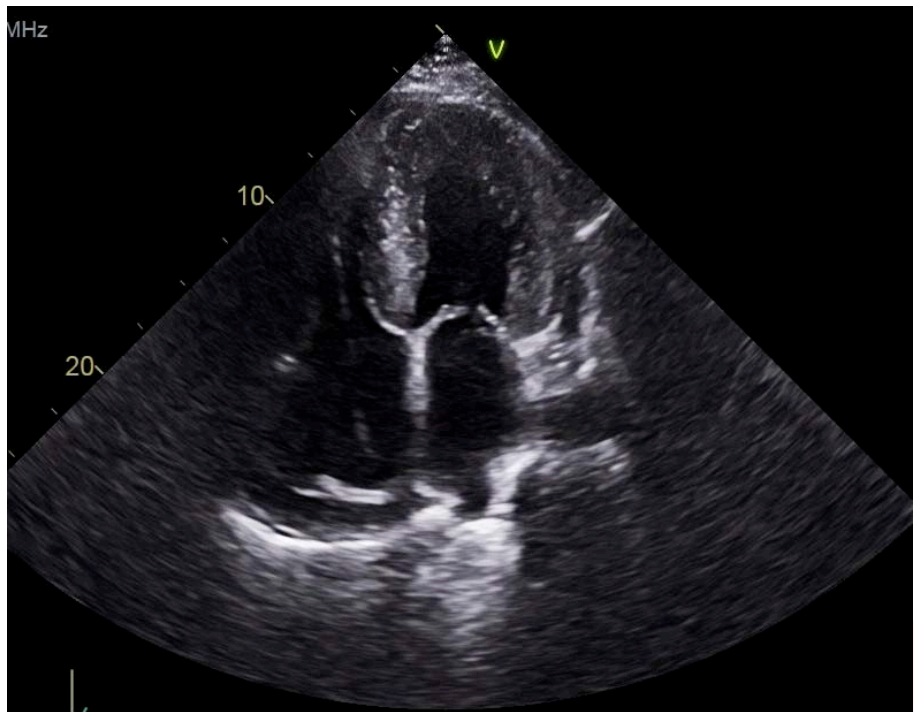
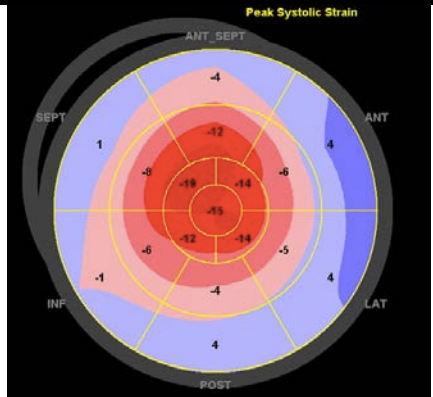
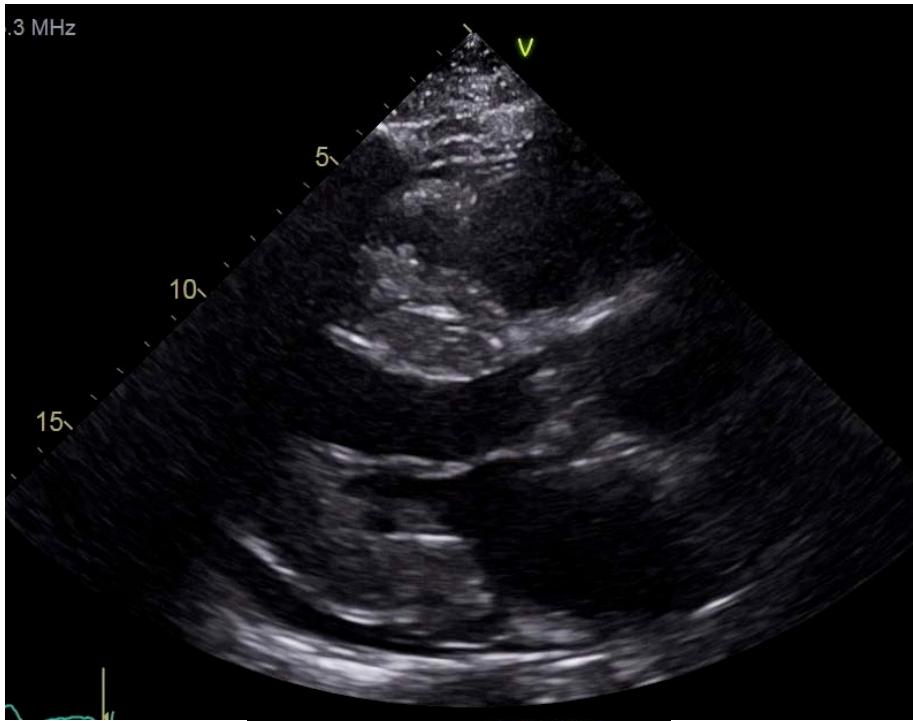
Patient B: what is the most likely unifying diagnosis?

- 54 year old male with multiple reviews for SOB. Has background of HTN, AF and asthma. Previous echo revealed EF of 50%, interventricular septal thickness of 1.3cm and no significant valvular dysfunction. Was recently treated for OSA. Presents with peripheral edema. Weight is 95 Kgs.
- Meds: Apixiban 2.5mg BD, amlodipine 10mg, digoxin 125mcg
- JVP raised, peripheral oedema.
- Creatine clearance 108

- Multiple myeloma
- HFrEF
- Fabry
- Amyloid
- Nephrotic syndrome



Echo



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Question: How would you optimize his treatment?

- Patient is on Apixiban 2.5mg BD, amlodipine 10mg, digoxin 125mcg, 80mg BD of frusemide
 - Apixiban 5mg BD
 - Increase Digoxin
 - Stop Digoxin
 - Education regarding fluid and weight

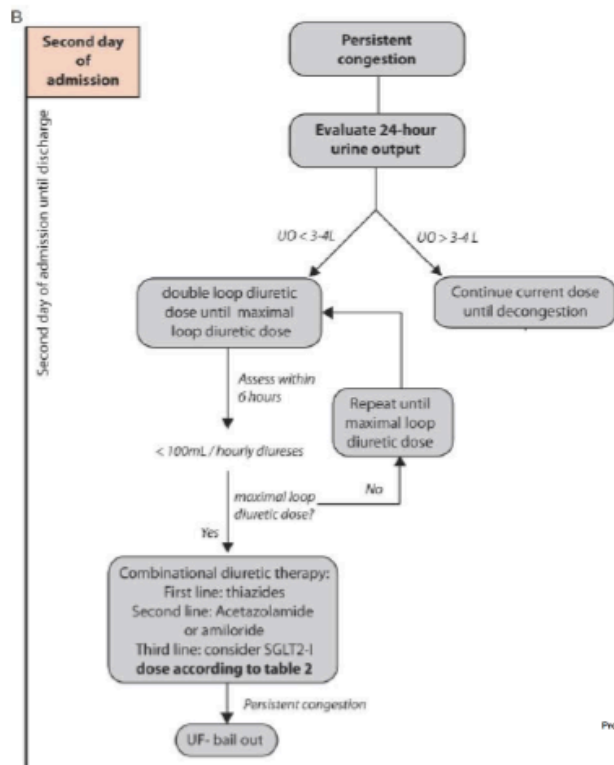


Question:

- Patient investigated and diagnosed with AL amyloid. He is on 40mg BD IV. Called as patient still orthopneic but eGFR worsened to 40. You review and JVP not seen at 45 degrees, tongue is dry, warm.
 - Stop frusemide
 - Increase frusemide to 80mg IV BD
 - Start Frusemide infusion 5mg an hour and initial 40mg IV push
 - Noradrenaline

Diuretic escalation

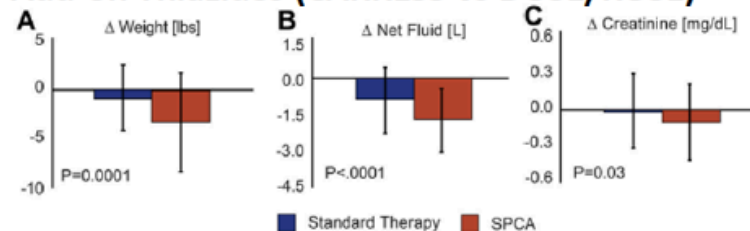
- Sequential renal blockade



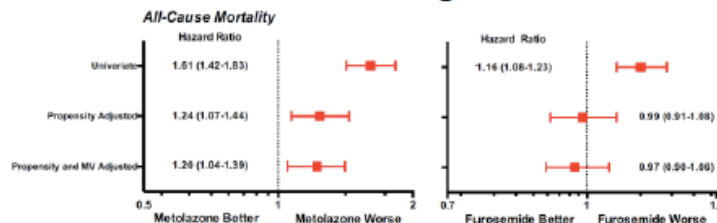
Stepped Pharmacological Care (CARRESS)

Current Dose		Suggested Dose (goal 3-5L urine/day)	
Loop (mg/day)	Thiazide	Loop (/day)	Thiazide
≤ 80	+/-	40mg IVB + 5mg/hr	0
81 – 160	+/-	80mg IVB + 10mg/hr	5mg MTZ qd
161 – 240	+/-	80mg IVB + 20mg/hr	5mg MTZ bid
> 240	+/-	80mg IVB + 30mg/hr	5mg MTZ bid

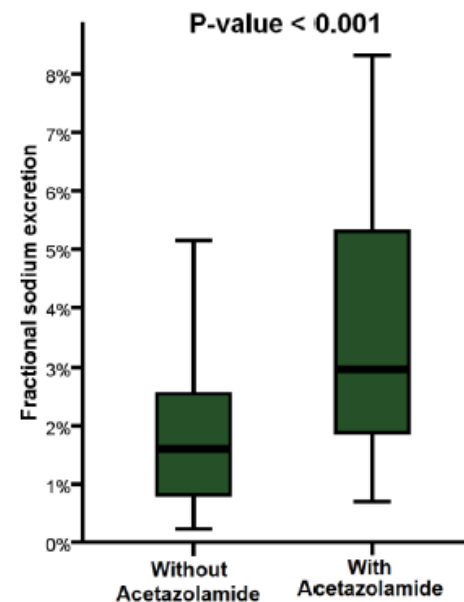
Add-on Thiazides (CARRESS vs DOSE/ROSE)



Add-on Metolazone vs High-dose furosemide

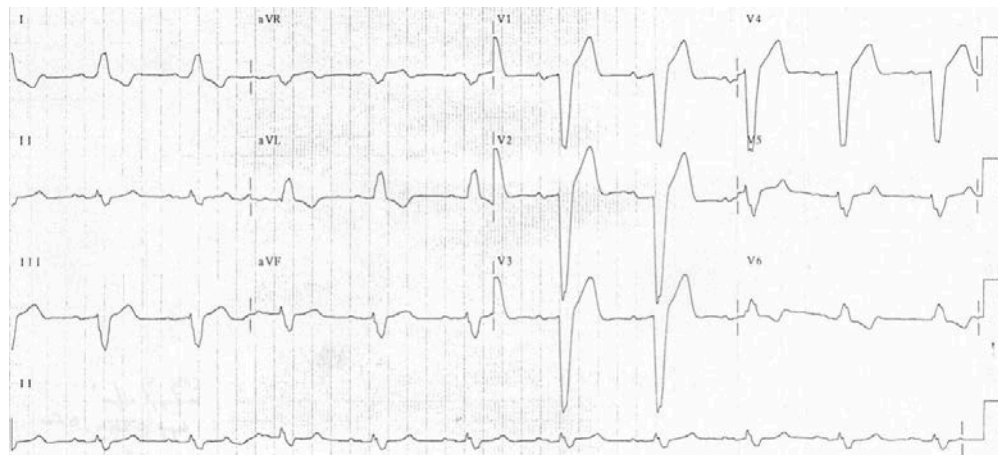


Add-on Acetazolamide



Patient AD

- Referred patient to advanced HF clinic. Patient on sacubitril/valsartan 73/77mg BD, spironolactone 25mg, bisoprolol 10mg, frusemide 80mg BD. He is morbidly obese with BMI 42. 3 admissions this year for decompensation. He cares for his mother and on multiple occasions has discharged early to care for her. Stable on follow up and optimized. Remains NYHA II/III.





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Question: What would you do?

- Start Transplant work up
- Stop spironolactone and increase sacubitril/valsartan to 97/103mg BD
- Refer for Device therapy
- Educate, loose weight



“I NEED HELP”

WHEN TO REFER PATIENTS FOR ADVANCED HEART FAILURE ASSESSMENT

REMEMBER THIS ACRONYM TO ASSIST IN DECISION MAKING FOR REFERRAL TO ADVANCED HEART FAILURE SPECIALIST ^(1,2)	
I	IV Inotropes
N	NYHA III/IV or persistently elevated natriuretic peptides
E	End-organ dysfunction
E	Ejection Fraction < 35%
D	Defibrillator shocks
H	Hospitalizations > 1
E	Edema Despite escalating diuretics
L	Low Blood Pressure – High Heart Rate
P	Prognostic medication – progressive intolerance or down-titration of GDMT

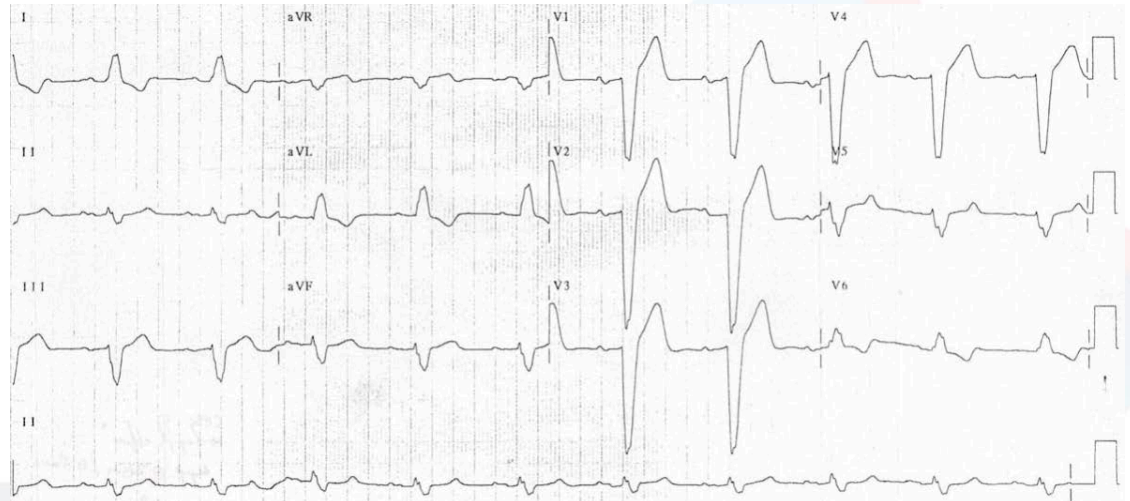
(1) Baumwol J. “I Need Help”—a mnemonic to aid timely referral in advanced heart failure. J Heart Lung Transplant. 2017;36:593–4.s

(2) The Journal of American College of Cardiology; Pathways for Optimization of Heart Failure Treatment; Vol. 71, No. 2, 2018:201–302017

Question

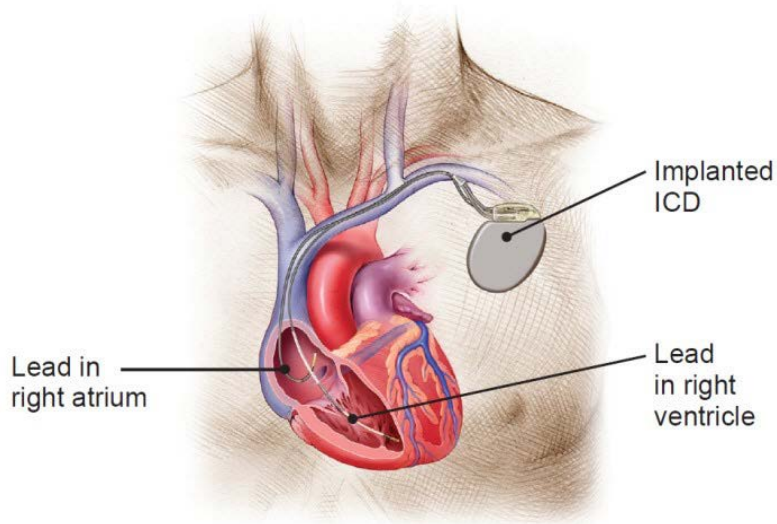
- Referred patient to advanced HF clinic. Patient on sacubitril/valsartan 73/77mg BD, spironolactone 25mg, bisoprolol 10mg, frusemide 80mg BD. He is morbidly obese with BMI 42. 3 admissions this year for decompensation. He cares for his mother and on multiple occasions has discharged early to care for her. Stable on follow up and optimized. Remains NYHA II/III. EF 17%

- ICD
- CRT
- CRT-D

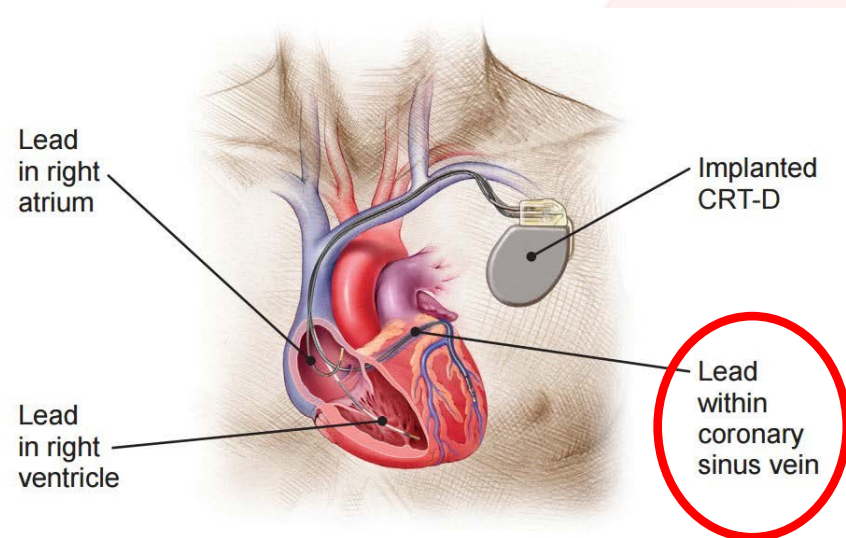


Indications for Cardiac Electronic Implantable Devices in HF – ICD & CRT-ICD

- Prevention of Sudden Cardiac Death



- Cardiac Resynchronization Therapy



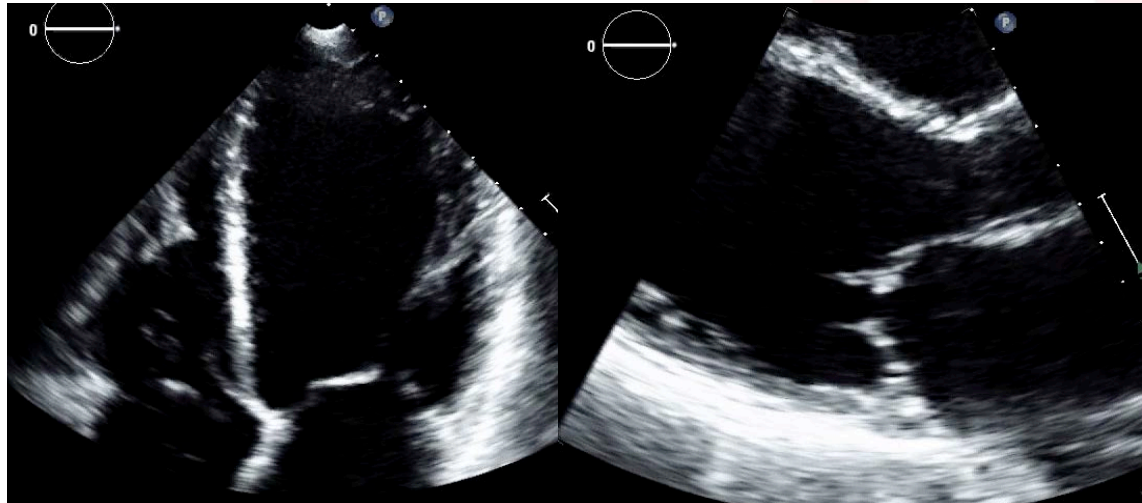
Figures from: <http://www.bostonscientific.com/en-US/patients/about-your-device>

CRT and AICD

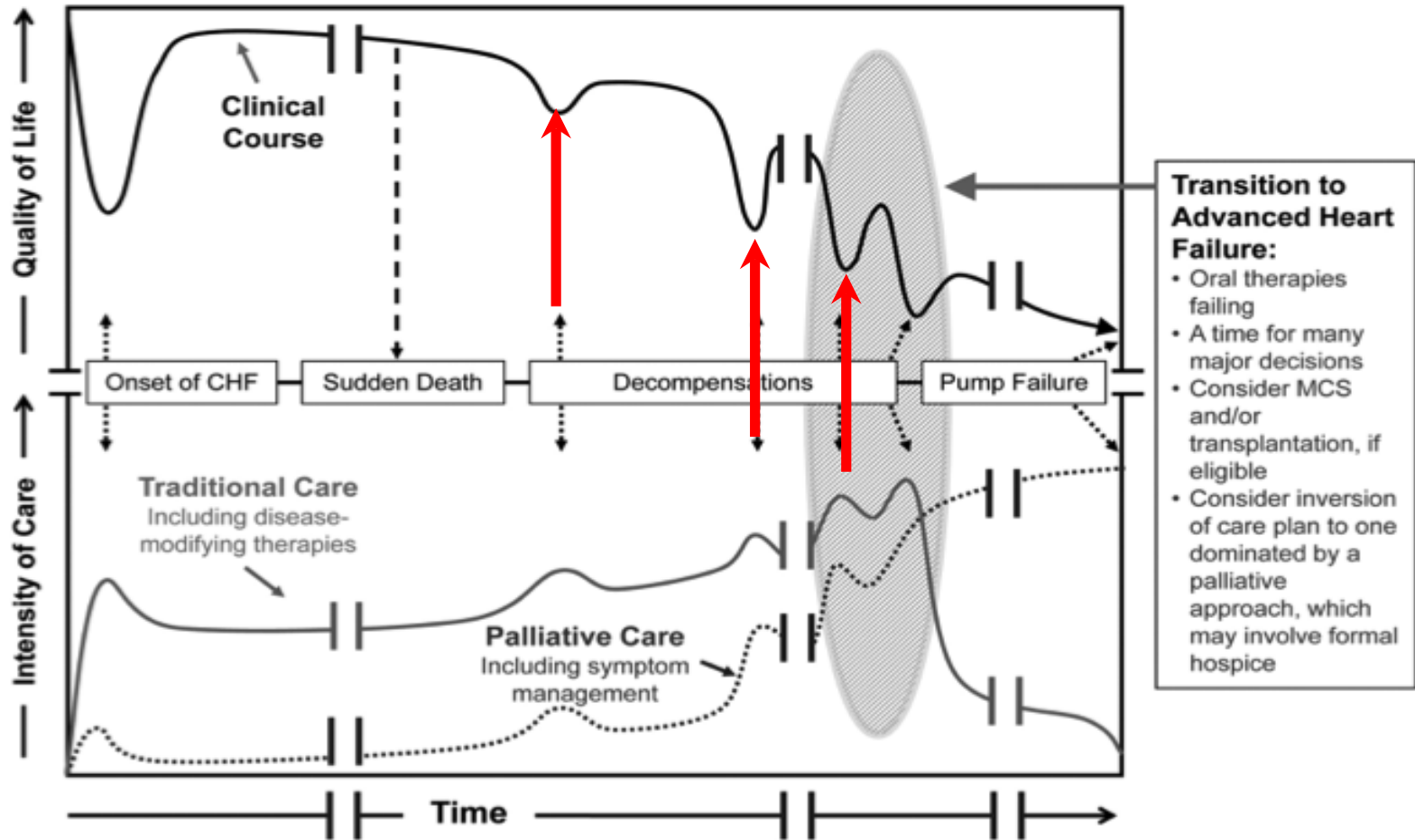
- CRT (Australian)
 - 1A – sinus rhythm, $\leq 35\%$, QRS > 150 , GDMT
 - 1B – 130-149
 - 3a - $< 130\text{ms}$
- AICD
 - MADIT II criteria – prior MI and LVEF $< 30\%$
 - SCD HEFT criteria – LVEF $< 35\%$ and NYHA II or III

Patient Referred to HF team: Mr A.T.

- 53 male with IDCM. 3 admissions this year for HF. EF last month was 19% with LVEDV 396ml. CKD III, weight 68kg, height 187 cm. HR is 64 and BP 94/70.
- Meds: sacubitril/valsartan 24/26mg BD (reduced dose), spironolactone 25mg, bisoprolol, CRT-D
- Social: reduced working to 3 days a week due to tiredness.
- **What red flags do you have?**
 - Reducing Tx
 - Repeat admissions
 - Reducing work load
 - Weight
 - Low BP
 - All of above



Clinical Course of HF



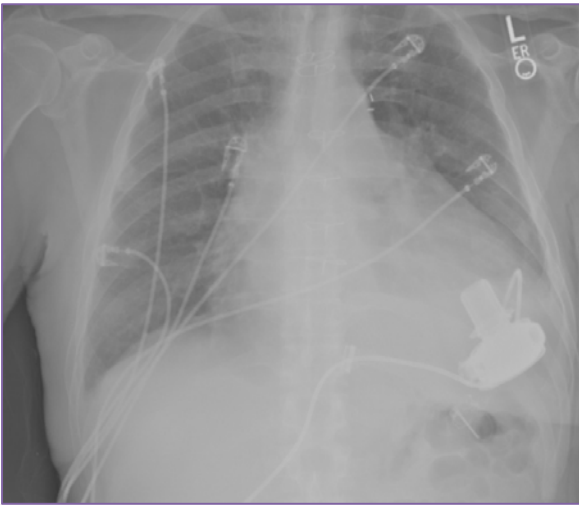
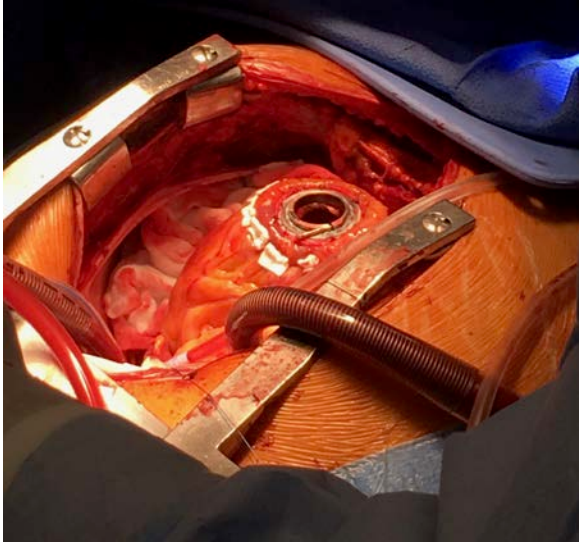
Palliative Care

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
Referral to palliative care should be considered in patients with advanced HF to alleviate end-stage symptoms , improve quality of life and decrease rehospitalisation. Involvement of palliative care should be considered early in the trajectory towards end stage HF. ¹	Strong	High

- In patients with an ICD, discussions concerning deactivation should occur between the patient, family and cardiologist.
- Patients should be encouraged to have an advanced care plan, regardless of clinical status and soon after diagnosis.

1.Kavalieratos D, et al. JAMA. 2016;316(20):2104-14.

Insertion of VAD as bridge to Tx



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A close-up photograph of a person's hands wearing blue nitrile gloves, gently cupping a bright red, realistic-looking heart. The heart is the central focus, and the word "Questions" is printed in white, bold, sans-serif font across its middle. The background is a soft-focus blue, likely a medical professional's scrubs, with a portion of a stethoscope visible in the upper left corner. The lighting is soft and even, highlighting the texture of the gloves and the smooth surface of the heart.

Questions