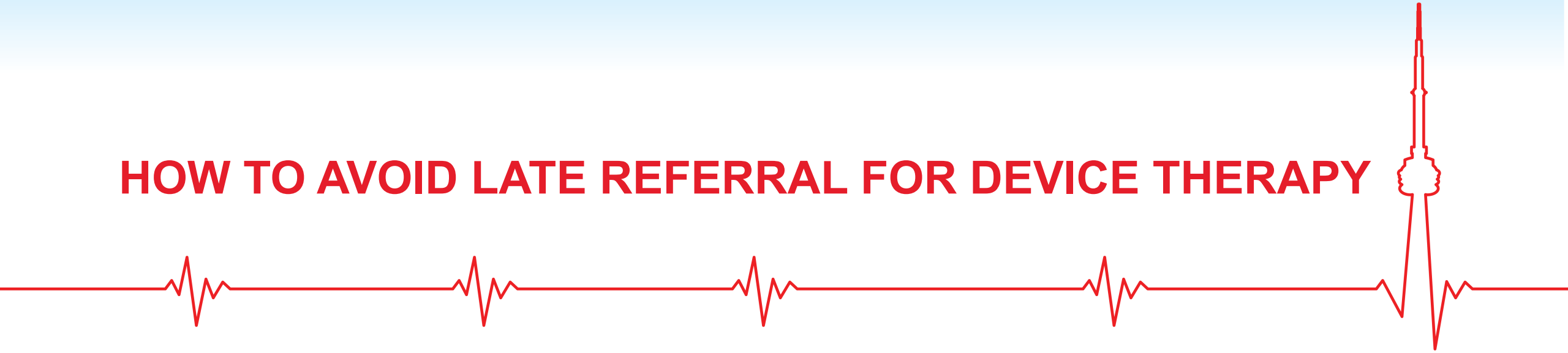
HOW TO AVOID LATE REFERRAL FOR DEVICE THERAPY



Anil Gupta, MD, FRCP

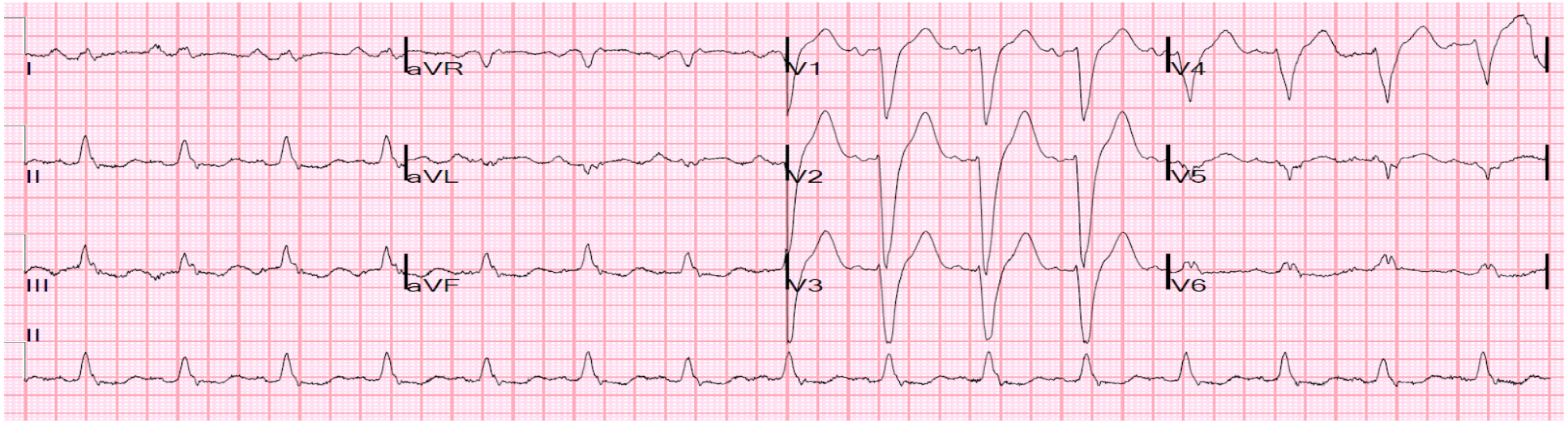
Staff Cardiologist
Trillium Health Partners
Lecturer, University of Toronto
Toronto, ON

68 year old woman

- Diabetes, HTN, eGFR 48 mL/min
- dilated cardiomyopathy, LVEF 25% by Echo
- NYHA 2-3

Medications:

- carvedilol 12.5 mg BID
- ramipril 5 mg OD
- aldactone 25 mg po OD

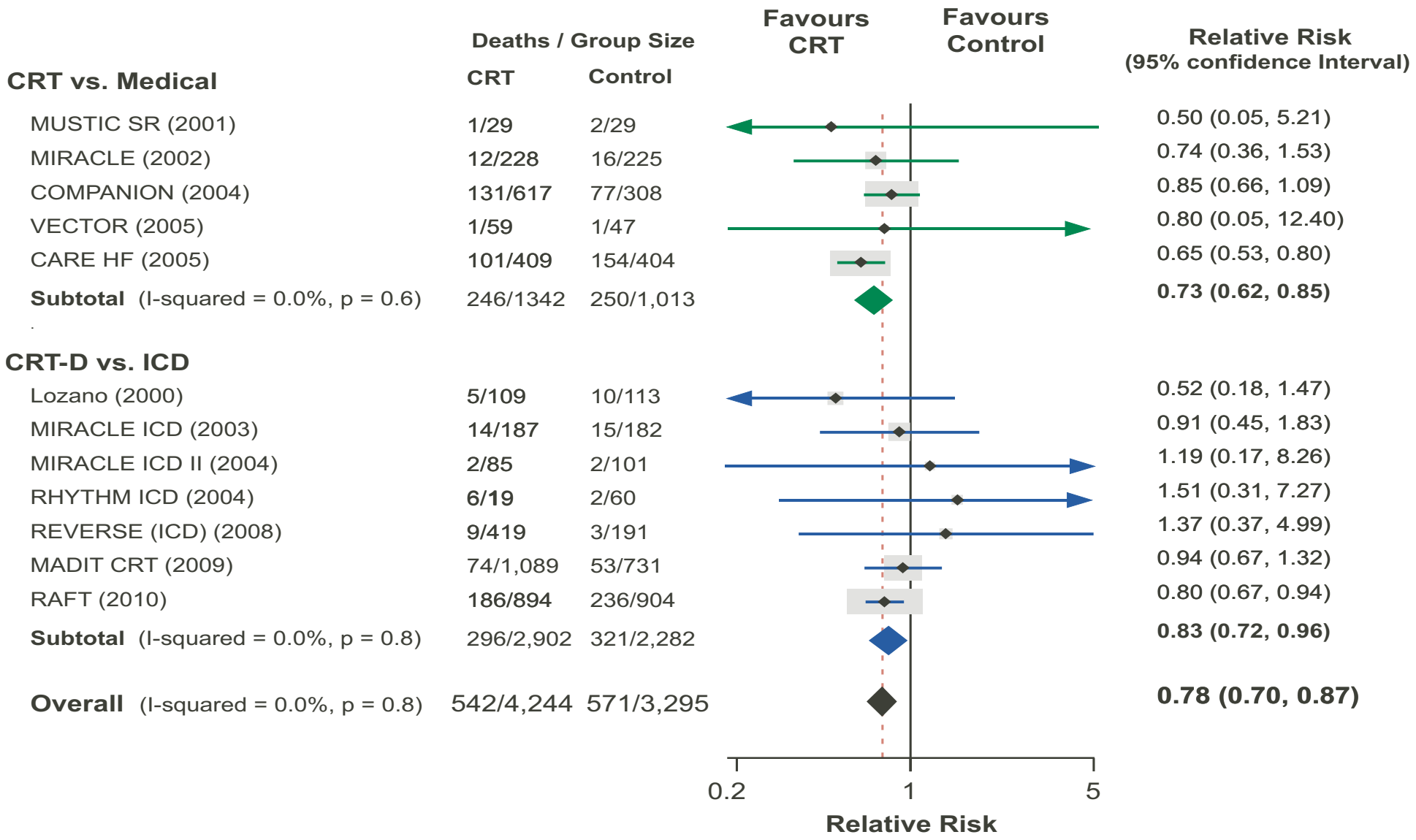


- Referred for consideration of CRT, by local community internist.
- Electrophysiologist astutely recognized further opportunity to optimize medical therapy
- Referred her to the HF clinic for further management
  - **Switched ramipril to sacubitril/valsartan 24/26 mg BID**
  - **1 month later titrated dose to 24/25 mg qAM and 49/51mg qPM**
  - **Switched carvedilol to bisoprolol 5mg po OD**
  - **With improved BP, able to further increase sacubitril/valsartan to 49/51mg mg po BID**

- Repeat assessment:
  - EF by MUGA scan 32%
  - ECG shows LBBB, QRS > 150 msec
  - eGFR 43 mL/min
  - NYHA 2-3
  - Relevant medications:
    - sacubitril/valsartan 49/51mg po BID
    - bisoproprolol 5mg po OD
    - aldactone 25mg po OD

- CRT successfully implanted
  - Patients improved to NYHA class 1-2
  - LVEF by echo now 41%

Clinical Trial Evidence



Can J Cardiol **2013**; 29(2):182-195

CRT Guidelines

Recommendation

CRT is recommended for patients

- Sinus rhythm
- NYHA class II or III
- Ambulatory IV heart failure symptoms
- LVEF ≤ 35%
- QRS duration ≥ 130 msec due to LBBB

CRT Guidelines

Recommendation

CRT is recommended for patients

- Sinus rhythm
- NYHA class II or III
- Ambulatory IV heart failure symptoms
- LVEF ≤ 35%
- QRS duration ≥ 150 msec not due to LBBB conduction

Recommendation

- There is insufficient evidence to recommend CRT for patients with NYHA class I or patients non-ambulatory class IV NYHA symptoms.

- There is also insufficient data to recommend CRT in patients with QRS duration < 130 ms.

- Patients with LBBB and QRS duration ≥ 150 ms appear more likely to benefit from CRT than patients with non-LBBB conduction and/or less QRS prolongation.

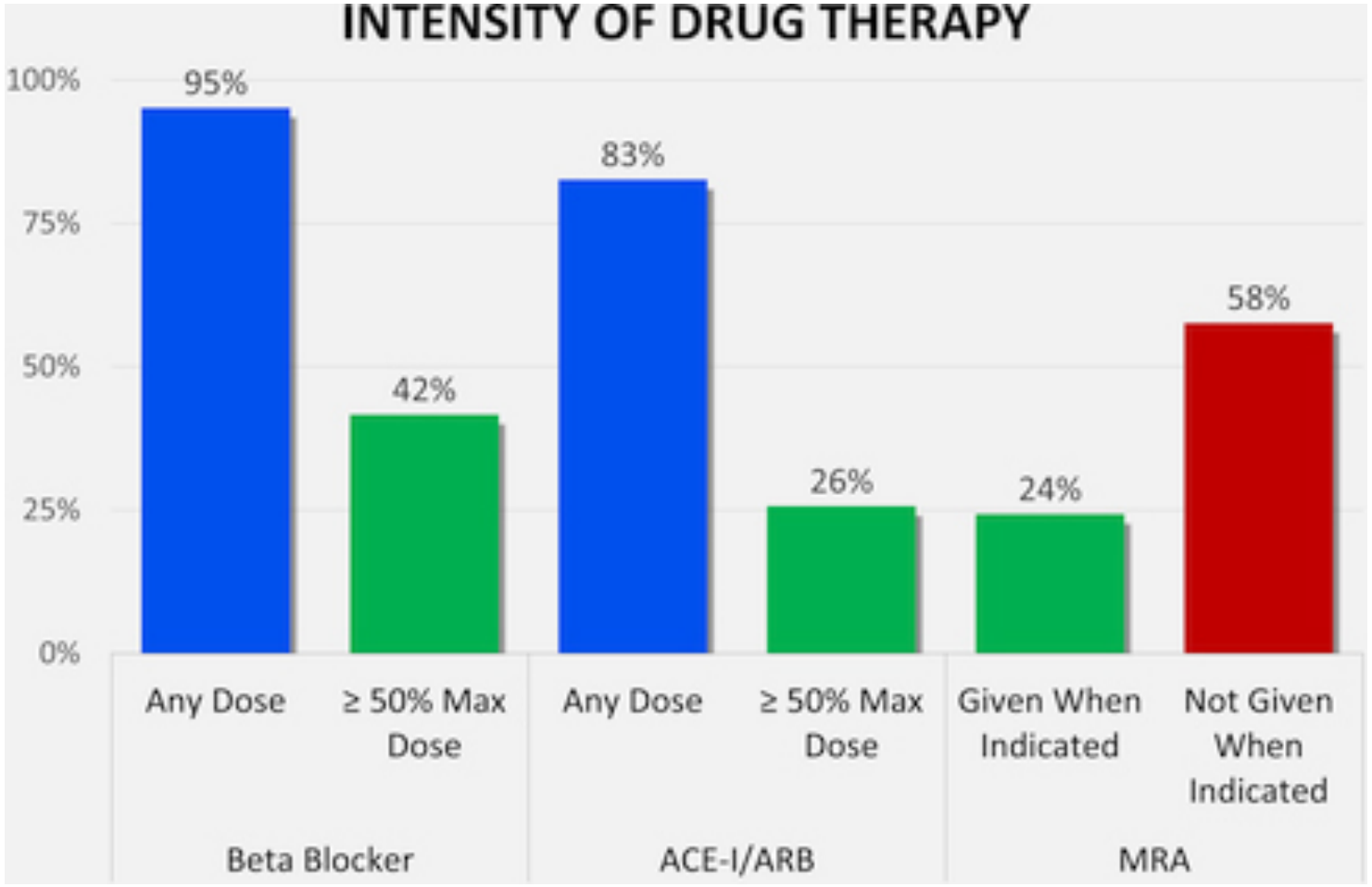
CRT Guidelines

Recommendation

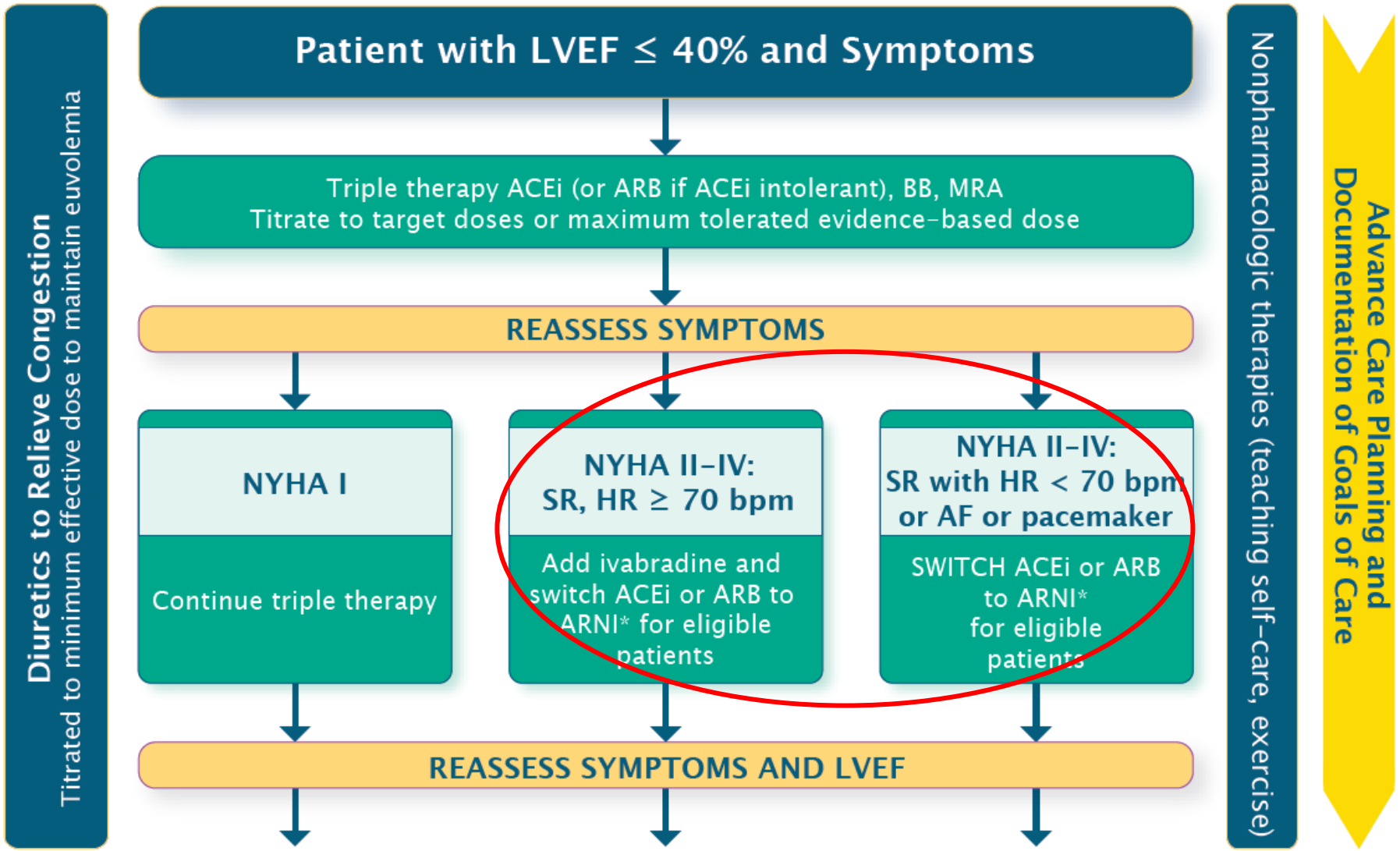
- Adequate medical therapy be implemented prior to the initiation of CRT
- Details of that assessment be recorded in their medical record.
- The reasons for non-use of recommended heart failure medications or the prescription of lower than the recommended doses of these agents should be recorded.

Are Heart Failure Patients Who Undergo Cardiac Device Implantation Receiving Optimal Guideline Directed Medical Therapy?

Nov 2018. Circulation. 2018;138:A12743



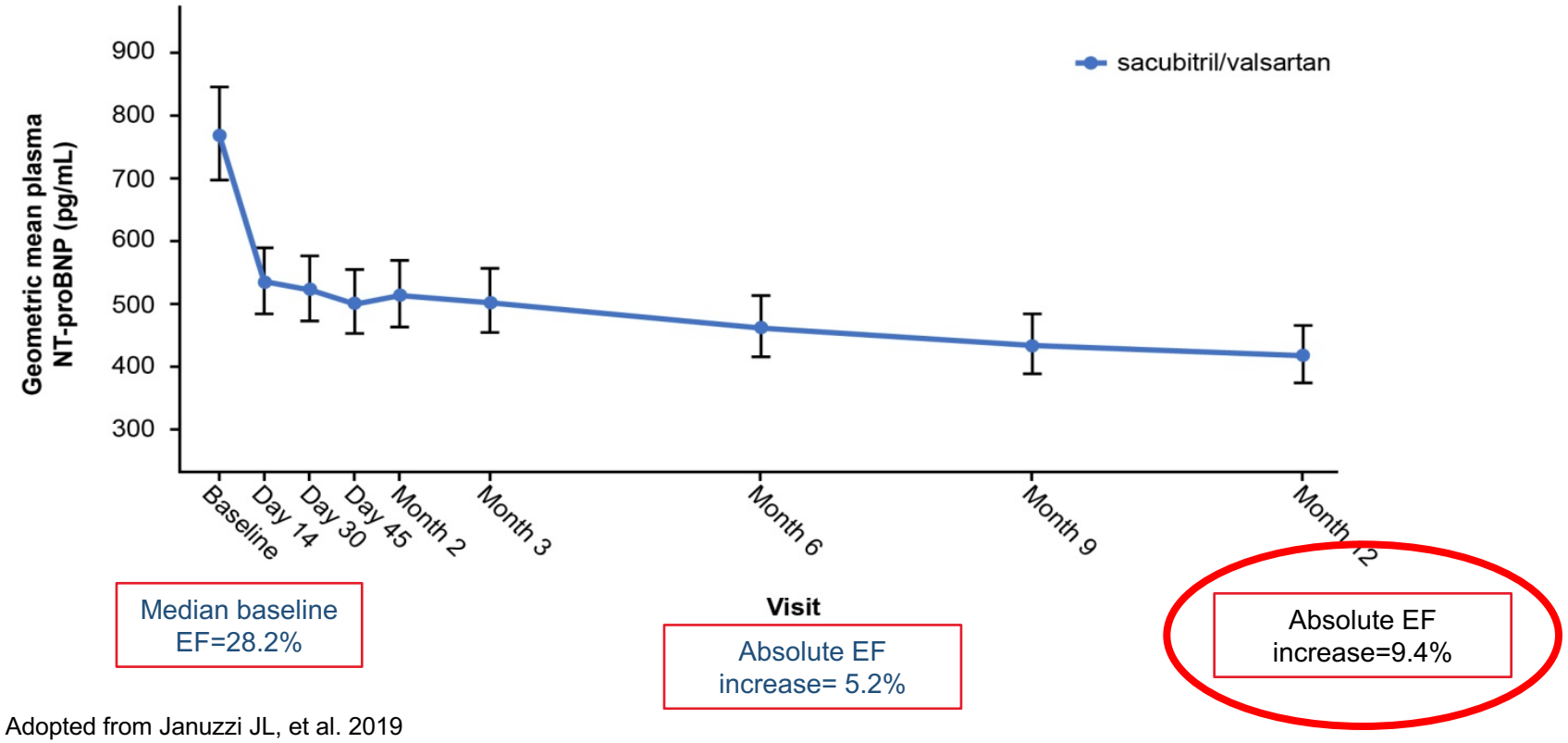
Therapeutic Approach to Patients With HFrEF



PROVE-HF

NT-proBNP concentrations

Initiation of sacubitril/valsartan was associated with a reduction in NT-proBNP concentrations with the majority of reduction seen at the first follow-up visit (day 14)[1,2]



Adopted from Januzzi JL, et al. 2019

NT-proBNP, N-terminal pro-B-type natriurietic peptide

1. Januzzi JL, et al. *JAMA* 2019; DOI: 10.1001/jama.2019.1282 2. Januzzi JL, et al. Late Breaker ESC 2019. Paris, France August 31-September 4, 2019

Summary of Evidence

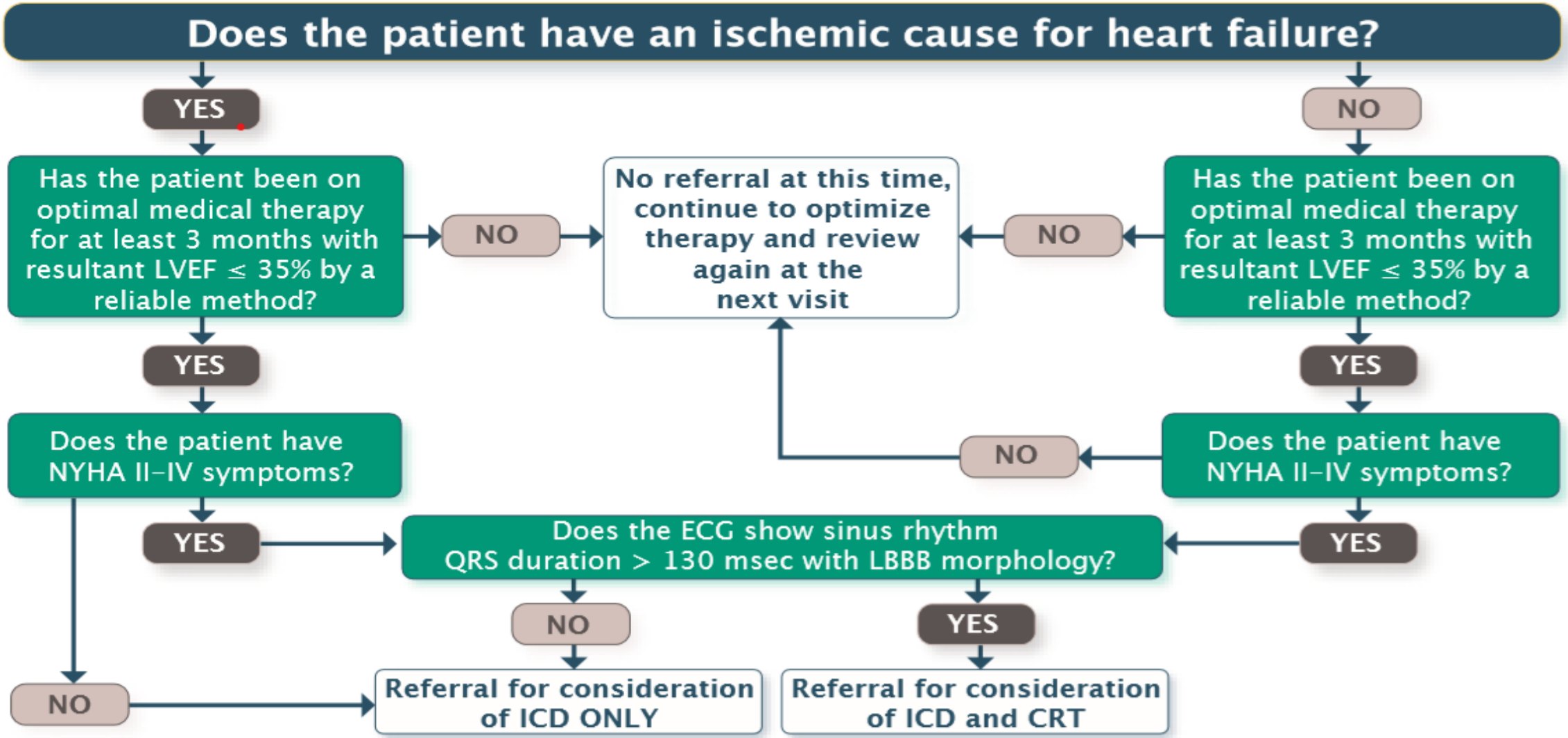
- Very few NYHA I or non-ambulatory IV patients
- Mean QRS: 153-173 msec
- Most had LBBB
- Patients with severe comorbidities excluded:
  - Severe pulmonary disease
  - Severe liver disease
  - Severe renal disease
  - Limited life expectancy

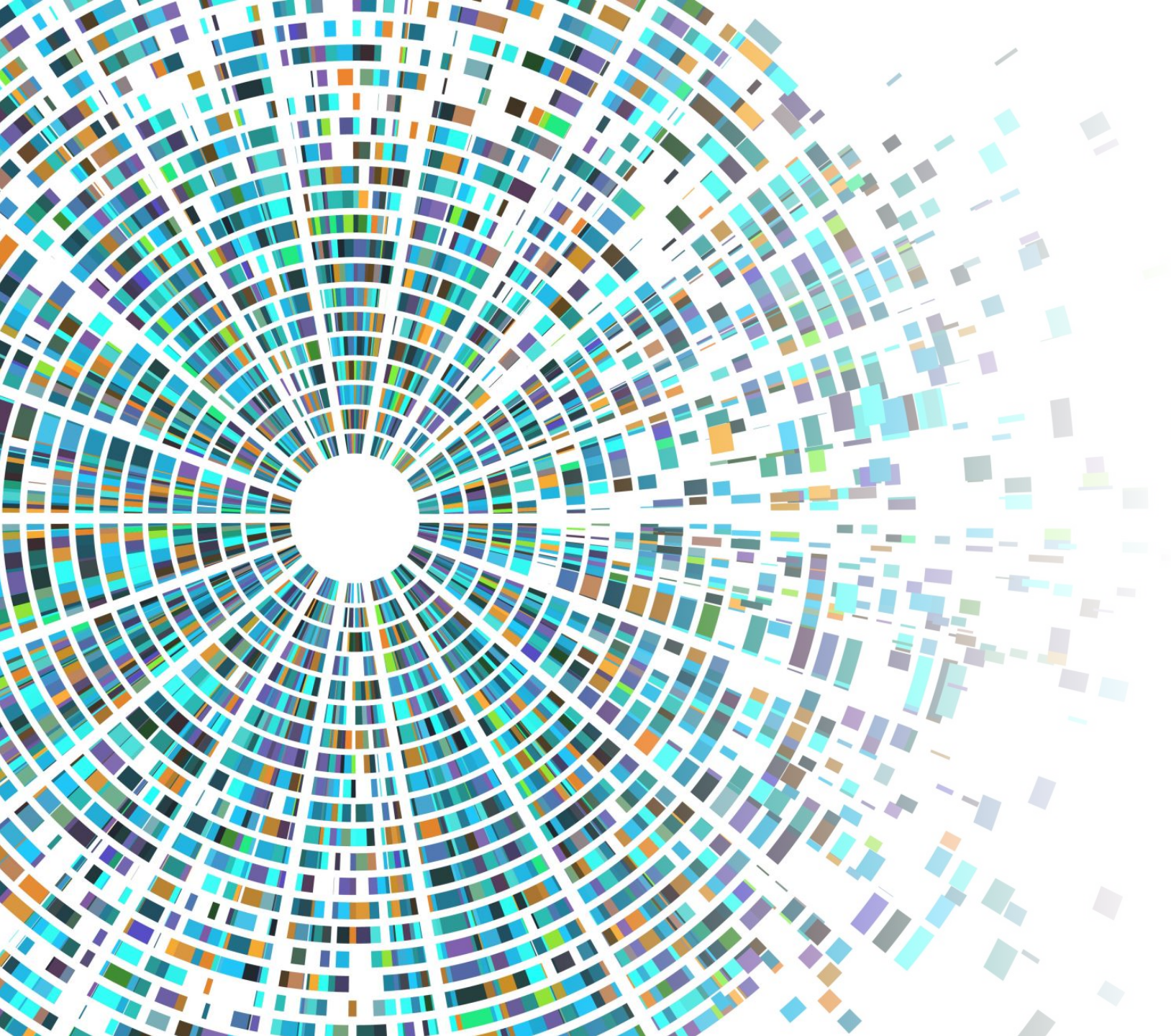
Other considerations…

- CRT *may be considered* for patients in permanent AF who are otherwise suitable for this therapy.
- Routine assessment of dyssynchrony with present echocardiographic techniques is *not recommended* to guide the prescription of CRT.
- CRT *may be considered* for patients who are chronically RV-paced or are likely to be chronically paced, have signs and/or symptoms of heart failure, and a LVEF ≤ 35%.
- Severe CKD (GRF<30) was an exclusion in landmark trials

Complication	Incidence	Suggested methods to prevent
Contrast-induced nephropathy	7-43%	Pre-hydration; ↓ dose of diuretics; ↓dose of contrast, dilution of contrast
Pneumothorax	0.6-1.0%	Extrathoracic puncture, echo or contrast-guided venous puncture, axillary preferred to subclavian; use of cephalic vein
Pericardial effusion	1.5%	Use of soft tip guides and access tools
Hematoma	3-6%	Avoid low molecular weight heparin peri-procedurally
Phrenic nerve stimulation	up to 13%	Conscious sedation; no paralytic agents; identify all available coronary vein branches; use of multi-polar leads
Lead related	3.5-18.7%	Appropriate training and adequate procedural volumes
Device infection	1.3-2.6%	Appropriate antibiotic prophylaxis; chlorhexidine skin preparation; limited shaving

Referral Pathway for Device Therapy in Patients with Heart Failure (HF)





HF update: How to avoid late referral for device therapy

Kiran Sidhu, MD FRCPC

Anil Gupta, MD FRCPC

Conflict of Interest

- **Grants/research support**: None
- **Consulting fees**: None
- **Speaker fees**: None
- **Other**: No relevant disclosures

- I will discuss off-label use for CRT

Objectives

1. Identify patient profiles that prompt you to refer for CRT

2. Identify patient profiles that prompt you to refer for VAD

Patient presentation

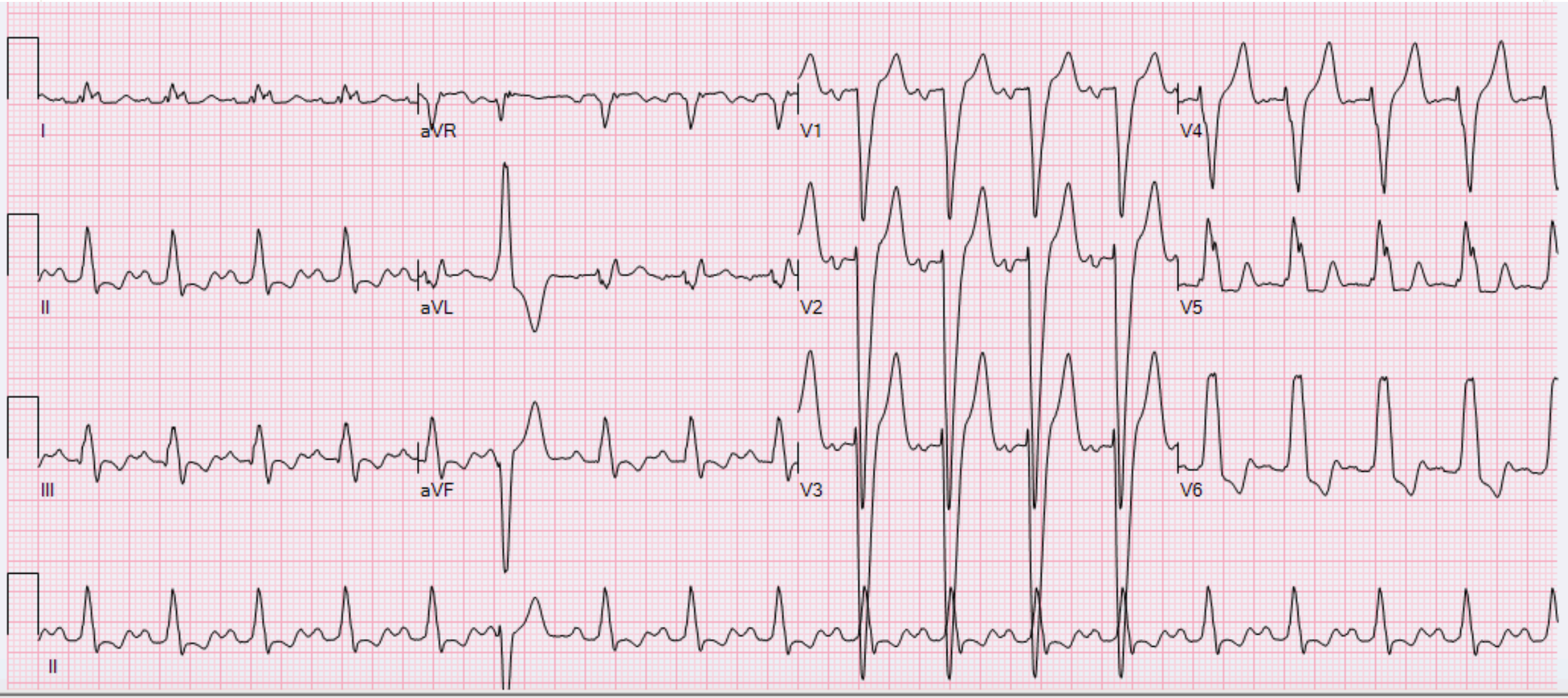
- 42 year old male, previously healthy, 6’2”, blood group O
- Admitted in Jan 2020 with cardiogenic shock
- Remarks on URTI symptoms since early December
- MRI shows EF 7%, severe RV dysfunction, LGE pattern consistent with possible prior myocarditis vs. idiopathic dilated cardiomyopathy
- Briefly on Dobutamine, then transitioned to Ramipril 2.5 mg bid, Metoprolol 12.5 mg BID, Lasix 20 mg daily
- Seen in clinic 3 days post-discharge, Ramipril uptitrated and able to walk > 438 m on 6MWT

Patient presentation

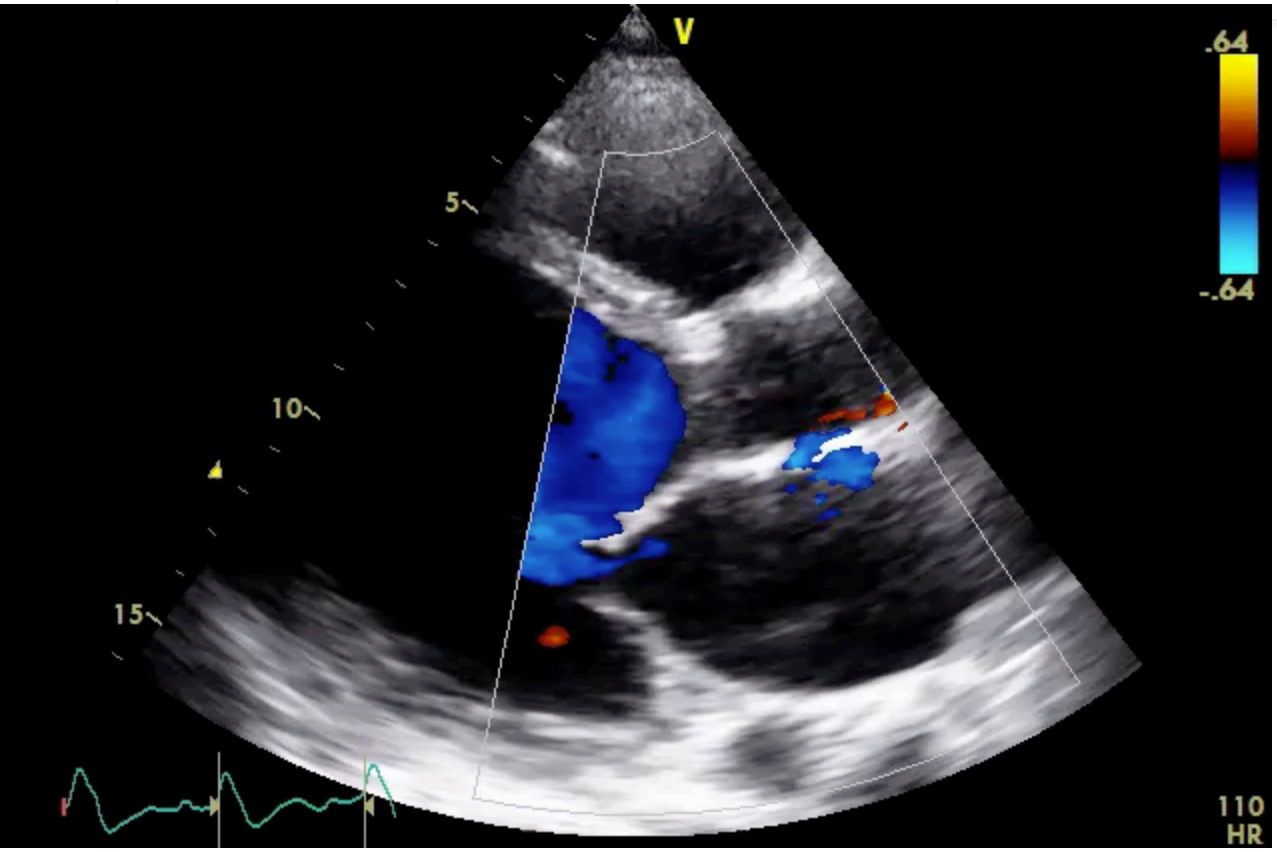
- Five days later, presents to ED with PND and HR>120 – sent home
- Over the course of the next week, progressive intolerance of medical therapy, new cough with hemoptysis
- Seen on a Friday afternoon in clinic – can only walk 50 steps before dyspneic, sleeping in a chair, abdominal bloating, vomiting, confusion

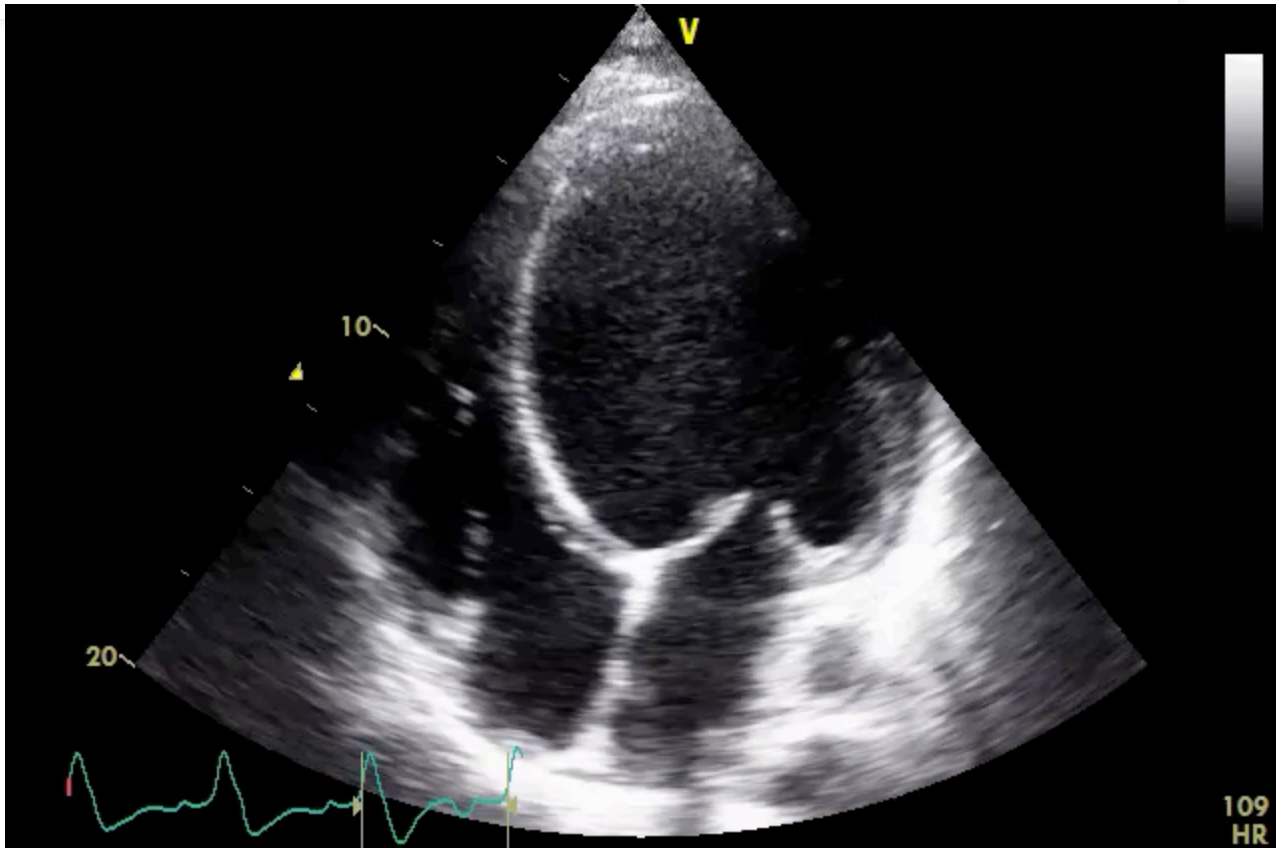
Objective data

- BP 76/60, HR 120 in clinic
- PA line: RA 19, PCWP 42, CO 2.9/CI 1.4, SVR 2246
- Labs: Na 129, K 4.2, SCr 126, lactate 2.3
- LFTs: Bili 58/18, AST 75, ALT 84, GGT 50, INR 1.8
- Started on IV Lasix infusion, Milrinone 0.25 mcg/kg/min


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

TTE on Milrinone





Course in Hospital

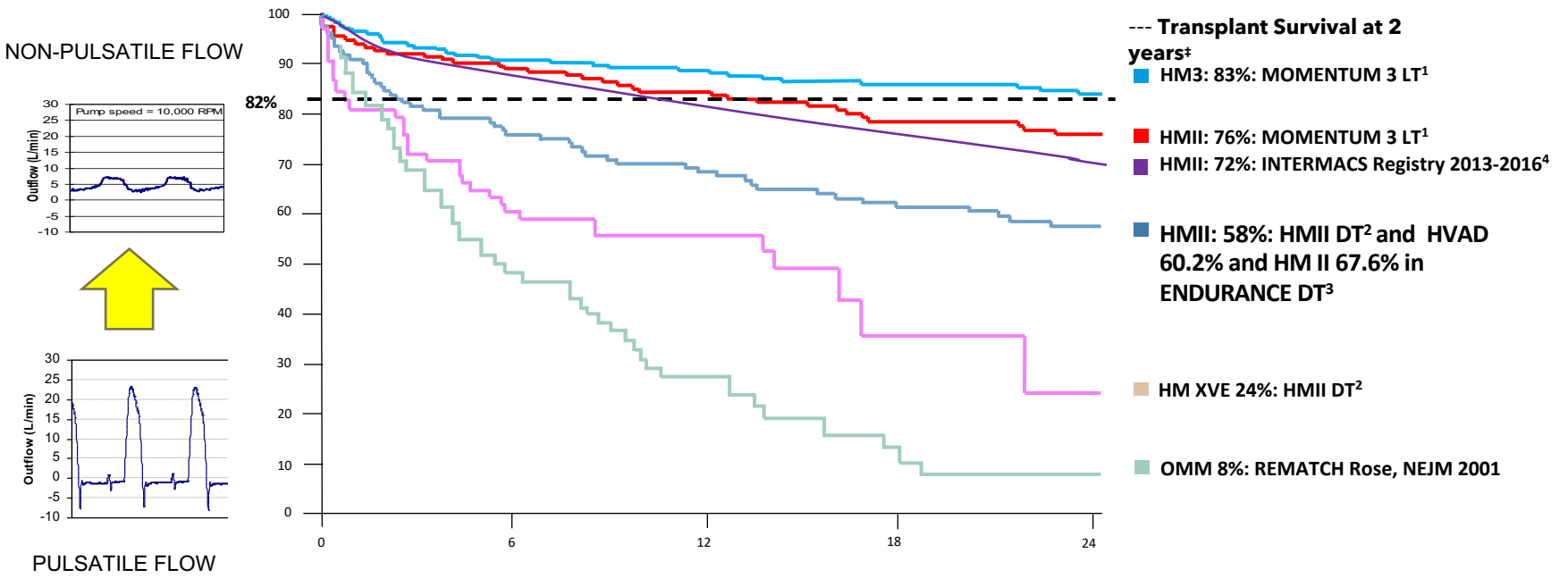
- Diuresed down to a RA 6, PCWP 14
- Captopril started and uptitrated to 50 mg TID, addition of Hydralazine resulted in marked lightheadedness
- Persistently tachycardic at 120 bpm
- Attempts at weaning Milrinone result in deterioration of mixed venous sats to < 50% and rise in CVP
- Any attempt at mobilization also results in marked drop in venous saturations

What would you do now?

1) Referral for CRT

2) Referral for LVAD

Advancing Survival in Advanced Heart Failure



1. Mehra MR, et al., for the MOMENTUM 3 investigators. N Engl J Med. 2018.
2. Slaughter, et al. NEJM.
3. Rogers J et al. ENDURANCE Investigators N Engl J Med. 2017.
4. The International Society for Heart & Lung Transplantation. http://www.ishlt.org/registries/slides.asp?slides=heartLungRegistry. Accessed March 11, 2018.

Slide courtesy of MR Mehra

INTERMACS
HEART FAILURE CLINICAL PROFILES

Profile 1 (Sickest)	Critical cardiogenic shock
Profile 2	Progressive decline on inotropic support
Profile 3	Stable but inotropic dependent
Profile 4	Resting symptoms – home on oral therapy
Profile 5	Exertion intolerant
Profile 6	Exertion limited
Profile 7	Advanced NYHA Class III symptoms

High risk features

- Other considerations for your ambulatory patients:
  - VO2 max < 14 or < 50% predicted
  - 6MWT < 300 m

Remember acronym to assist in decision making for referral to advanced heart failure specialist:

I-NEED-HELP (also see *Table 6*)

I: IV inotropes

N: NYHA IIIB/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

Yancy et al. J Am Coll Cardiol. 2018 Jan 16;71(2):201-230

Considerations pre-LVAD implant

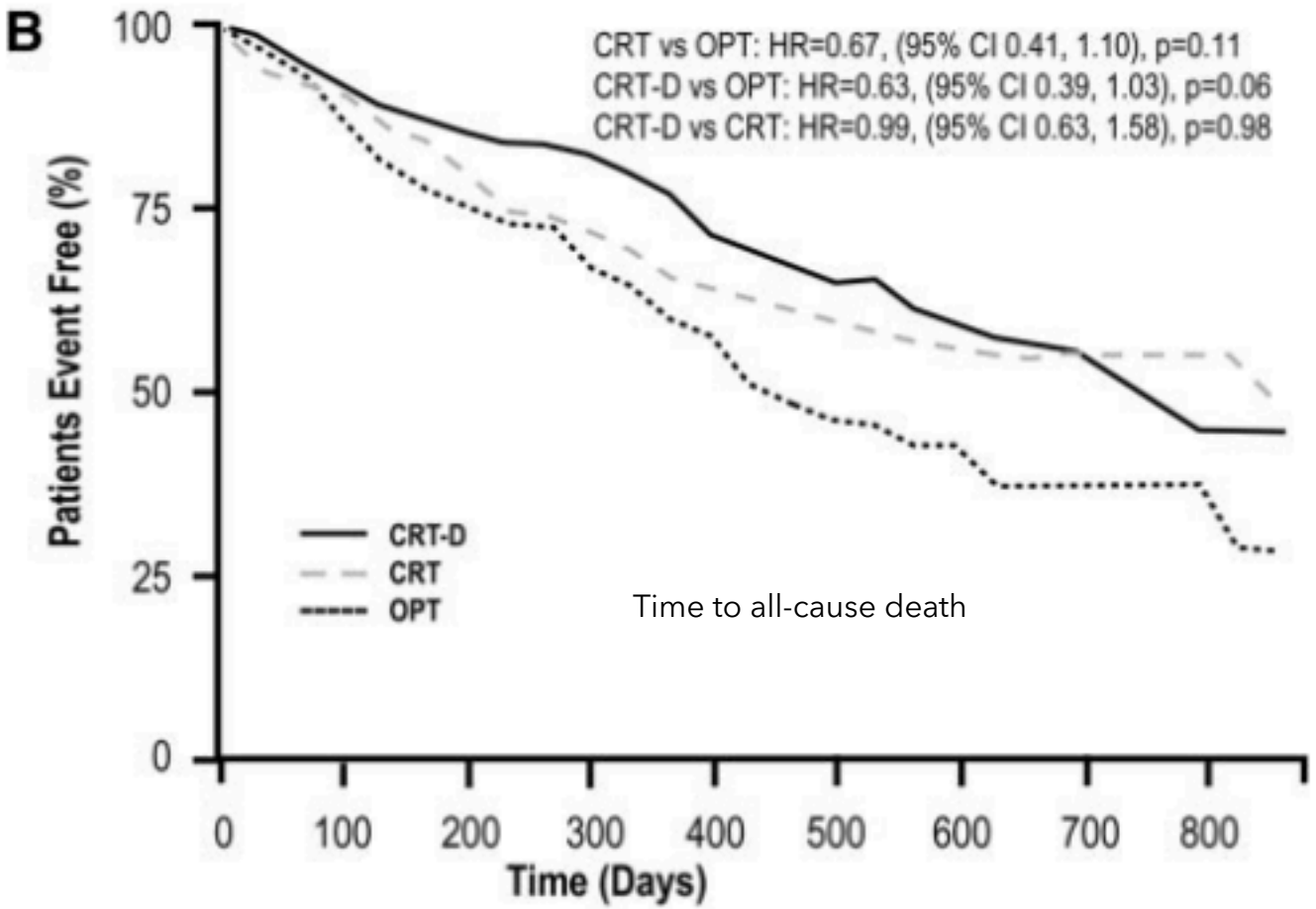
- Age
- RV function
- Pulmonary hypertension
- Aortic insufficiency
- Renal function
- Hepatic function
- Recent malignancy
- BMI
- Prior sternotomy
- Bleeding risks
- Infection
- Psychosocial evaluation

Gustafsson, Rogers et al. Eur J Heart Fail. 2017 May;19(5):595-602.

What if my patient does not qualify for a VAD?

COMPANION trial

- 1520 pts with NYHA III/IV HF, EF≤ 35% , wide QRS and 1 HFH in the last year
- Randomized to OMT vs. CRT-P vs. CRT-D
- 14% of patients were NYHA IV – post-hoc analysis of the data was carried out
- Excluded patients who had a HFH in the last month or needed inotropes
- Improvements in NYHA class seen in 67% of Class IV pts with CRT vs. 31% on OMT



Treatment	Events (%)	Censored (%)	Median FU Time
CRT-D (n=83)	37 (45%)	46 (55%)	14.1 months
CRT (n=79)	35 (44%)	44 (56%)	15.5 months
OPT (n=55)	30 (55%)	25 (45%)	10.1 months

Lindenfeld et al. Circulation. 2007 Jan 16;115(2):204-12.

CRT in inotrope dependent HF patients

TABLE 1 Baseline Characteristics of Included Studies

First Author (Ref. #)	N	Follow-Up, days	Age, yrs	Male	HF Etiology		NYHA Functional Class IV	QRS Duration, ms	QRS Configuration	LVEF, %	CRT-D
					ICM	NICM					
Milliez et al. (18)	20	547 ± 365	67 ± 10	18 (90)	12 (60)	8 (40)	20 (100)	174 ± 25	–	18 ± 3	–
Cowburn et al. (19)	10	361 ± 221	71 ± 7	10 (100)	8 (80)	2 (20)	10 (100)	205 ± 21	–	20 ± 8	–
Herweg et al. (20)	10	1,088 ± 284	55 ± 13	9 (90)	4 (40)	6 (60)	10 (100)	153 ± 25	LBBB: 7 (70) IVCD: 3 (30)	23 ± 4	10 (100)
Hara et al. (21)	14	–	58 ± 14	11 (79)	3 (21)	11 (79)	14 (100)	159 ± 48	LBBB: 3 (21) RBBB: 1 (7) IVCD: 2 (14) Paced: 5 (36) None: 3 (21)	20.9 ± 6.3	13 (93)
Sokal et al. (22)	11	1,163 ± 538	63.7 ± 12.6	9 (82)	8 (72)	3 (28)	11 (100)	190 ± 34	LBBB: 6 (55)	19 ± 4	11 (100)
Konstantino et al. (23)	10	–	68.6 ± 5.0	9 (90)	10 (100)	0	10 (100)	170 ± 17	LBBB: 8 (80) Paced: 2 (20)	–	8 (80)
Nakajima et al.(24)	26	1,033 ± 742	55 ± 18	19 (73)	19 (73)	7 (27)	26 (100)	159 ± 38	LBBB: 11 (42) RBBB: 5 (19) IVCD: 10 (38)	23 ± 7	–
Bhattacharya et al. (25)	50	927 ± 730	68.3 ± 9.2	36 (72)	32 (64)	18 (36)	20 (40)	172 ± 34	RBBR: 6 Non-RBBB: 44	20.3 ± 7.4	50 (100)
Total	151	877 ± 620	64 ± 12	121 (80)	96 (64)	55 (36)	121 (80.1)	171 ± 33	LBBB: 35 (50.2) RBBB: 6 (8.5) IVCD: 15 (21.1) Paced: 7 (9.9)	20.6 ± 6.3	92 (96.8)

Hernadez et al. JACC Heart Fail. 2018 Sep;6(9):734-742

CRT in inotrope dependent patients

- 7 out of 8 studies reported successful inotrope wean
- Improvement in NYHA class in 6 studies, 35% to II, 43% to III
- 12 month survival: 69% (56-83%)
- 6 patients underwent heart transplant (incl. in 1 yr survival)
- 53 pts died at 1 year or had undergone LVAD

Hernadez et al. JACC Heart Fail. 2018 Sep;6(9):734-742

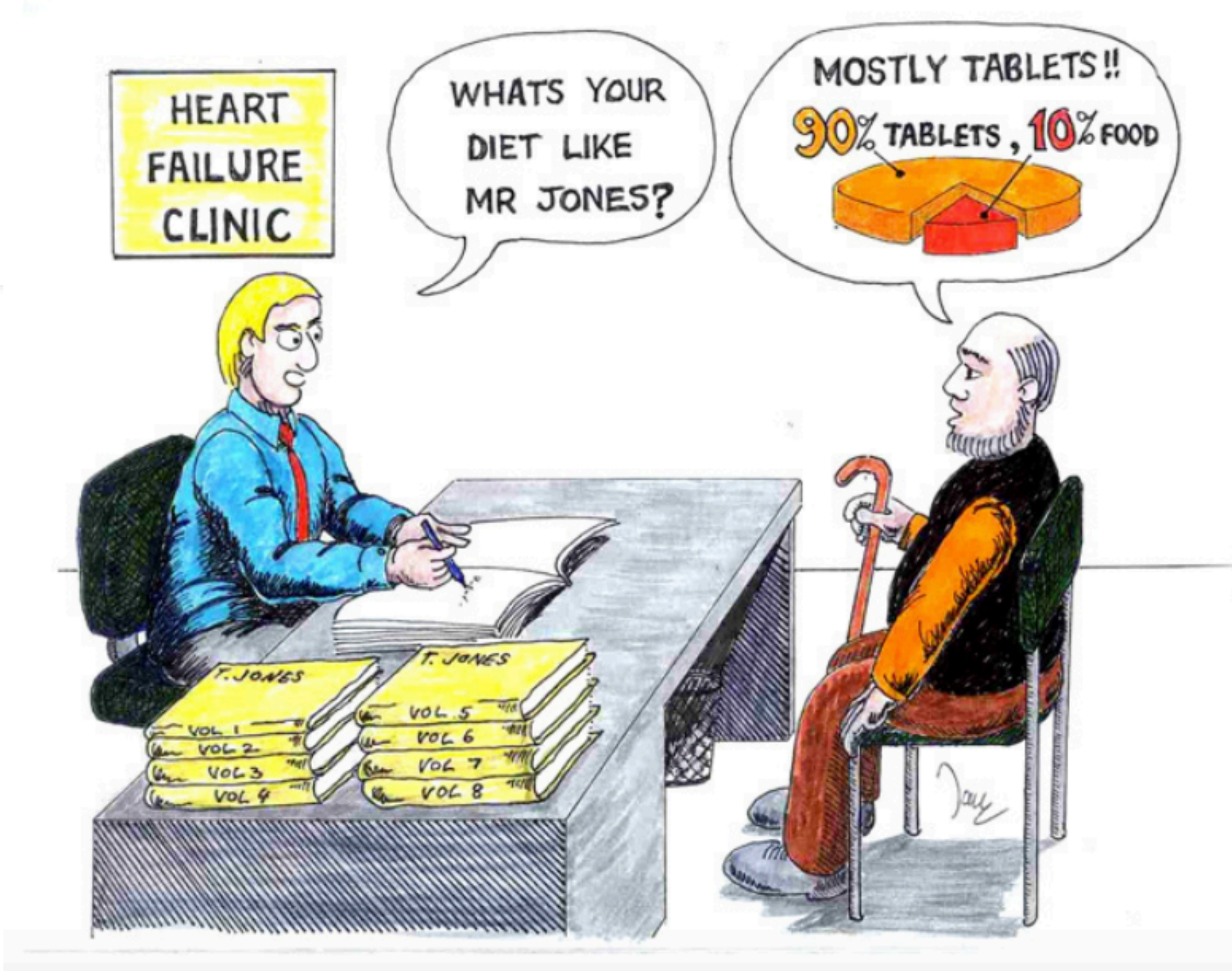
Back to the case

- Successful LVAD implant end of February
- Early RV dysfunction requiring slow Milrinone wean
- Discharged home ~ 1 month post-implant
- Seen in clinic early April, mobilizing freely at NYHA I-II level!

Conclusion

- Be vigilant for signs of deterioration in HF patients
- Early referral to HF clinic to ensure timely consideration for advanced therapies
- CRT implant should be considered in appropriately selected NYHA IV patients; data is quite limited in inotrope dependent patients and is still considered “off label”

Questions?


HEART FAILURE CLINIC
WHATS YOUR DIET LIKE MR JONES?
MOSTLY TABLETS!!
90% TABLETS, 10% FOOD
T. JONES
VOL 1
VOL 2
VOL 3
VOL 4
T. JONES
VOL 5
VOL 6
VOL 7
VOL 8