My HFrEF patient now has a normal ejection fraction - what's next?

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Conflict of Interest Disclosures

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- **Speaker fees**: Novartis, Servier, Boehringer Ingelheim

- I will discuss off-label uses for ____none_____

Case 1

- 68 yo man
- 2018: Presents to ER with SOB, orthopnea, trace edema: found to be in CHF L> R, Admitted to hospital -> ECG: narrow QRS, echo: EF 25%, angio: no CAD, MRI: no fibrosis
- Medical history consistent with smoking 10py, Etoh 8-10 beers per day x 10 years
- Treated medically, compliant with cessation of cigarettes and Etoh, follow-up in CHF clinic. No recurrent admission
- 2019: NYHA 2 echo EF 40%, no signs of volume overload
- 2020: Routine Echo, EF is now 55%, NLV size, feels perfect.
  - BP always between 100-110 syst, HR in the 60s
  - Sacubitril/valsartan max dose, Bisoprolol10mg die, spironolactone 25mg die

Patients asks, can I stop my meds, I feel perfect.
Now what?

Question

Case 1 - Now what?

- 1) stop all meds, he is cured
- 2) repeat another echo in 6 months to 1 year and then consider dc meds
- 3) repeat another echo in 6 months to 1 year and then consider simplifying meds
- 4) keep these meds indefinitely
- 5) simplify meds and keep indefinitely

Case 2

- 68 yo man
- 2016: Presents to ER with SOB, orthopnea, edema: found to be in CHF L> R, Admitted to hospital -> ECG: narrow QRS, echo: EF 25%, angio: no CAD, MRI: no fibrosis
- Medical history consistent with viral infection, flu-like symptoms about 3 weeks ago
- Treated medically, compliant with meds and lifestyle. No recurrent admission
- 2017: EF 30%
- 2018: EF 45%
- 2019: EF 50%
- 2020: Routine Echo, EF is now 55%, NLV size, feels perfect.
  - BP at home about 100 systolic, HR 60s
  - Sacubitril/valsartan max dose, Carvedilol 25mg bid, spironolactone 25mg die

Question

Case 2 - Now what?

- 1) stop all meds, he is cured
- 2) repeat another echo in 6 months to 1 year and then consider dc meds
- 3) repeat another echo in 6 months to 1 year and then consider simplifying meds
- 3) keep these meds indefinitely
- 4) simplify meds and keep indefinitely

Guidelines

Canadian Journal of Cardiology 33 (2017) 1342–1433

Society Guidelines

2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure

Primary Panel: Justin A. Ezekowitz, MBBCh (Chair),[a] Eileen O'Meara, MD (Co-chair),[b] Michael A. McDonald, MD,[c] Howard Abrams, MD,[c] Michael Chan, MBBS,[d] Anique Ducharme, MD,[b] Nadia Giannetti, MD,[e] Adam Grzeslo, MD,[f] Peter G. Hamilton, MBBCh,[a] George A. Heckman, MD,[g] Jonathan G. Howlett, MD,[h] Sheri L. Koshman, Pharm D,[a] Serge Lepage, MD,[i] Robert S. McKelvie, MD,[j] Gordon W. Moe, MD,[k] Miroslaw Rajda, MD,[l] Elizabeth Swiggum, MD,[m] Sean A. Virani, MD,[n] Shelley Zieroth, MD,[o] **Secondary Panel:** Abdul Al-Hesayen, MD,[k] Alain Cohen-Solal, MD,[p] Michel D'Astous, MD,[q] Sabe De, MD,[j] Estrellita Estrella-Holder, RN,[o] Stephen Fremes, MD,[r] Lee Green, MD,[a] Haissam Haddad, MD,[s] Karen Harkness, RN,[f] Adrian F. Hernandez, MD,[t] Simon Kouz, MD,[u] Marie-Hélène LeBlanc, MD,[v] Frederick A. Masoudi, MD,[w] Heather J. Ross, MD,[c] Andre Roussin, MD,[x] and Bruce Sussex, MBBS[y]

Guidelines

- The term **“recovered EF”** has also been added to the literature referring to patients who previously had HFrEF and now have an EF > 40%.
- These patients might eventually be classified in the HFmEF or HFpEF group but deserve recognition because despite their recovered imaging parameters, they might still carry additional risk for adverse clinical events.
- Uncertainty exists on strategies for management of individuals with HFmEF including surveillance, treatment, and prognosis

Guidelines

Table 12. Potential scenarios in which evidence-based medical therapy for heart failure might be withdrawn

Clinical presentation	Conditions to justify stepwise withdrawal of GDMT after 6-12 months of full medical therapy	Comments
Tachycardia-related CM	• Normal EF and LV volumes • NYHA I • Underlying tachycardia controlled	Usually due to atrial fibrillation/flutter with increased HR, might rarely occur because of PVCs. Might need long-term BB for rate control
Alcoholic CM	• Normal EF and LV volumes • NYHA I • Abstinence ETOH	Nutritional deficiency, obesity, and obstructive sleep apnea might coexist and require therapy
Chemotherapy-related CM	• Normal EF and LV volumes • NYHA I • No further drug exposure	Certain types of chemotherapy are more likely to reverse than others (trastuzumab—high rate of LVEF improvement when it is discontinued whereas patients who received anthracyclines should continue LV enhancement therapy) Long-term surveillance strongly recommended
Peripartum CM	• Normal EF and LV volumes • NYHA I	Repeat pregnancy might be possible for some. Consultation at high-risk maternal centre should be undertaken
Valve replacement surgery	• Normal EF and LV volumes • NYHA I • Normally functioning valve	Less consensus on regurgitant lesions with ongoing dilation of LV

BB, β-blocker; CM, cardiomyopathy; EF, ejection fraction; ETOH, ethanol; GDMT, guideline-directed medical therapy; HR, heart rate; LV, left ventricle; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PVC, premature ventricular contraction.

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 Lota, Zohya Khalique, 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

Lancet 2019; 393: 61–73

TRED-HF trial

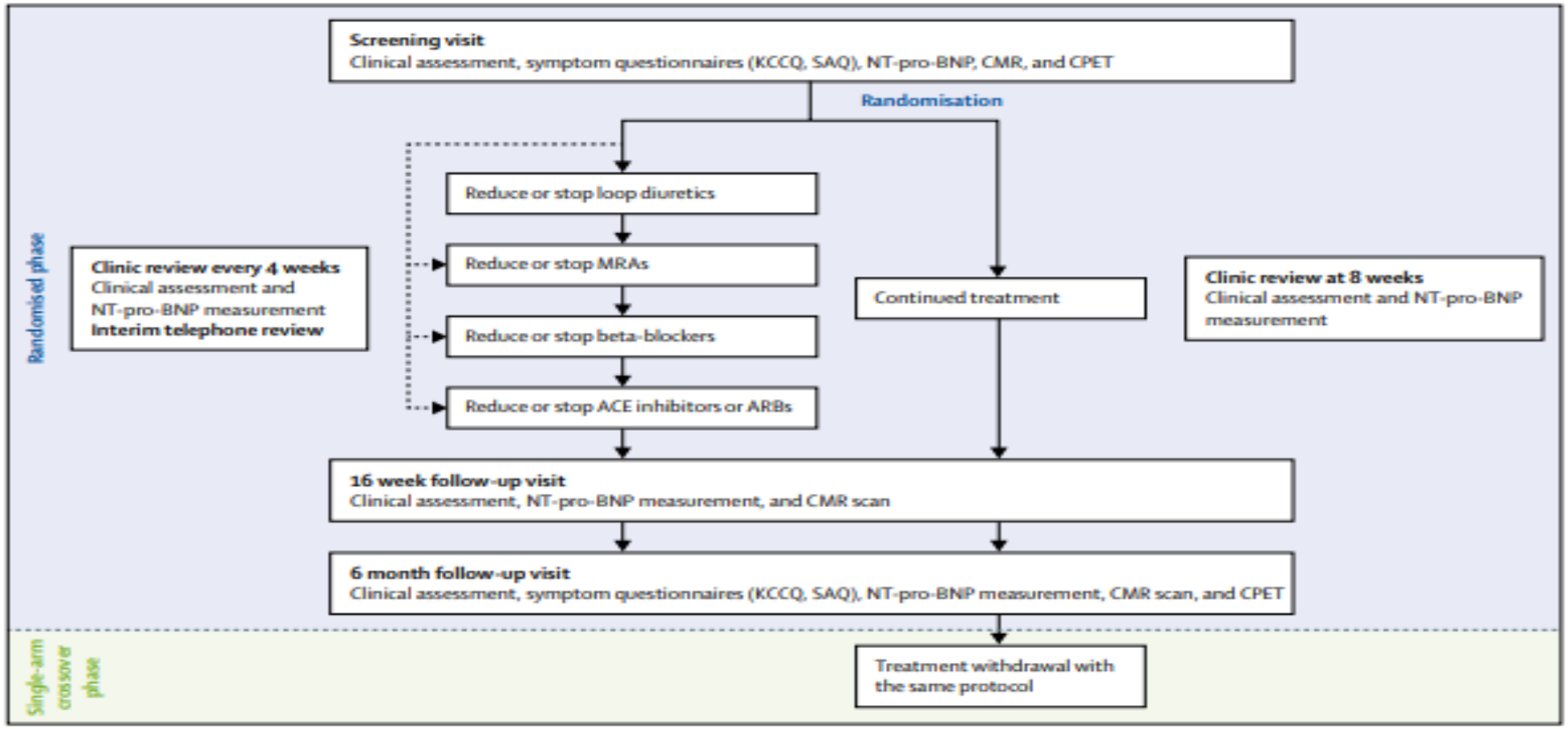

Figure 1: **Flowchart of TRED-HF study design**
ACE=angiotensin converting enzyme. ARB=angiotensin receptor blocker. CMR=cardiovascular magnetic resonance. CPET=cardiopulmonary exercise test. KCCQ=Kansas City Cardiomyopathy Questionnaire. MRA=mineralocorticoid receptor antagonist. NT-pro-BNP=N-terminal pro-B-type natriuretic peptide. SAQ=symptom assessment questionnaire.

TRED-HF

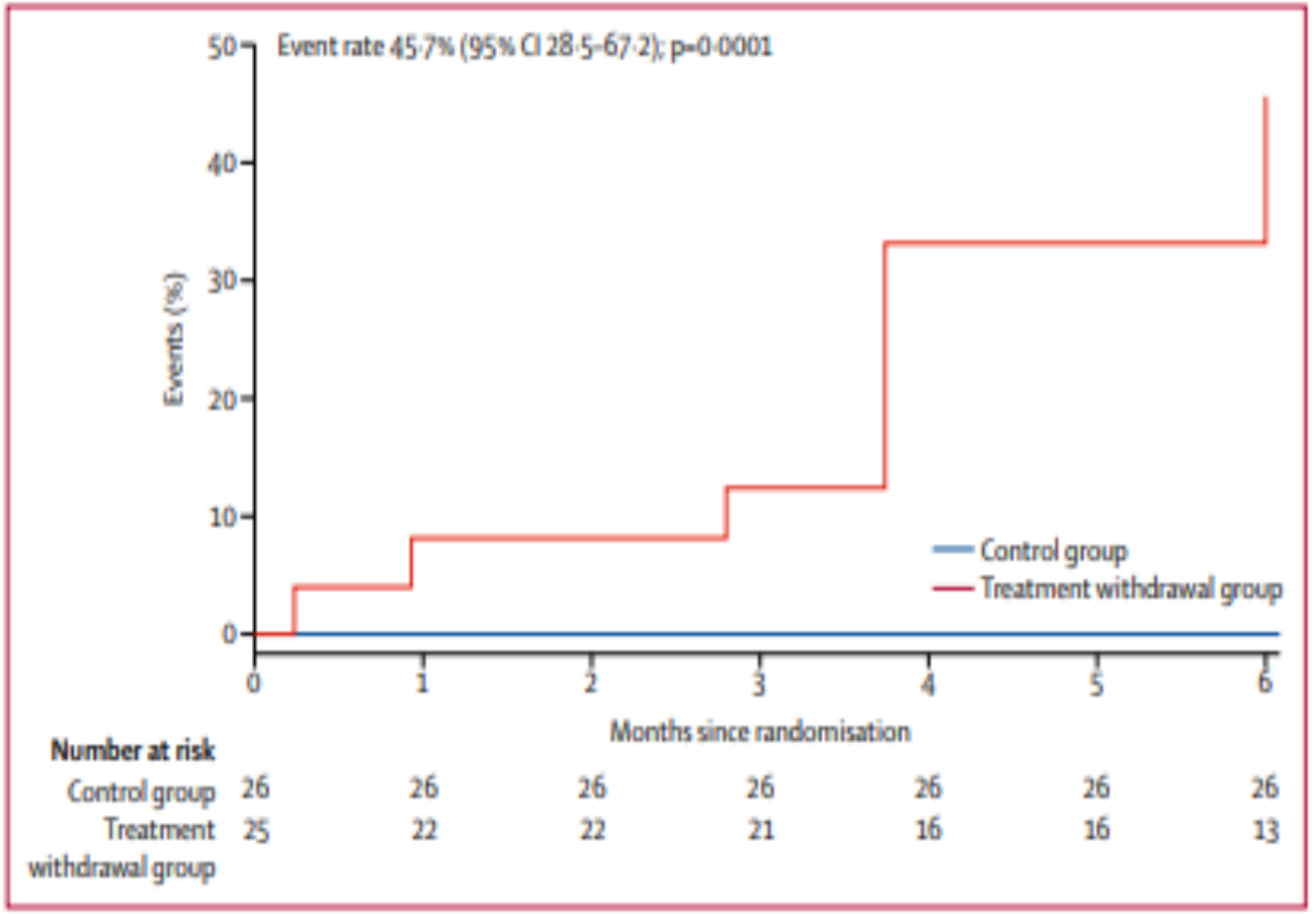

***Figure 3*: Kaplan-Meier curve of time to primary endpoint in randomised phase, according to treatment group**
One patient dropped out at 7 days.

TRED-HF

	Overall			Primary endpoint met			Primary endpoint not met		
	Patients	Estimated mean change between baseline and 6 months (95% CI)	p value	Patients	Estimated mean change between baseline and 6 months (95% CI)	p value	Patients	Estimated mean change between baseline and 6 months (95% CI)	p value
LVEF, %	49	−6·9 (−9·6 to −4·3)	<0·0001	20	−12·0 (−16·6 to −7·4)	0·0001	29	−3·5 (−5·8 to −1·1)	0·0190
LVEDVi, mL/m²	47*	6·5 (3·1 to 9·8)	0·0003	20	11·8 (8·2 to 15·3)	<0·0001	27*	2·5 (−2·0 to 7·0)	0·2107
LAVi, mL/m²	47*	2·0 (−0·6 to 4·6)	0·1224	20	6·6 (3·3 to 9·9)	0·0009	27*	−1·4 (−4·5 to 1·7)	0·3702
Heart rate, bpm	49	13·2 (9·3 to 17·1)	<0·0001	20	16·4 (9·1 to 23·6)	0·0003	29	11·7 (7·9 to 15·6)	<0·0001
Systolic blood pressure, mm Hg	49	8·7 (4·6 to 12·9)	0·0001	20	8·9 (2·3 to 15·4)	0·0101	29	8·7 (3·4 to 13·9)	0·0020
Diastolic blood pressure, mm Hg	49	6·7 (3·2 to 10·1)	0·0003	20	6·4 (1·7 to 11·0)	<0·0001	29	6·9 (2·2 to 11·5)	0·0033
Log NT-pro-BNP, ng/L	49	0·3 (0·0 to 0·6)	0·0246	20	0·4 (0·2 to 0·6)	0·0022	29	0·0 (−0·1 to 0·05)	0·4276
VO_2 max (mL/kg per min)	41†	−0·7 (−2·1 to 0·7)	0·3294	17†	−1·5 (−3·5 to 0·4)	0·1476	24†	0·0 (−1·9 to 2·0)	0·9737
Exercise time (s)	41†	−0·6 (−14·9 to 13·8)	0·9376	17†	−19·7 (−40·9 to 1·5)	0·0873	24†	12·0 (−4·4 to 28·3)	0·1646
KCCQ, 0–100	49	−2·2 (−4·7 to 0·3)	0·0777	20	−3·9 (−7·7 to −0·11)	0·0582	29	−1·2 (−4·2 to 1·8)	0·4480
SAQ, 0–100	49	0·1 (−0·1 to 0·3)	0·3782	20	1·5 (−2·9 to 5·9)	0·5110	29	0·77 (−1·9 to 3·4)	0·5754

Measurements taken at the start of treatment withdrawal (at baseline for those randomly assigned to treatment withdrawal and at the start of the single-arm crossover phase for those initially randomly assigned to continue treatment) and follow-up. A maximum of 49 patients completed follow-up. bpm=beats per min. KCCQ=Kansas City Cardiomyopathy Questionnaire. LAVi=left atrial volume indexed to body surface area. LVEDVi=left ventricular end diastolic volume indexed to body surface area. LVEF=left ventricular ejection fraction. NT-pro-BNP=N-terminal pro-B-type natriuretic peptide. SAQ=symptom assessment questionnaire. VO_2 max=maximum oxygen consumption. *Two patients had absent LVEDVi and LAVi at follow-up because of new contraindication to cardiovascular magnetic resonance; three-dimensional echocardiography used for LVEF follow-up. †Eight patients were unable to complete the cardiopulmonary exercise test because of musculoskeletal pain or injury.

Table 4: **Non-randomised comparison of secondary outcomes before and after treatment withdrawal for all patients, according to occurrence of primary endpoint**

TRED-HF

- In conclusion, in this pilot study,
  - Withdrawal of pharmacological HF treatment in patients with recovered dilated cardiomyopathy associated with relapse in 40% of cases
  - Suggests that complete withdrawal of treatment should not usually be attempted in such patients
  - Future work could identify patient subgroups who have permanent recovery of myocardial function for whom withdrawal is safe or for whom only some medications need to be continued in the long term

Single centre study

Withdrawal of Beta Blockers and Angiotensin Converting Enzyme Inhibitors After Left Ventricular Systolic Function Recovery in Patient with Dilated Cardiomyopathy a Randomized Control Trial

Abeer Bakhsh[1], Thao Huynh[1], George Thanassoulis[1], James C. Engert[1,2], Abhinav Sharma[1], Eleanor Elstein[1], Nadia Giannetti[1]

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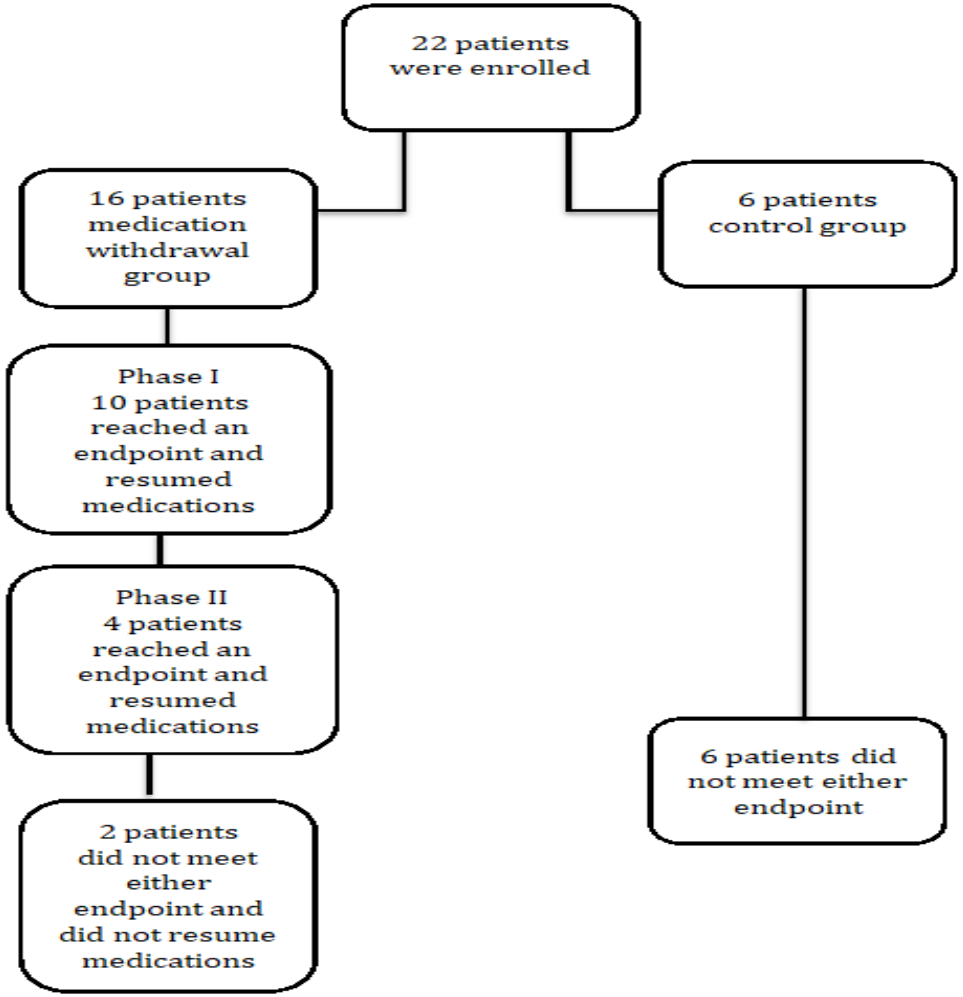
Single centre study



Single centre study

Table 1: Baseline Characteristics

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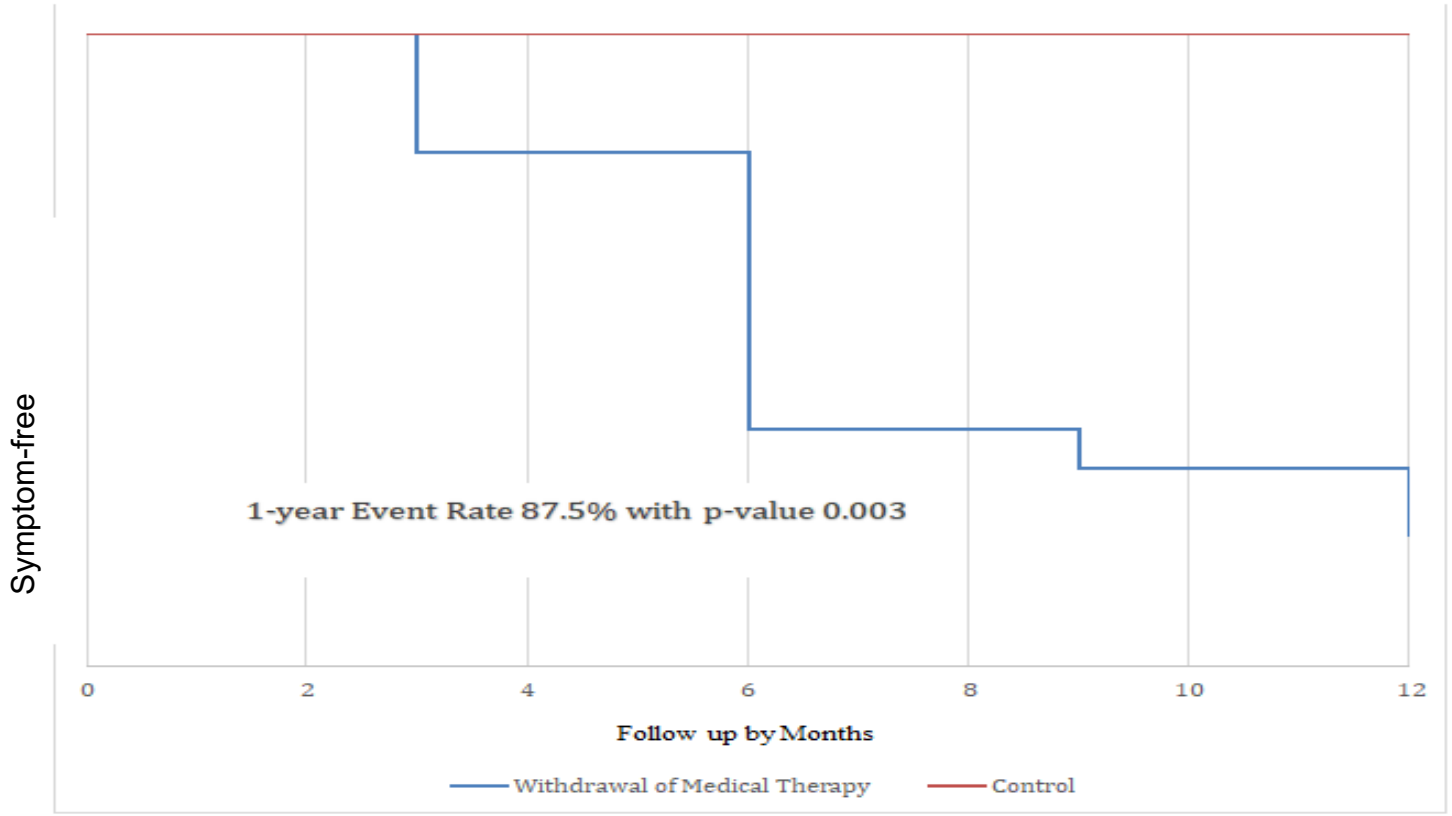
	All Patients	Randomized	Control
Number of Patients (%)	22 (%)	16 (%)	6 (%)
Age	59y ± 13y	63y ± 12y	53y ± 8y
Gender:			
Male	12 (55)	8 (50)	4 (67)
Female	10 (45)	8 (50)	2 (33)
Etiology of dilated cardiomyopathy:			
Idiopathic	10 (45)	8 (50)	2 (33)
Arrhythmia	2 (9)	2 (13)	0
Hypertension	2 (9)	2 (9)	0
Alcohol use	4 (18)	4 (25)	0
Others	6 (27)	2 (13)	4 (67)
Co-morbidity:			
Diabetes	3 (14)	1 (6)	2 (33)
Hypertension	6 (27)	5 (31)	1 (17)
Dyslipidemia	7 (32)	6 (38)	1 (17)
Atrial Fibrillation	7 (32)	5 (31)	2 (33)
Obstructive Sleep Apnea	7 (32)	7 (44)	0
Transient ischemic attack	3 (14)	3 (19)	0
Cancer	3 (14)	3 (19)	0
Duration of Heart Failure (month):			
>18	3 (14)	3 (19)	0
24-48	5 (23)	4 (25)	1 (17)
>48	14 (64)	9 (56)	5 (83)
Left Ventricle Ejection Fraction (%): At Randomization	58 ± 6 %	59 ± 5 %	57 ± 7 %

Single centre study

Figure 2: Kaplan Meier Curve of 1ry outcome



Single centre study

Table 2: Change in LVEF over time in patients in the medical therapy withdrawal group

Table 2: Change in LVEF over time in patients in the medical therapy withdrawal group

Time of Assessment	Number of patients	Mean LVEF (SD)
Enrollment	16	59±5
3-months	4	53±6
6-months	9	51±9
9-months	6	40±12
1-year	15	47±12
2-year	15	50±12

LVEF: Left Ventricle Ejection Fraction
SD: Standard Deviation

Return to cases. Question:

CASE 1- NOW WHAT?

- 1) stop all meds, he is cured
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- 4) keep these meds indefinitely
- 5) simplify meds to once daily and keep indefinitely

Return to cases. Question:

CASE 2- NOW WHAT?

- 1) stop all meds, he is cured
- 2) repeat another echo in 6 months to 1 year and then consider dc meds
- 3) repeat another echo in 6 months to 1 year and then consider simplifying meds
- 4) keep these meds indefinitely
- 5) simplify meds to once daily and keep indefinitely

Question

Should the patients have follow-up?

- 1) discharge to follow-up annually with a physician
- 2) discharge, no need for any follow-up

Conclusion

- Paucity of data on how to manage patients who have recovered their LVEF and symptoms
- In a minority of cases with a clear insult has been identified and “abolished”, can consider slow cessation of meds
- In majority of cases, simplify medication and ensure a regular follow-up with a physician

QUESTIONS?

To submit your questions click on the Q&A icon on your screen