My Biggest Mistakes and Lessons Learned

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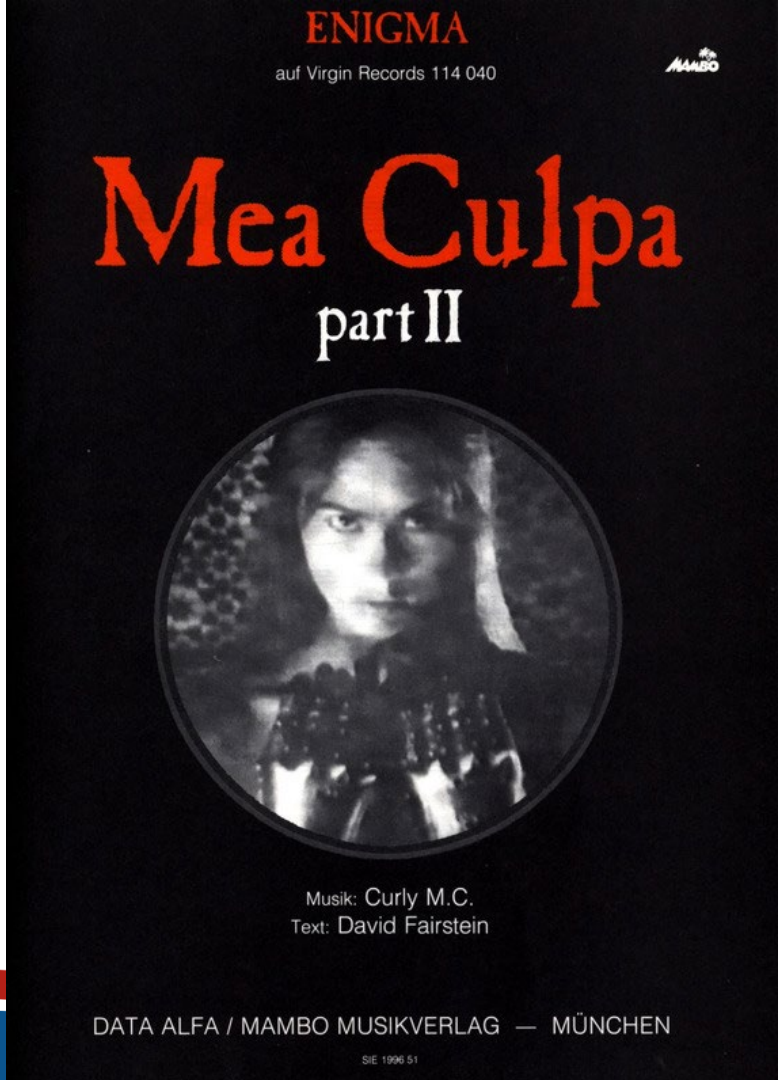
Disclosure #2

This is a genuine mistake

Recently

Made by me…



Case History

56-year-old male referred from the emergency for dyspnoea

In ED (two weeks earlier)

- SOB, wheezing diaphoretic.
- BP 152/76, his heart rate 80 and his oxygen saturation normal.
- CT chest showed no evidence of pulmonary embolism.
- HS Troponin was slightly elevated with no delta.
- NT BNP was significantly elevated at 1,267.
- COVID negative.

Referred for echo and cardiac consult

When I saw him…

HPI

- Vague historian
- Short of breath for “quite a while”. NYHA III

PH

- Hypertension (indeterminate, treated, ?adherence). BP at recent echo 186/97
- Pre-diabetes
- Polysomnography severe OSA, but did not follow-up, no CPAP.
- HIV status is negative.

MEDICATIONS

- Amlodipine 5 mg daily
- Chlorthalidone 50 mg daily
- Telmisartan 40 mg daily. Page 1 of 3

NKA

SOCIAL HISTORY

- Lives alone in basement unemployed. He recently lost his job.
- 15 pack year smoking history but stopped 20 years ago. Denied misuse alcohol or substances, no anabolic steroids.

FAMILY HISTORY

- Foster child, limited details of his biological family
- Natural mother died from causes unknown.

PHYSICAL EXAM

Unremarkable appearance with marked central obesity

Sweaty, wheezy.

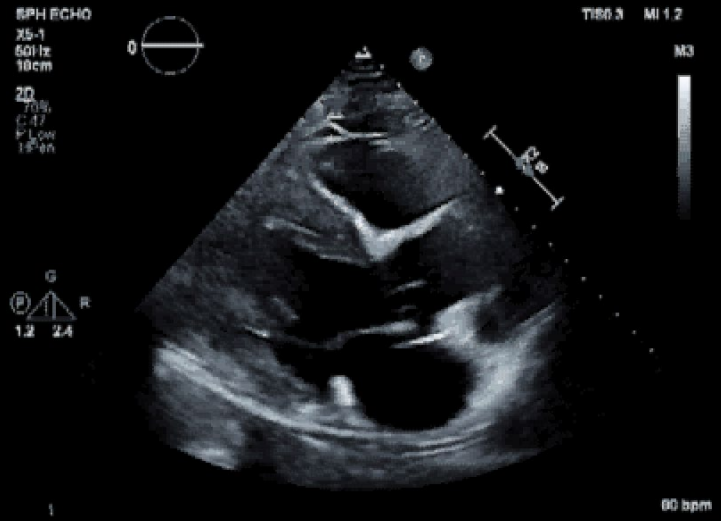
BP 120/75. HR 90

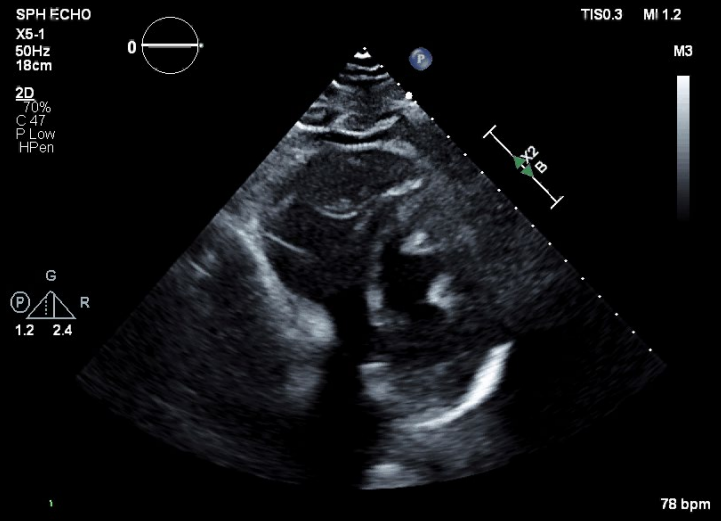
venous pressure not assessable

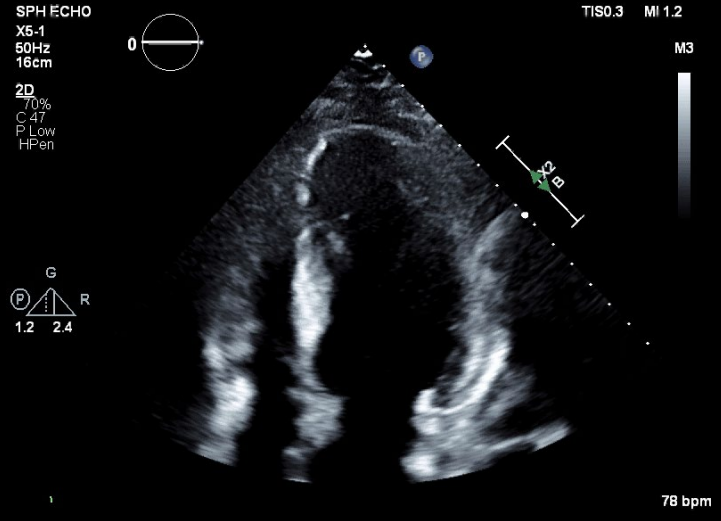
Heart sounds 1 and 2, quiet. No murmurs, no systolic murmur induced with Valsalva.

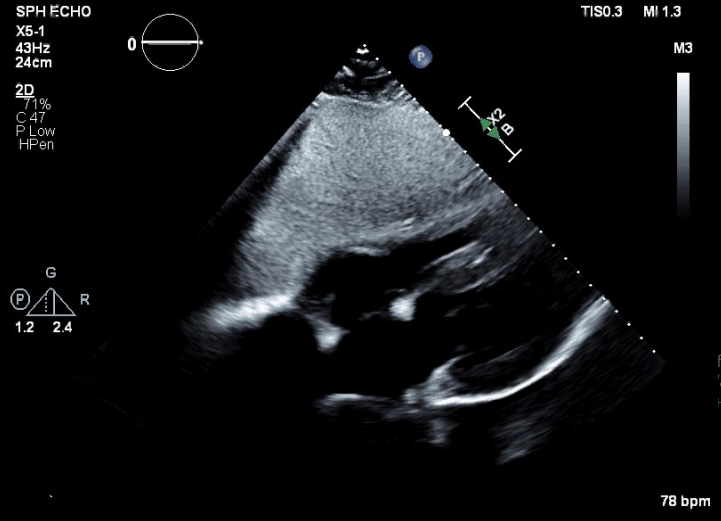
Breath sounds were reduced to the lung bases no crackles or wheezes.

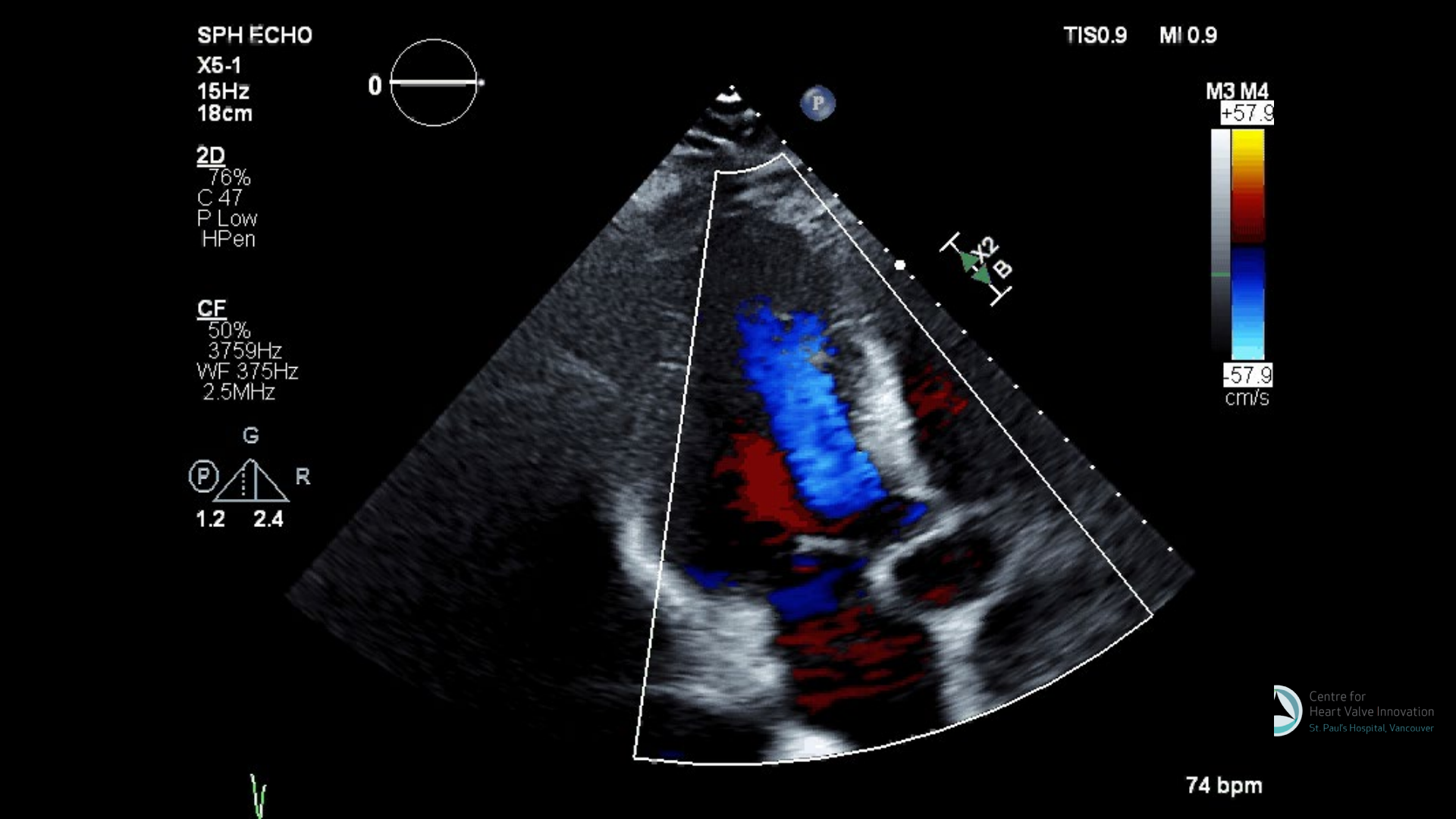
3+ peripheral edema.










SPH ECHO
X5-1
15Hz
18cm
2D
76%
C 47
P Low
HPen
CF
50%
3759Hz
WF 375Hz
2.5MHz
G
P
R
1.2
2.4
0
TIS0.9
MI 0.9
M3 M4
+57.9
-57.9
cm/s
74 bpm
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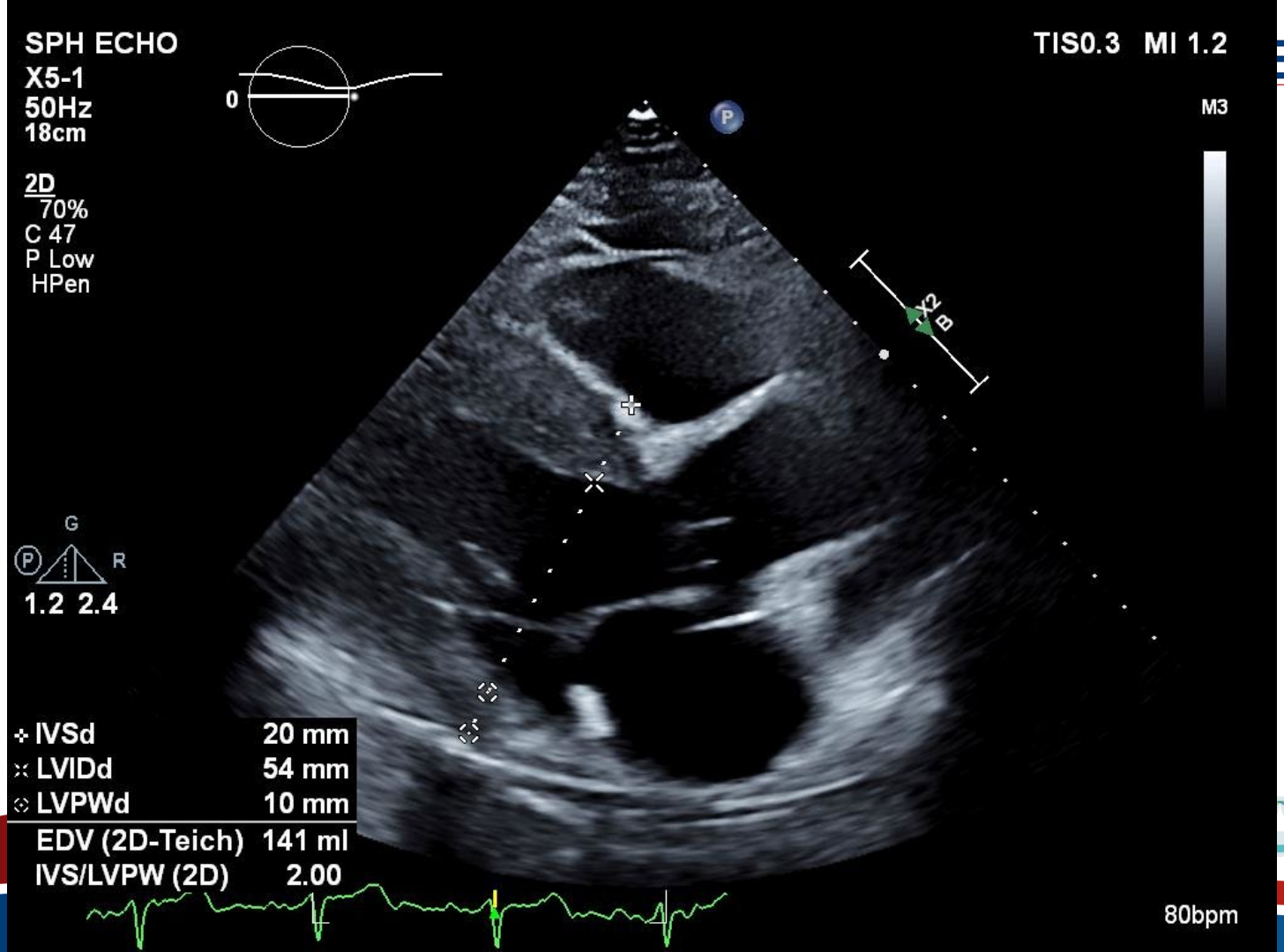
Heart Valve Innovation
St. Paul's Hospital, Vancouver



American Society of Echocardiography
Sound Saves Lives

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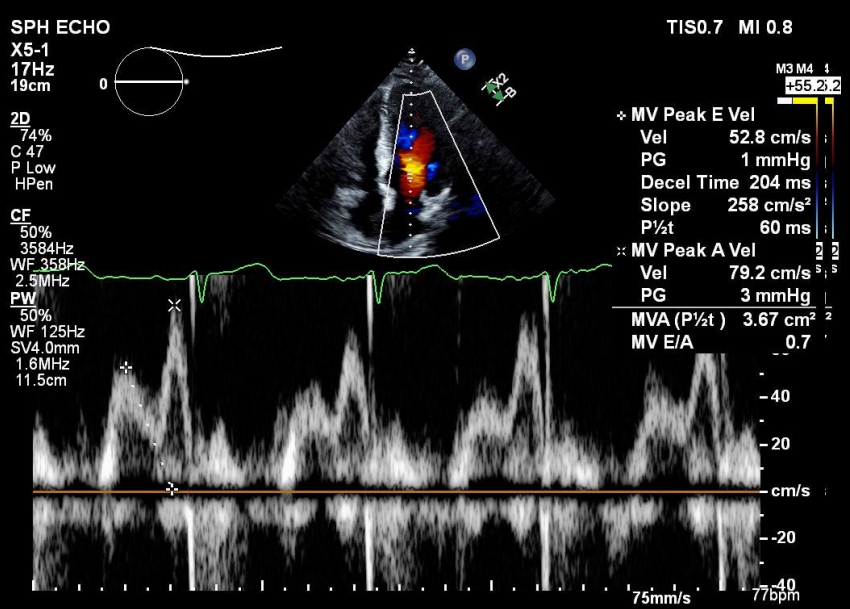
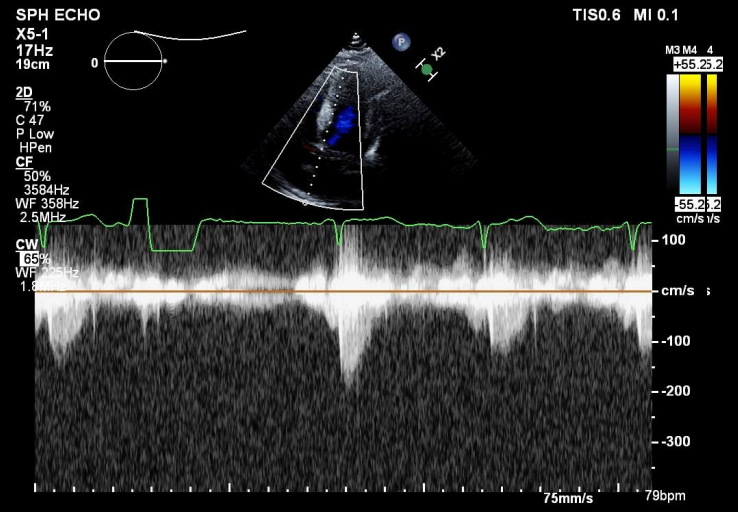
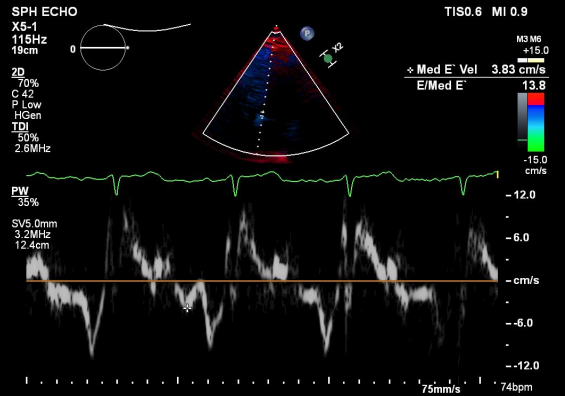
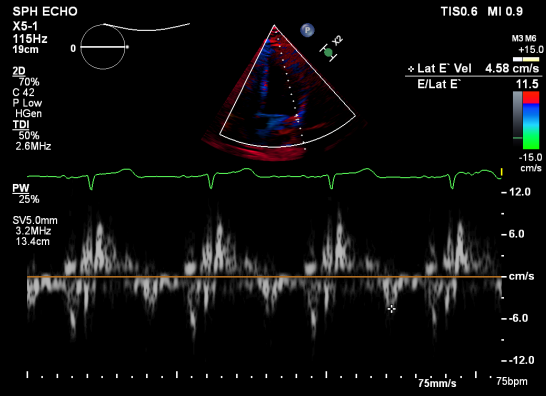
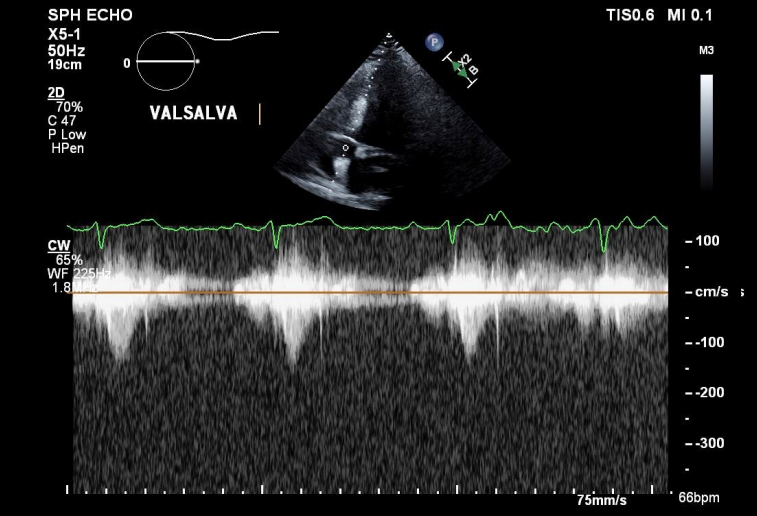

SPH ECHO
X5-1
17Hz
19cm
2D
74%
C 47
P Low
HPen
CF
50%
3584Hz
WF 358Hz
2.5MHz
PW
50%
WF 125Hz
SV4.0mm
1.6MHz
11.5cm
TIS0.7 MI 0.8
M3 M4
+55.2
MV Peak E Vel
Vel 52.8 cm/s
PG 1 mmHg
Decel Time 204 ms
Slope 258 cm/s²
P½t 60 ms
MV Peak A Vel
Vel 79.2 cm/s
PG 3 mmHg
MVA (P½t) 3.67 cm²
MV E/A 0.7
40
20
cm/s
-20
-40
75mm/s
77bpm


SPH ECHO
X5-1
17Hz
19cm
2D
71%
C 47
P Low
HPen
CF
50%
3584Hz
WF 358Hz
2.5MHz
TIS0.6 MI 0.1
M3 M4
+55.2
-55.2
cm/s
CW
65%
100
cm/s
-100
-200
-300
75mm/s
79bpm


SPH ECHO
X5-1
115Hz
19cm
2D
70%
C 42
P Low
HGen
TDI
50%
2.6MHz
TIS0.6 MI 0.9
M3 M6
+15.0
Med E` Vel 3.83 cm/s
E/Med E` 13.8
-15.0
cm/s
PW
35%
SV5.0mm
3.2MHz
12.4cm
12.0
6.0
cm/s
-6.0
-12.0
75mm/s
74bpm


SPH ECHO
X5-1
115Hz
19cm
2D
70%
C 42
P Low
HGen
TDI
50%
2.6MHz
TIS0.6 MI 0.9
M3 M6
+15.0
Lat E` Vel 4.58 cm/s
E/Lat E` 11.5
-15.0
cm/s
PW
25%
SV5.0mm
3.2MHz
13.4cm
12.0
6.0
cm/s
-6.0
-12.0
75mm/s
75bpm


SPH ECHO
X5-1
50Hz
19cm
2D
70%
C 47
P Low
HPen
VALSALVA
TIS0.6 MI 0.1
M3
CW
65%
100
cm/s
-100
-200
-300
75mm/s
66bpm

Echo Report Summary

Normal LV size and function LVEF 70%

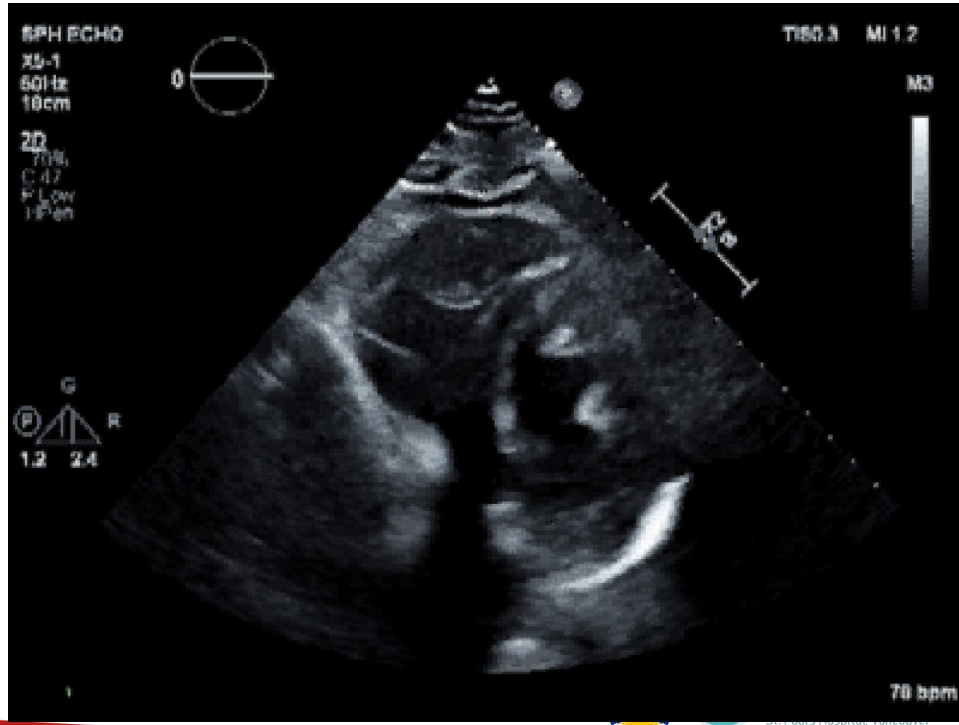
BP 186/97

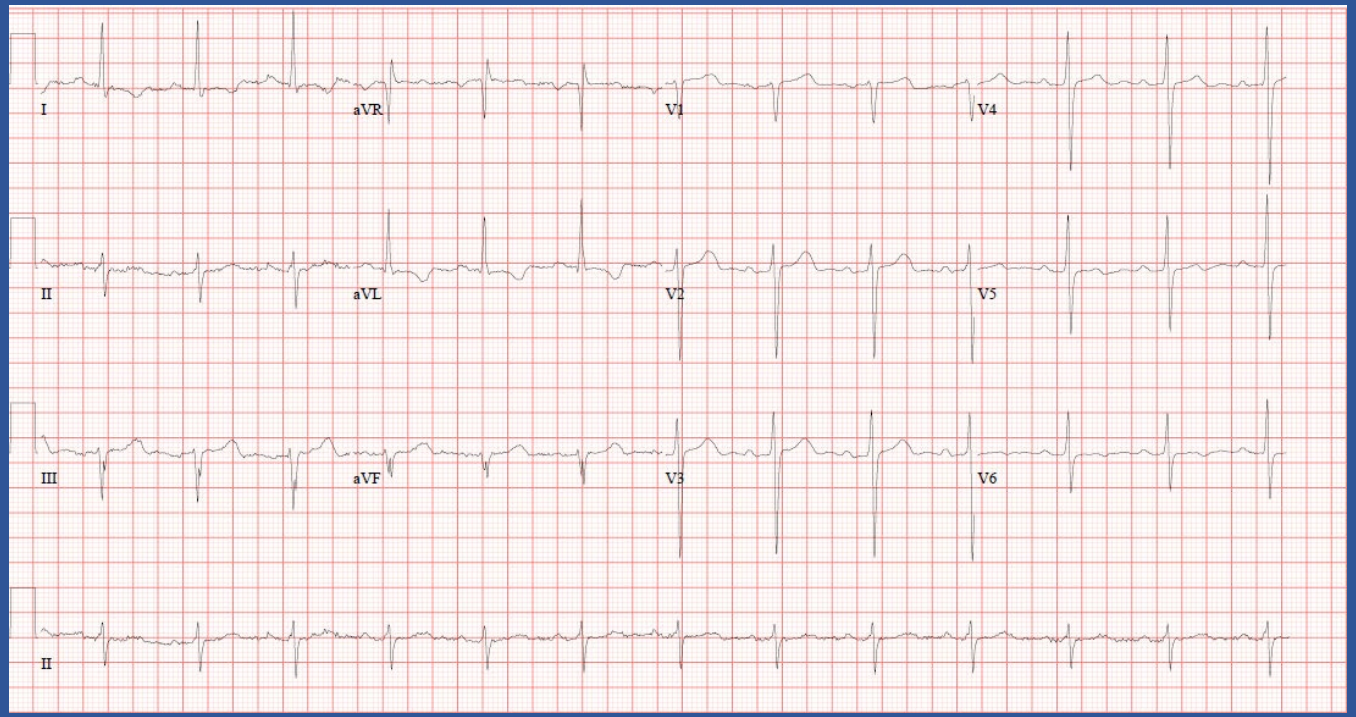
Severe eccentric LV hypertrophy

Septal asymmetric(?) hypertrophy

Hypertrophic cardiomyopathy

Image quality was insufficient for strain





General Chemistry		
Sodium	140	
Potassium	3.7	
Chloride	104	
Carbon Dioxide Total	30	
Calcium		
Magnesium		
Phosphate		
Glucose Random	6.0	
Lactate		
Urea	7.2	
Creatinine	106 (H)	1.2 mg/dL
Glomerular Filtration Rate Estimated	67	
Uric Acid		
Bilirubin Total		
Alanine Aminotransferase		
Aspartate Aminotransferase		
Alkaline Phosphatase		
Gamma Glutamyltransferase		
Creatine Kinase		
Lactate Dehydrogenase		
Troponin T Cardiac High Sensitivity	37 - 38 [2](H)	
NT-proBNP	1,267 * (H)	

UBC

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Differential Diagnosis

HFPEF

Cardiomyopathy with increased LV wall thickness, NYD

Consider:

- Hypertensive heart
- HCM
- phenocopy

Labile hypertension

OSA

Poor adherence with clinic FU and investigation, difficult to contact

Unusual features

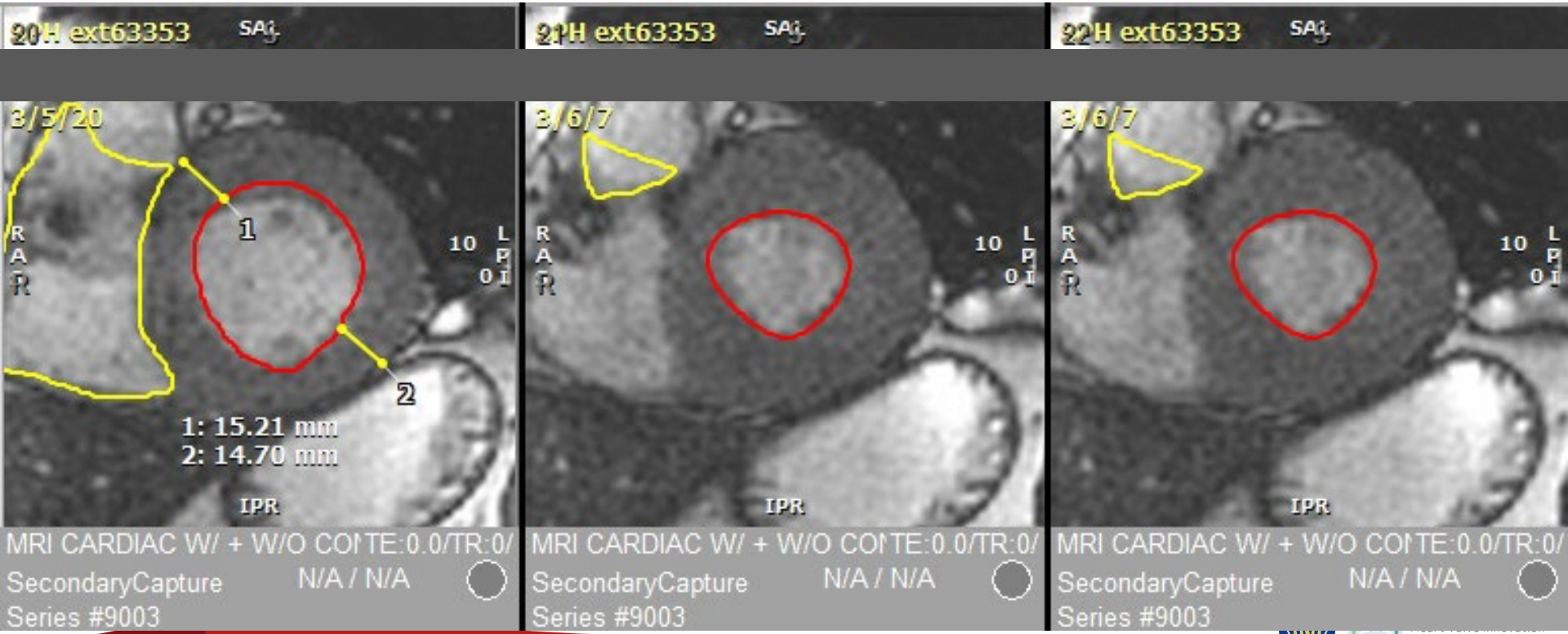
Lability of hypertension

A lot of HF clinically and biomarker abnormality for echo findings, diastology

A lot of HF for HCM

Was HT sufficient to account for cardiomyopathy and HFPEF?

Next test anyone?


20 H ext63353 SAg
3/5/20
1
2
1: 15.21 mm
2: 14.70 mm
IPR
MRI CARDIAC W/ + W/O CO TE:0.0/TR:0/
SecondaryCapture N/A / N/A
Series #9003
21 H ext63353 SAg
3/6/7
IPR
MRI CARDIAC W/ + W/O CO TE:0.0/TR:0/
SecondaryCapture N/A / N/A
Series #9003
22 H ext63353 SAg
3/6/7
IPR
MRI CARDIAC W/ + W/O CO TE:0.0/TR:0/
SecondaryCapture N/A / N/A
Series #9003

Cardiac MRI (1.5 T)

IISTORY:
rom CareConnect: 57-year-old male with heart failure with preserved ejection fraction. Increased left ventricular wall thickness. Diastolic dysfunction. Suspected HCM. History of hypertension.

OMPARISON:
lo prior cross-sectional cardiac imaging available for review on our system

ECHNIQUE
rotocol: Cardiomyopathy
ield Strength: 1.5T

INDINGS:

ardiac Dimensions

tria: The left atrium is normal in size (26cm2 or 12cm2/m2 on 4ch view; normal 7-15cm/m2). The right atrium is normal in size (32cm2 or 14.5cm2/m2 on 4ch; normal: 8-16cm/m2)

eft ventricle: The left ventricle is normal in size with preserved ejection fraction. No RWMA identified. There is moderate concentric left ventricular hypertrophy (basal IVSd 15mm PWd 15mm).

ight ventricle: The RV is normal in size with preserved function. There is normal wall thickness.

olumetric Analysis

orrected for BSA of 2.21m^2

eft ventricle
F 54%
DV 160ml or 72ml/m2
SV 73ml or 33ml/m2
V 87ml or 39ml/m2

ight ventricle
F 50%
DV 163ml or 74ml/m2
SV 81ml or 36ml/m2
V 82ml or 37ml/m2

ate Enhancement

Normal myocardial nulling pattern. In the late phase following gadolinium contrast there is no enhancement.

alves

No clinically relevant stenotic or regurgitant lesion identified.

ericardium

lormal pericardial thickness. No pericardial effusion.

lon-Cardiac Findings

MPRESSION:
lormal biventricular size and function. Moderate concentric LVH (maximal wall thickness 15 mm).
he findings are most likely representative of LV remodeling secondary to hypertension. Concentric type HCM should also be considered.

Impression:

- Normal biventricular size and function
- Moderated concentric LVH most likely hypertension
- Consider concentric HCM
- No LGE

Serum, urine immuno-fixation electrophoresis: negative

Mild albuminuria

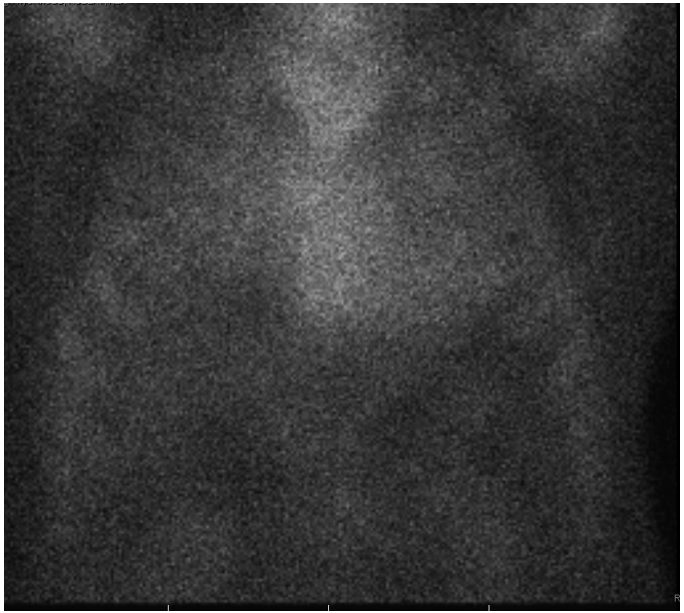
Serum free light chains negative

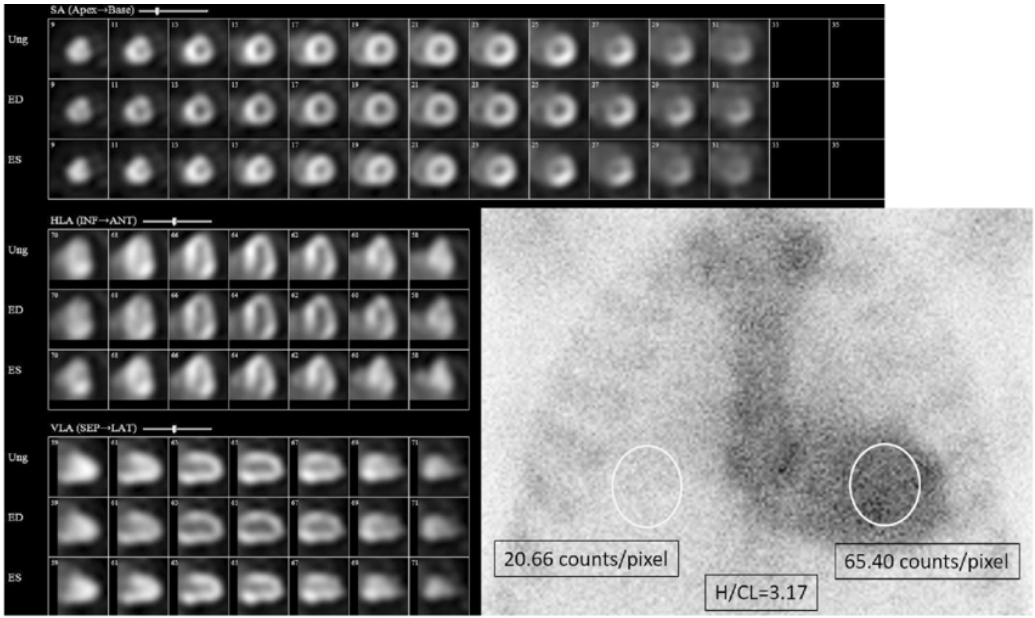
Ferritin normal

Alpha-galactosidase negative

Next steps?

Tc99m Pyrophosphate scan





No late cardiac uptake

Not suggestive of cardiac amyloidosis

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TEST RESULTS

Negative

SEQUENCING PERFORMANCE METRICS

PANEL	GENES	EXONS / REGIONS	BASES	BASES > 20X	MEDIAN COVERAGE	PERCENT > 20X
Hypertrophic Cardiomyopathy (HCM) Panel	40	618	112654	112617	183	99.97

TARGET REGION AND GENE LIST

The Blueprint Genetics Hypertrophic Cardiomyopathy (HCM) Flex Panel (version 1, Oct 05, 2018) Plus Analysis includes sequence analysis and copy number variation analysis of the following genes: ABCC9, ACAD9, ACADVL, ACTA1, ACTC1, ACTN2, AGK*, AGL, ALPK3, APOA1, BAG3, BRAF*, CBL, COX15, CSRP3, ELAC2, EPG5, FHL1*, FLNC*, FXN*, GAA, GLA, HRAS, JPH2, LAMP2, MYBPC3, MYH7, MYL2, MYL3, NDUFAF2, PLN, PRKAG2#, RAF1, SLC25A4, SOS1, TNNC1, TNNI3, TNNT2, TPM1 and TTR. The following exons are not included in the panel as they are not covered with sufficient high quality sequence reads: PRKAG2 (10, 13). This panel targets protein coding exons, exon-intron boundaries (± 20 bps) and selected non-coding, deep intronic variants (listed in Appendix 5). This panel should be used to detect single nucleotide variants and small insertions and deletions (INDELs) up to 220 bps and copy number variations defined as single exon or larger deletions and duplications. This panel should not be used for the detection of repeat expansion disorders or diseases caused by mitochondrial DNA (mtDNA) mutations. The test does not recognize balanced translocations or complex inversions, and it may not detect low-level mosaicism.

Genes added by the clinician: PLN and TNNC1

*Some, or all, of the gene is duplicated in the genome. Read more: https://blueprintgenetics.com/pseudogene/
#The gene has suboptimal coverage when >90% of the gene's target nucleotides are not covered at >20x with mapping quality score (MQ>20) reads.
The sensitivity to detect variants may be limited in genes marked with an asterisk (*) or number sign (#).

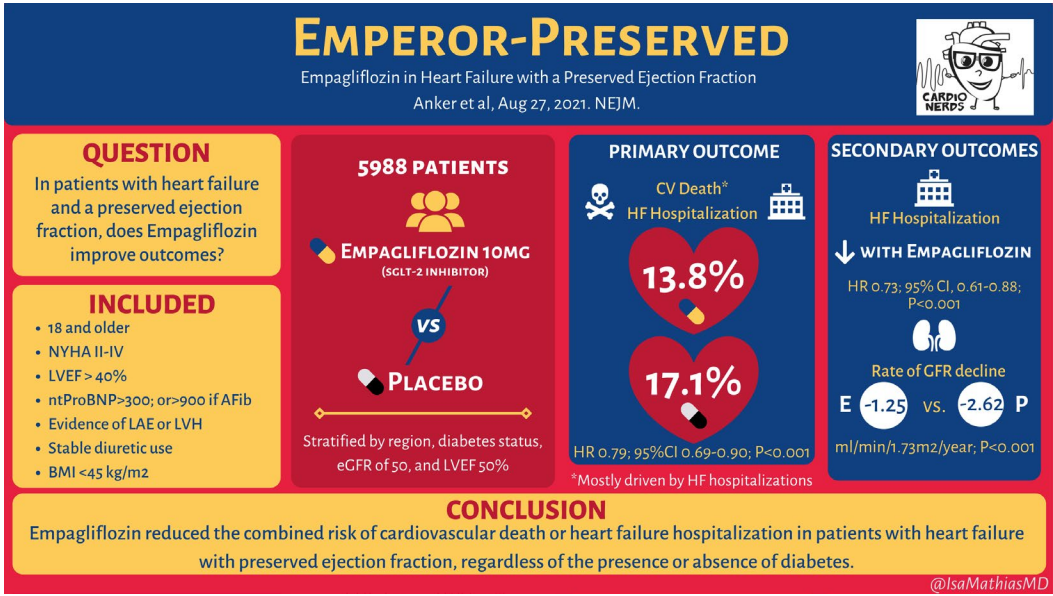
Family Extension Service includes free familial mutation testing of five first degree relatives within 12 months of the original index patient report date for likely pathogenic and pathogenic variants.

Clinical Course

Given frusemide (40 mg daily) spironolactone 25 mg daily

Poor response clinically

Empagliflozin 10 mg daily added



Within one month, baseline creatinine 121(1.37 mg/dL) had increased to creatinine was 302 (3.42 mg/dL, or GFR of 19).

K=2.9

Told to go to ED:

Nephrology consult:

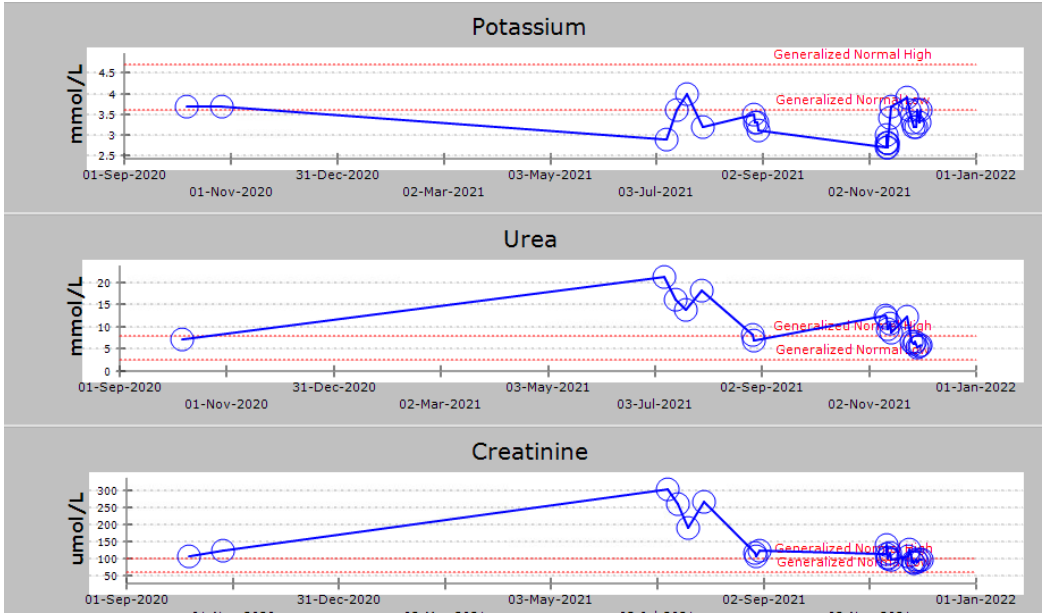
- Fluid restricting to less than 4 cups of fluid daily.
- Hypertensive nephrosclerosis
- ‘Does not misuse alcohol or substances’

Saw a lot of doctors: Heart failure, nephrology, GIM, Hypertension

Ongoing difficulties in management

Labile BP, renal function, K

Ongoing HF symptoms, edema




PENNY
ONE
1966

Current diagnosis: Amphetamine use disorder

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Current diagnosis (work-up is ongoing)

Amphetamine use disorder

Labile HT (?secondary HT)

Hypertensive cardiomyopathy

Modulated by amphetamine use disorder?

HFPEF

Secondary hyperaldosteronism

OSA

Cardiovascular effects of Methamphetamine

Methamphetamine increases postsynaptic catecholamine concentrations (via several mechanisms)

Cardiovascular effects reflect a heightened catecholaminergic state (elevated HR, BP, myocardial contractility),

- Direct vasoconstriction or vasospasm,
- Possible modulation of reactive oxygen species, inflammation, and
- Reduced NO-mediated vasodilation.

Kevil CG, Methamphetamine use and cardiovascular disease. *Arterioscler Thromb Vasc Biol*. 2019;39:1739–1746

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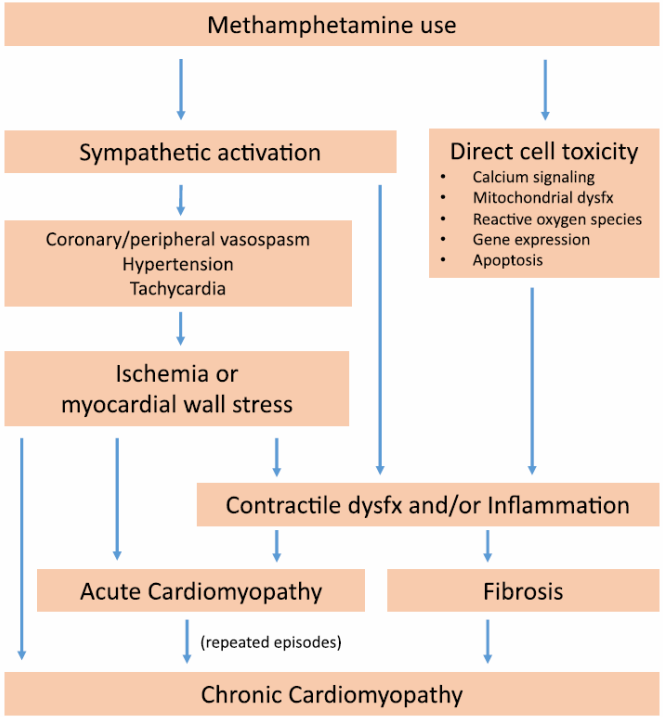
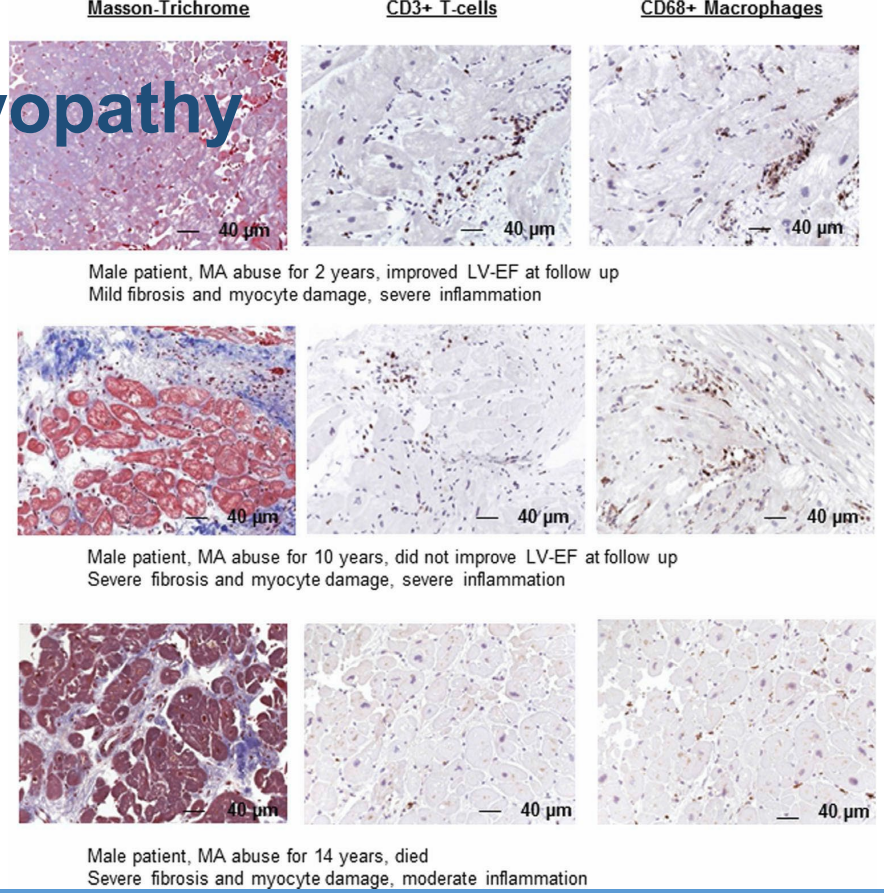
Methamphetamine cardiomyopathy





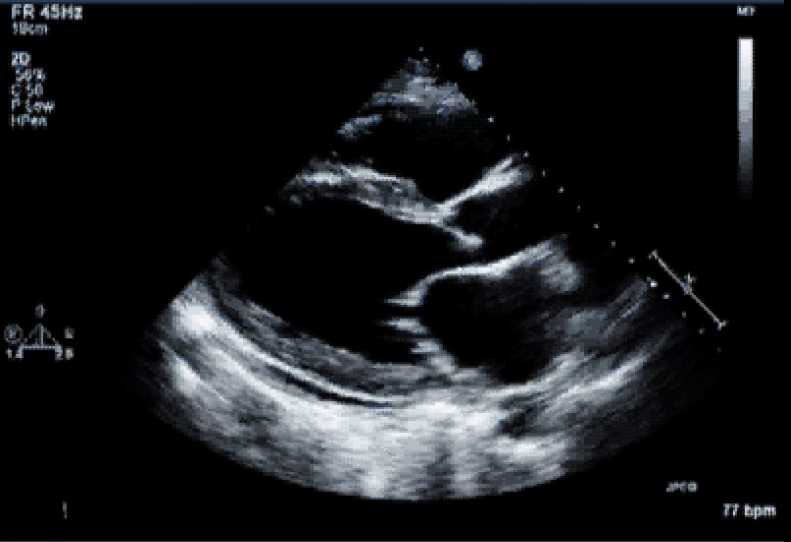
Histological examples of patients with discontinued and continued methamphetamine (MA) abuse over different time periods.
Longer and continued MA abuse (>5 years) is associated with a high degree of fibrosis and myocyte damage

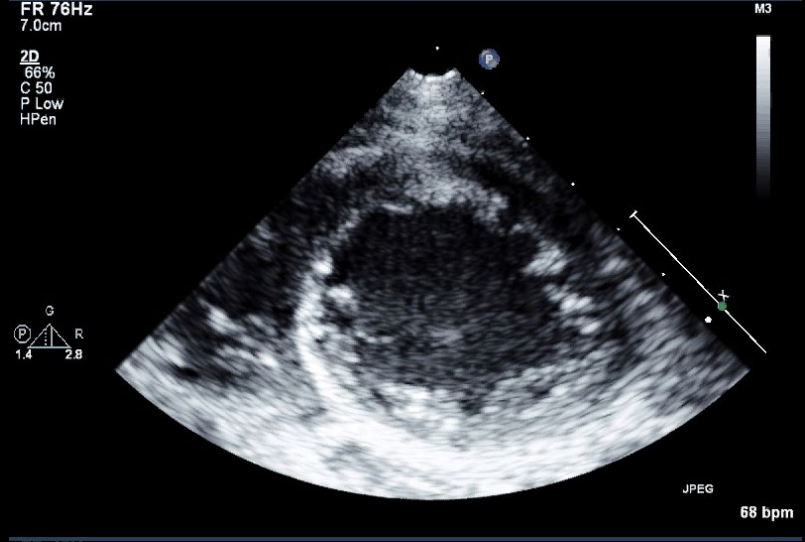
Schürer J Am Coll Cardiol HF 2017
Reddy Clinical Characteristics and Management of Methamphetamine-Associated Cardiomyopathy: State-of-the-Art Review*J Am Heart Assoc.* 2020

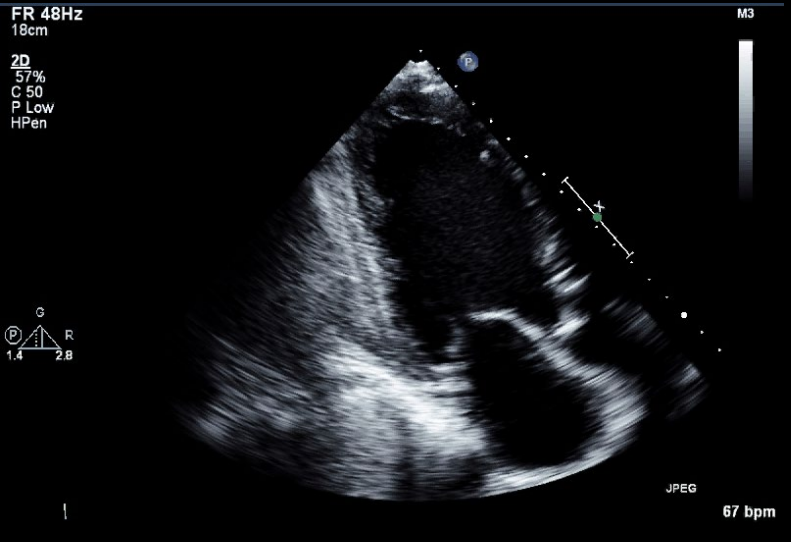
TABLE 1 Baseline Characteristics and Therapy of Patients With Methamphetamine-Associated Cardiomyopathy

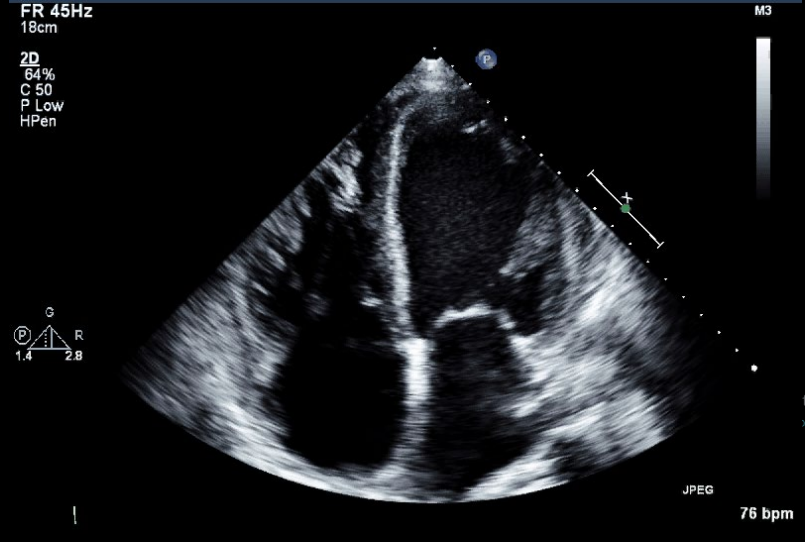
Schürer J Am Coll Cardiol HF 2017;5:435–45

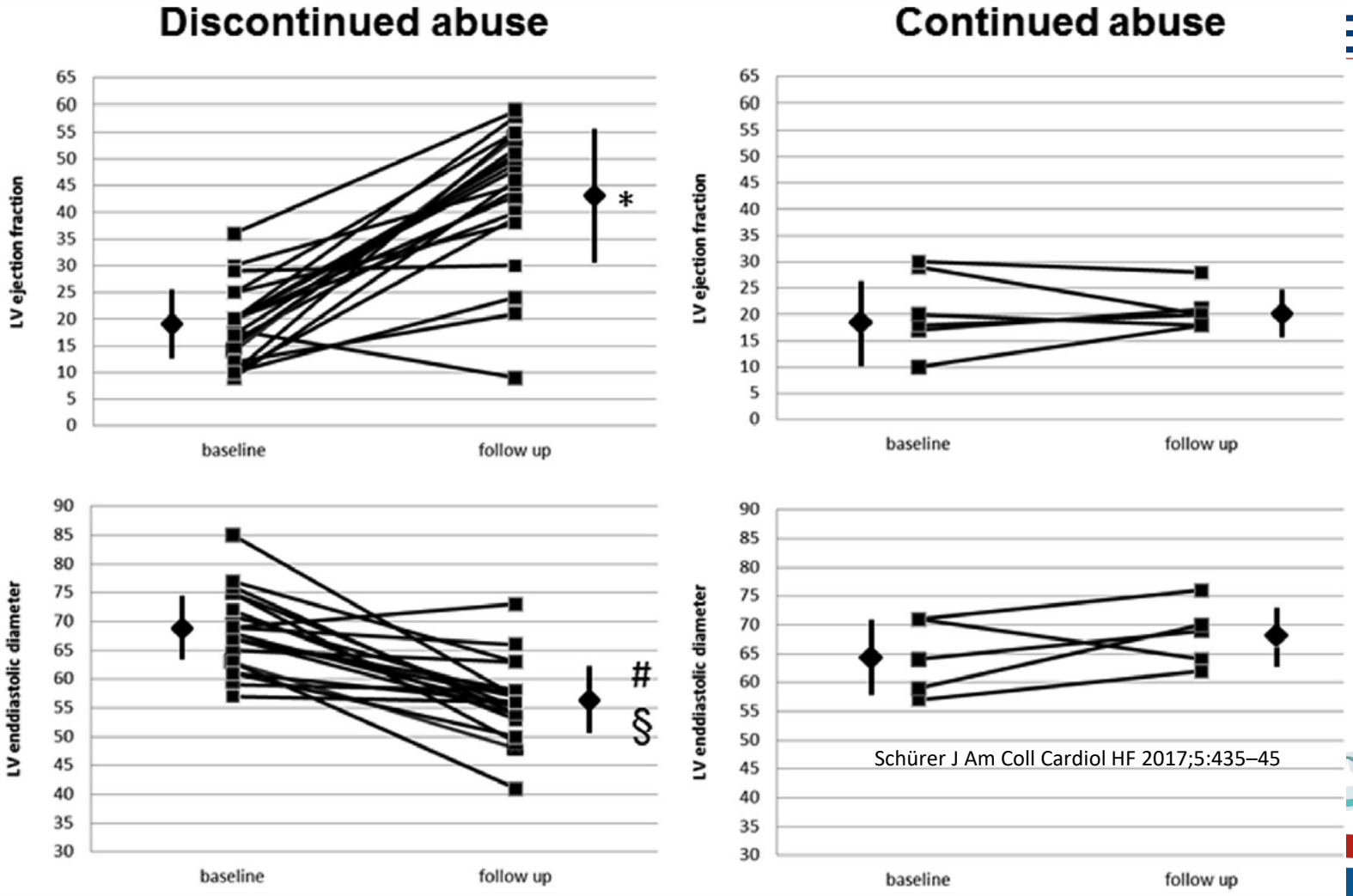
	All (N = 30)	Patients With Discontinued Abuse at Follow-Up (n = 23)	Patients With Discontinued Abuse at Follow-Up (n = 7)	p Value
Echocardiographic findings				
LVEF, %	19 ± 6	19 ± 8	19 ± 8	0.993
LVEDD, mm	67.1 ± 7.4	68.0 ± 7.4	64.6 ± 7.1	0.297
LVESD, mm	58.1 ± 6.2	58.2 ± 6.9	58.0 ± 5.0	0.959
RV diameter	36.6 ± 6.7	38.1 ± 7.4	33.5 ± 3.7	0.174
LA diameter, mm	46.4 ± 7.0	46.8 ± 7.4	45.2 ± 5.9	0.621
TAPSE, mm	17 ± 5	16 ± 5	17 ± 4	0.841
LV thrombus	10/30 (33.3)	7/23 (30.4)	3/7 (42.9)	0.657
RV thrombus	1/30 (3.3)	1/23 (4.3)	0/7 (0)	1.000
Pleural effusion	17/30 (56.7)	15/23 (65.2)	2/7 (28.6)	0.190
Pericardial effusion	12/30 (40)	10/23 (43.5)	2/7 (28.6)	0.669
Ascites	4/28 (14.3)	4/21 (19.0)	0/7 (0)	0.545


FR 45Hz
2D
77 bpm

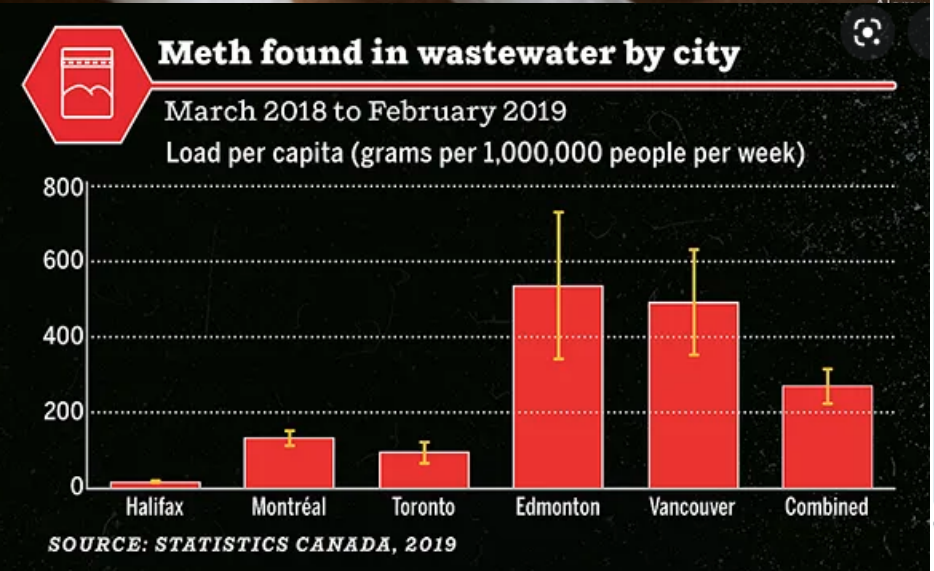

FR 76Hz
7.0cm
2D
66%
C 50
P Low
HPen
M3
JPEG
68 bpm

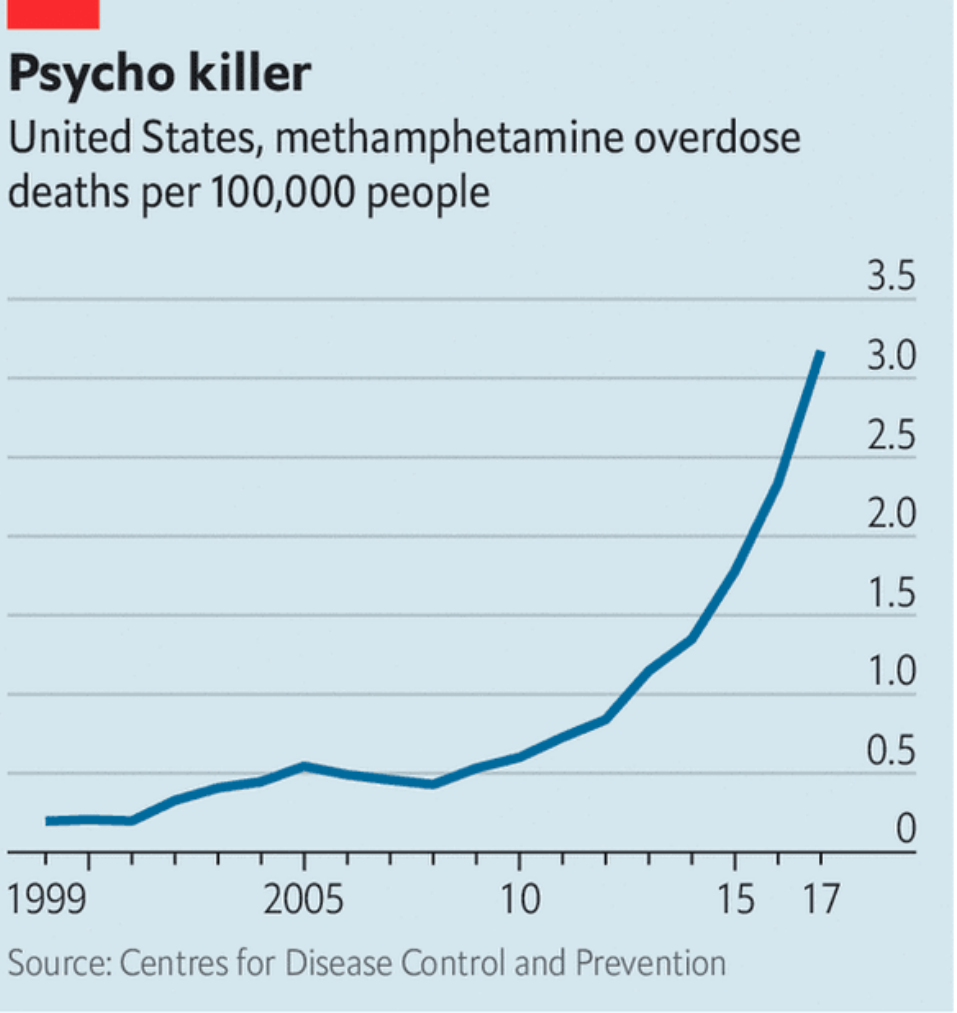

FR 48Hz
18cm
2D
57%
C 50
P Low
HPen
M3
JPEG
67 bpm


FR 45Hz
18cm
2D
64%
C 50
P Low
HPen
M3
JPEG
76 bpm



Schürer J Am Coll Cardiol HF 2017;5:435–45





The Economist 2019

Take-homes

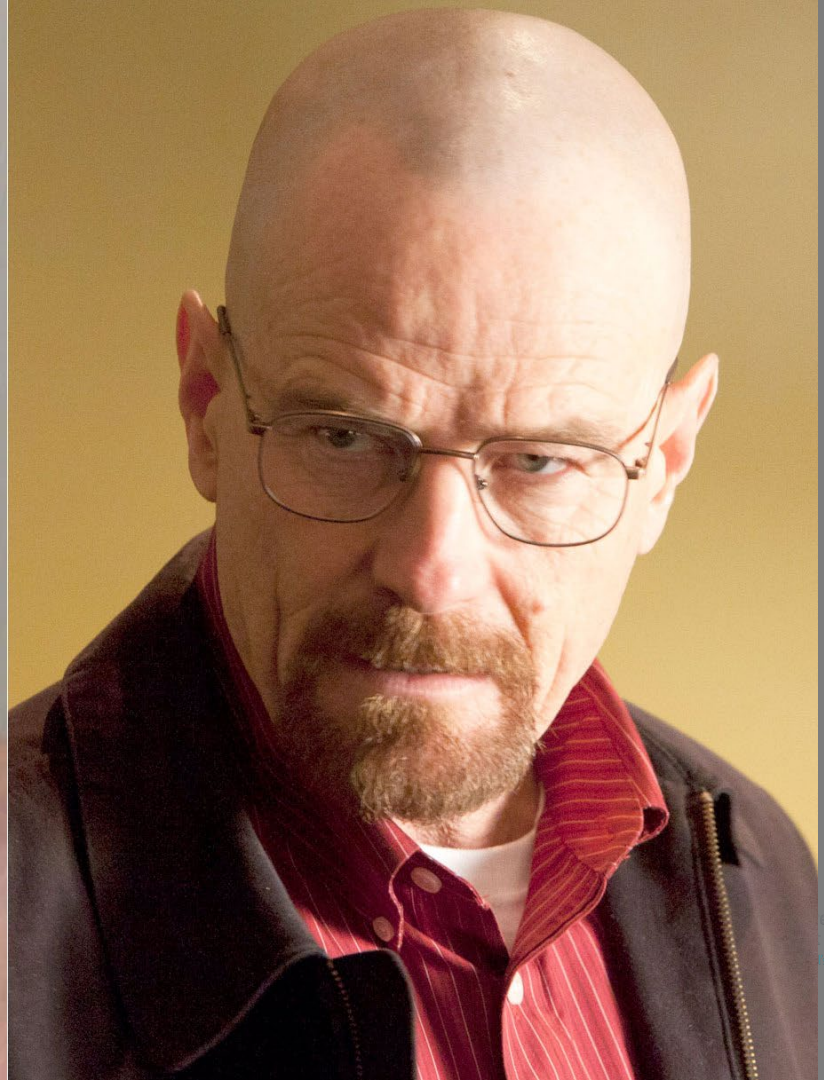
Case is atypical for meth associated cardiomyopathy

But AUD contributed significantly to atypical features of this case, and difficulties with management.

This is a growing epidemic with cardiac implications

When things don't make sense, go back to the history, especially substance history

(Or do a urinary drug screen)



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