Mavacamten for the treatment of obstructive hypertrophic cardiomyopathy

Assoc. Prof. Priv.-Doz. DDr. Martin R. Grübler, BSc FESC

Oberarzt

UK Wiener Neustadt

Disclosures

Forschung: Universitätsklinik Graz, Universitätsspital Zürich, SFU Wien,

Grants: EU FP 7 Horizon 2020

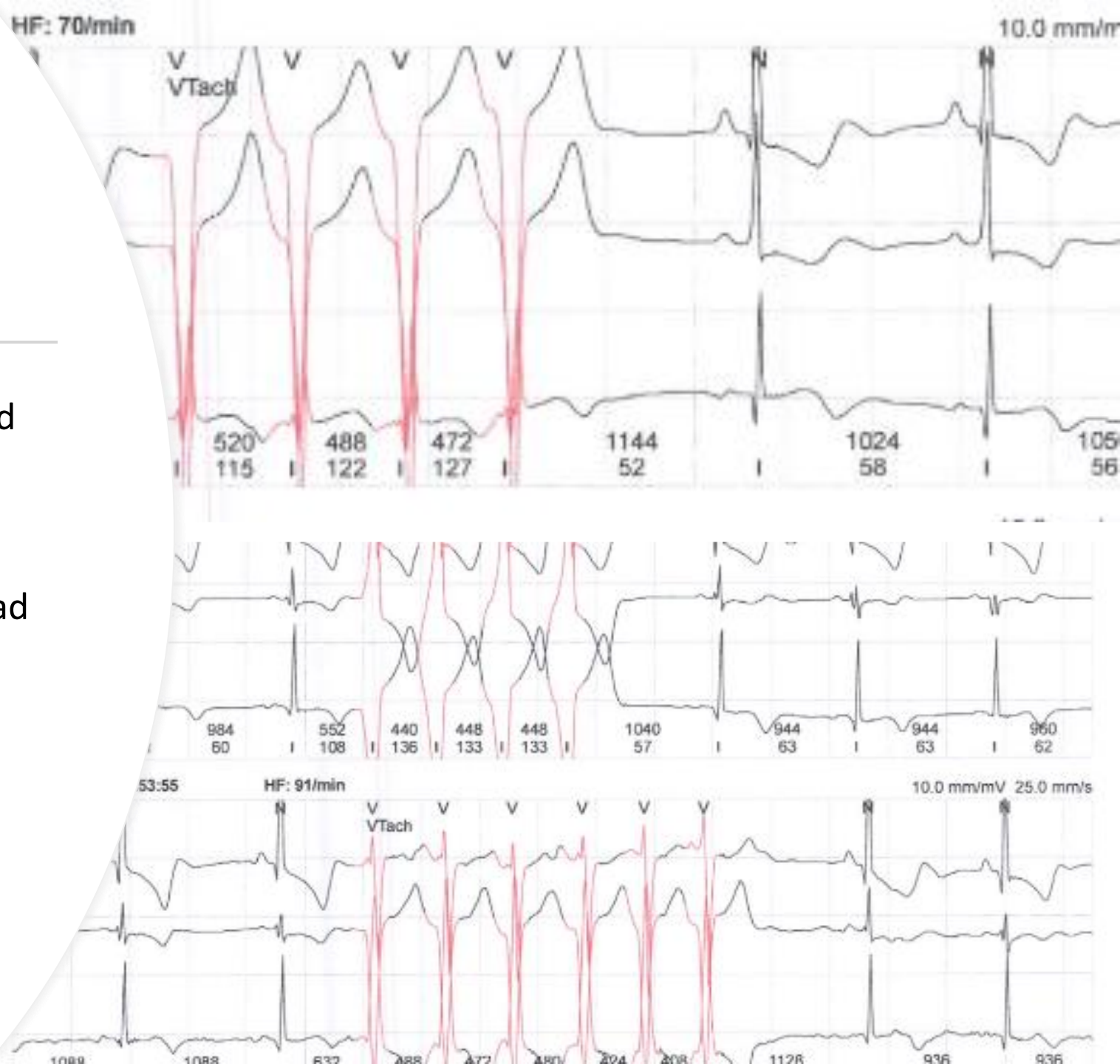
Anstellungsverhältnisse: LKNOE, DPU

Reisen, Kongresse, Honorare inkl. Fortbildungen: Amgen, Daiichi-Sanko, AOP health, Boehringer-Ingelheim, Vifor, Pfizer, Alnylam, Bayer, BMS.

Bristol Myers Squibb®

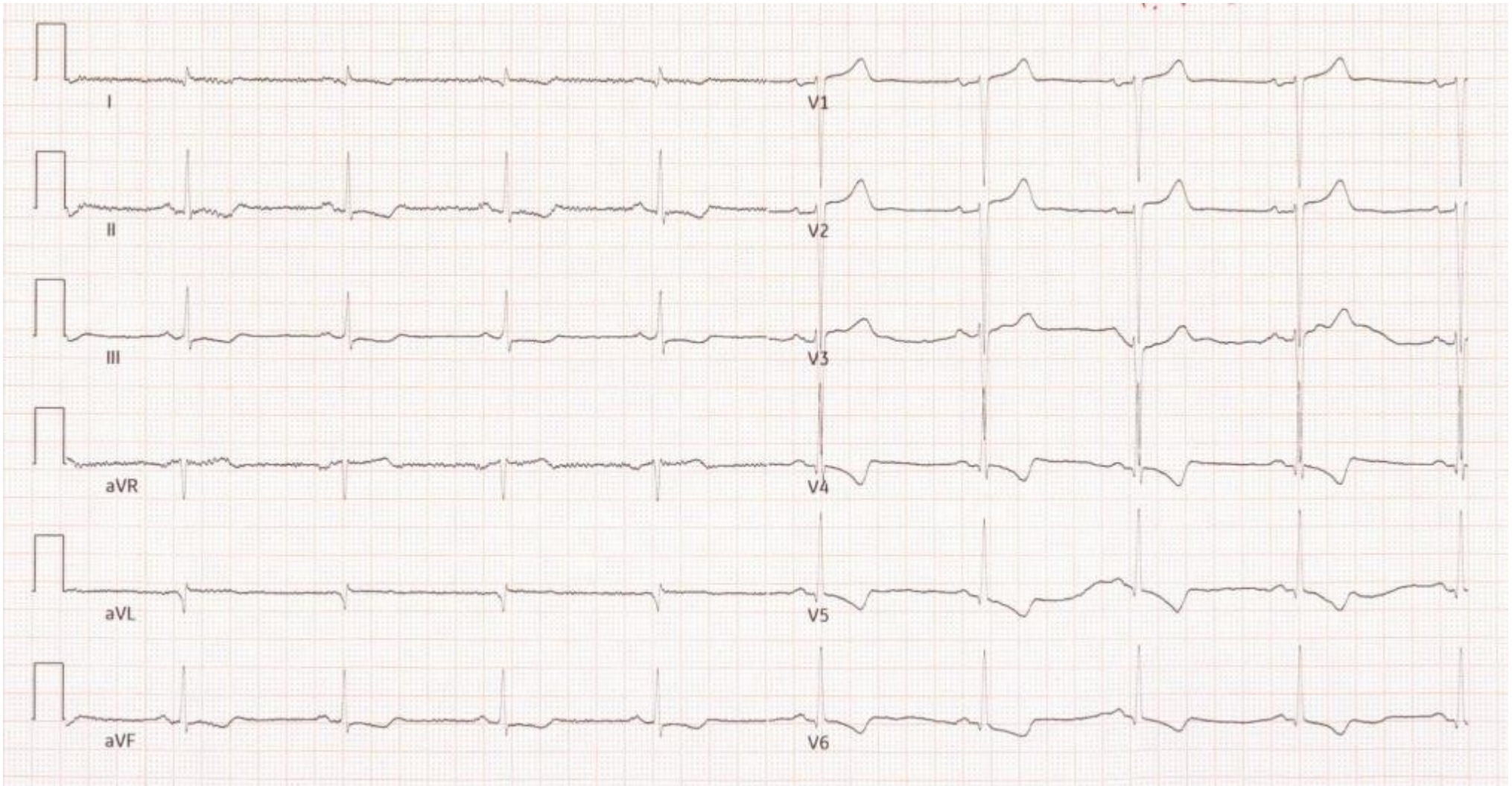
Case

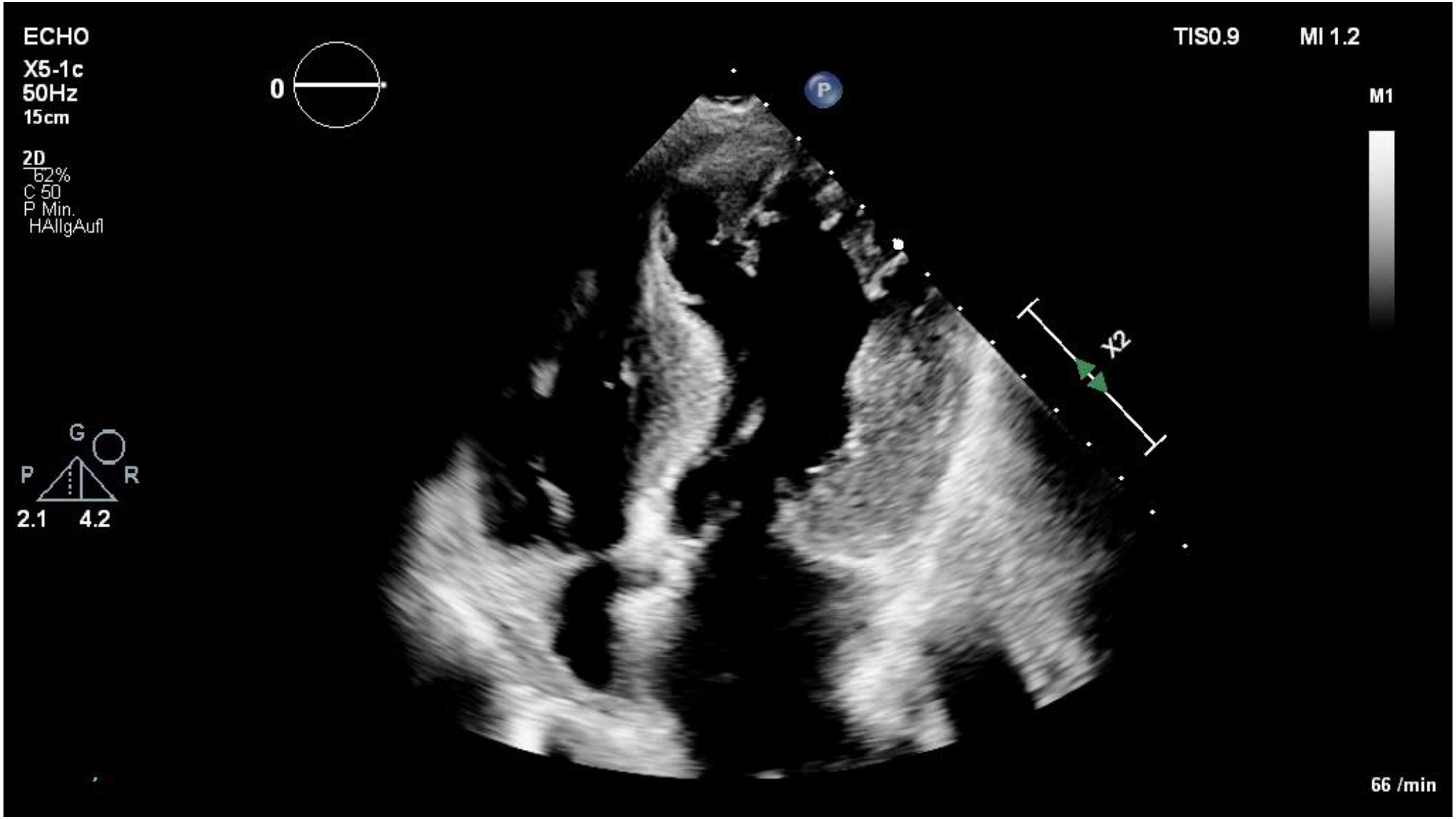
- Asymptomatic women, initially diagnosed 2013 (age 38) at NYHA I with HOCM with peak Valsalva 33mmHg (DF II°, IVSd 17mm)
- NSVT on routine follow-up Holter EKG lead to ICD implantation 2020

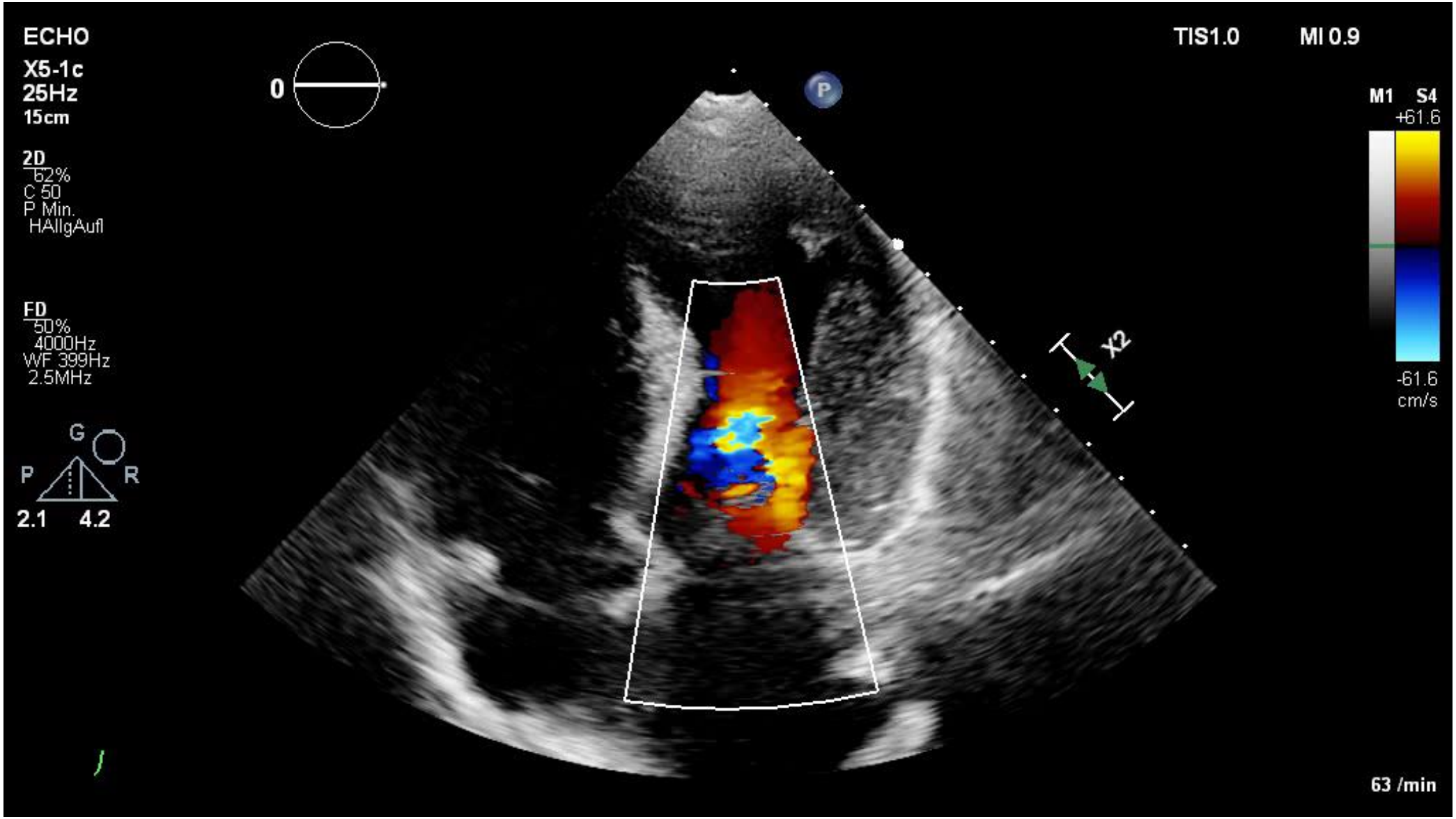


- Progressively symptomatic 2020 – 2023, NYHA III
- No ICD shocks, but pre-syncope
- Exercise intolerance, especially after a meal
- Heat and alcohol intolerance

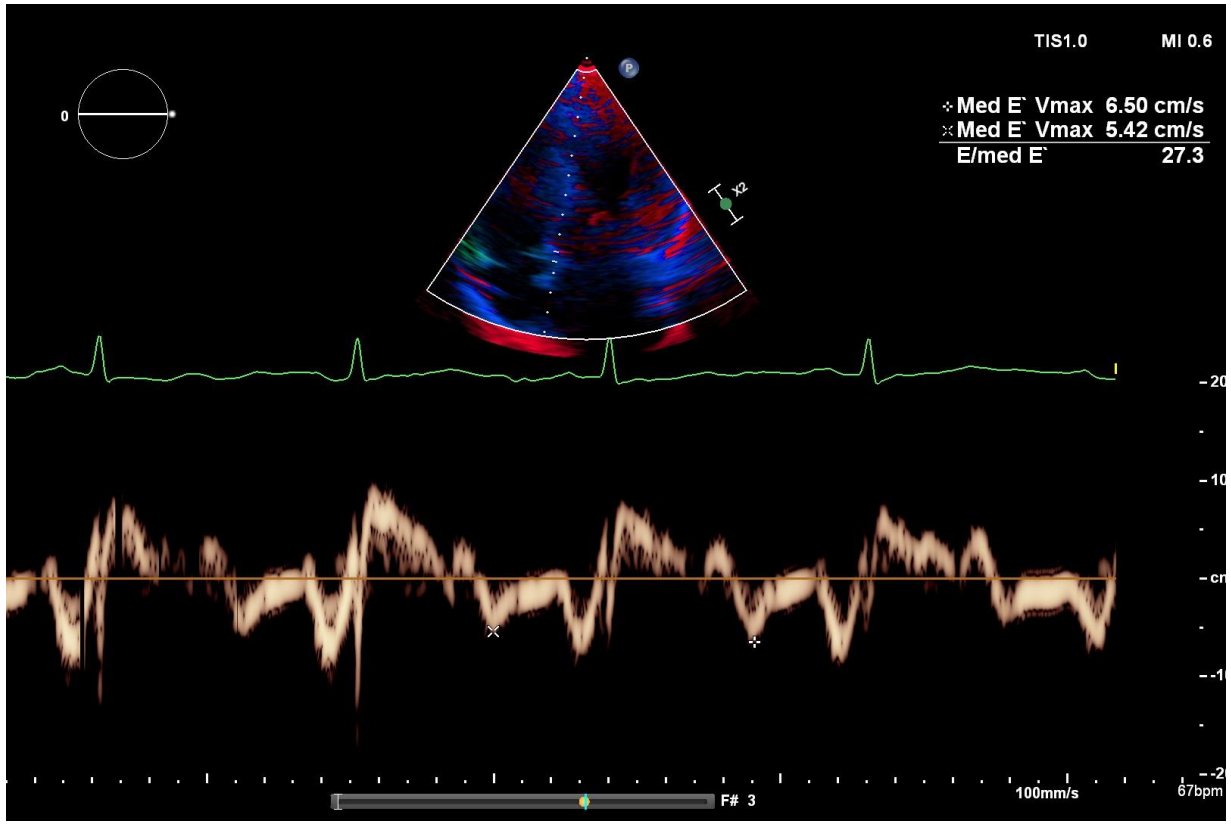
EKG

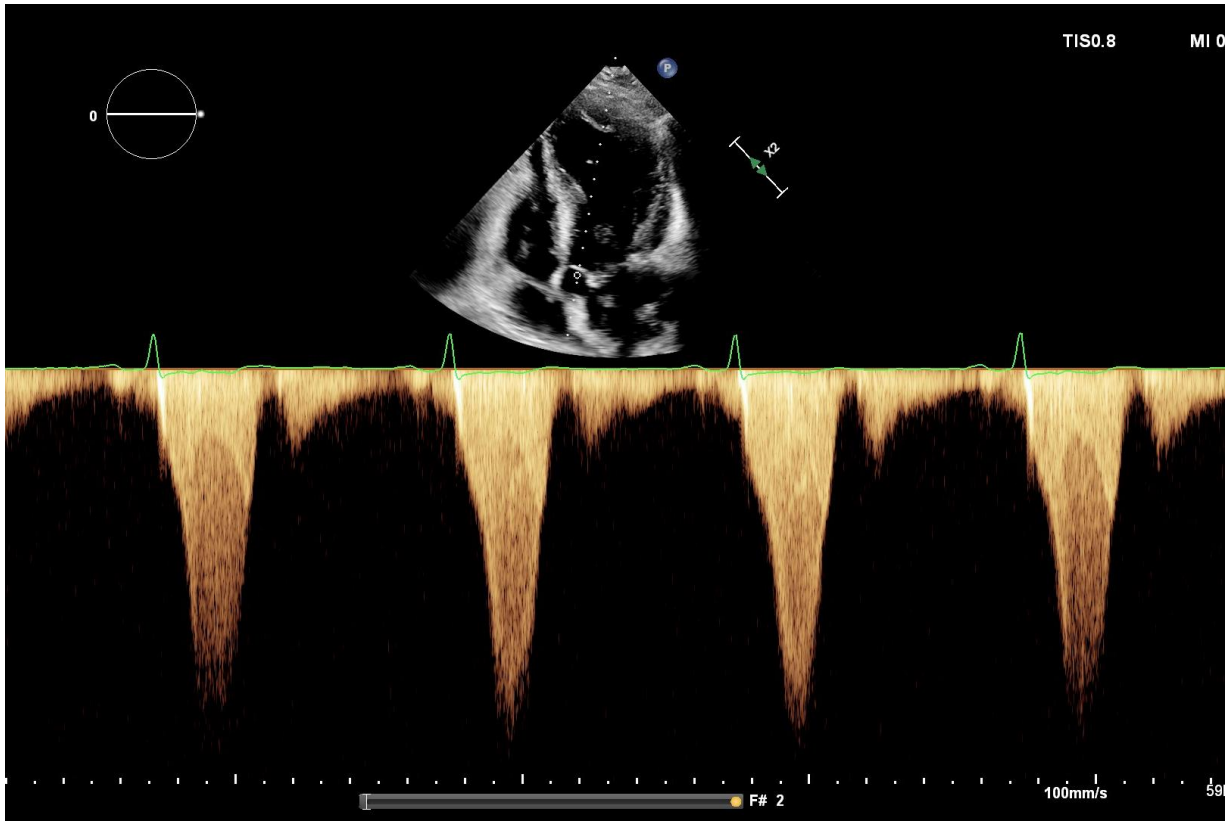



ECHO
X5-1c
50Hz
15cm
2D
62%
C 50
P Min.
HAllgAufl
0
TIS0.9
MI 1.2
M1
P
X2
G
P
R
2.1
4.2
66 /min


ECHO
X5-1c
25Hz
15cm
2D
62%
C 50
P Min.
HAllgAufl
FD
50%
4000Hz
WF 399Hz
2.5MHz
G
P
R
2.1
4.2
0
P
TIS1.0
MI 0.9
M1 S4
+61.6
-61.6
cm/s
X2
63 /min

LVOTO – peakG at rest 108mmHg





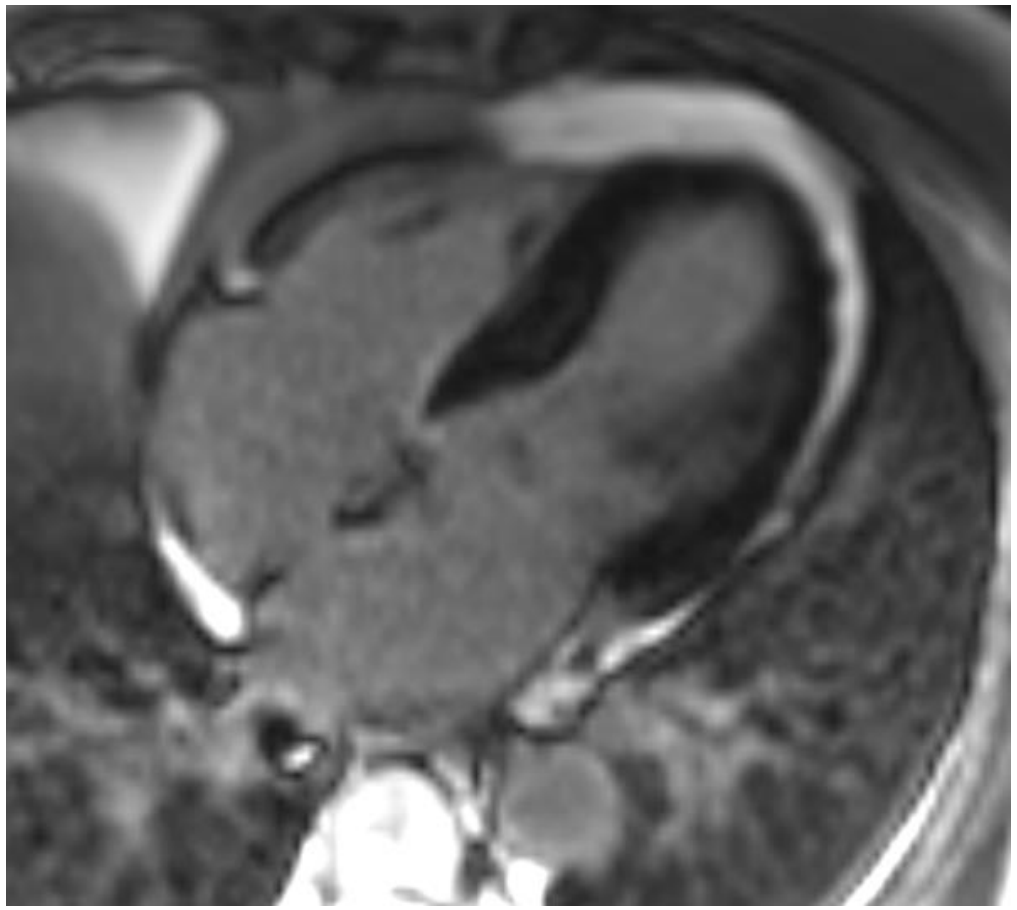
Genetics

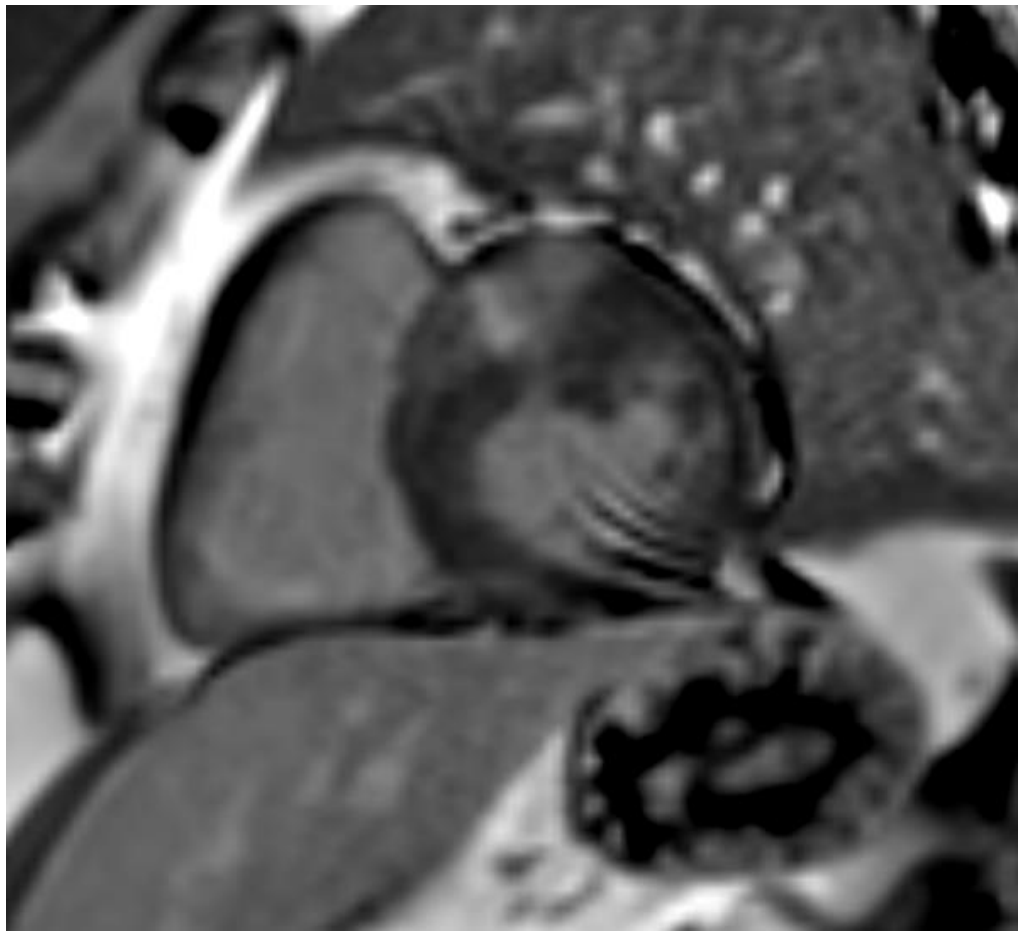
2. Resultat:

Gen	Accession-Nr. LRG-Nr	rs ID	Variante	Zygotie	Erbgang	Klassierung
MYBPC3	**NM_000256.3 LRG_386t1**	**NV**	**Deletion der Exons 1-5**	**het**	**AD**	**wahrscheinlich pathogen**

AD: autosomal dominant; AR: autosomal rezessive; het: heterozygot; Klassierung gemäss ACMG-Kriterien (Richards S et al. 2015, *Genet Med* 17 : 405-424); ACMG = American College of Medical Genetics and Genomics. NV: Nicht verfügbar

CMR





CPET

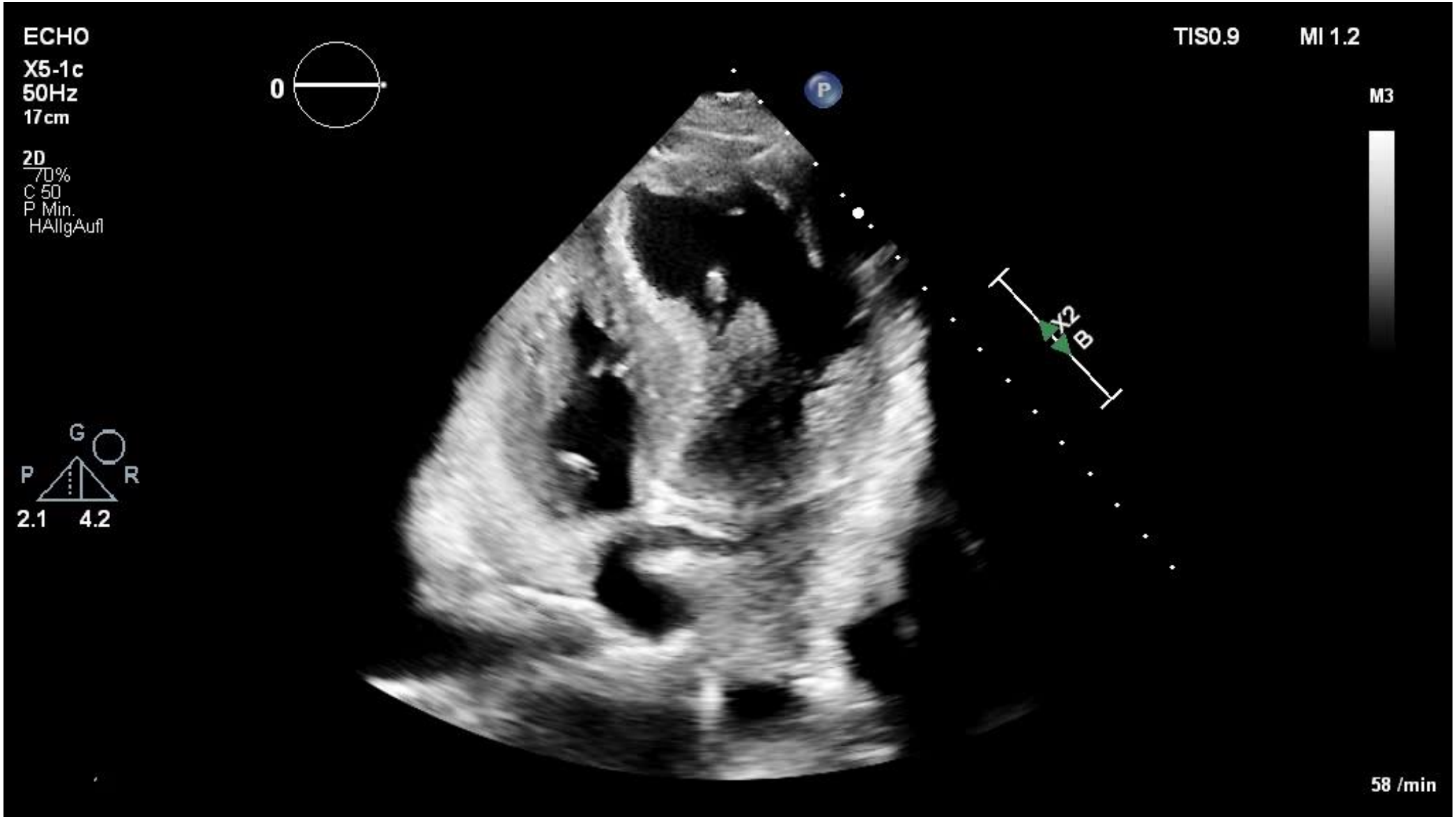
- Would not tolerate exercise for more than 4 minutes, so exam was cancelled

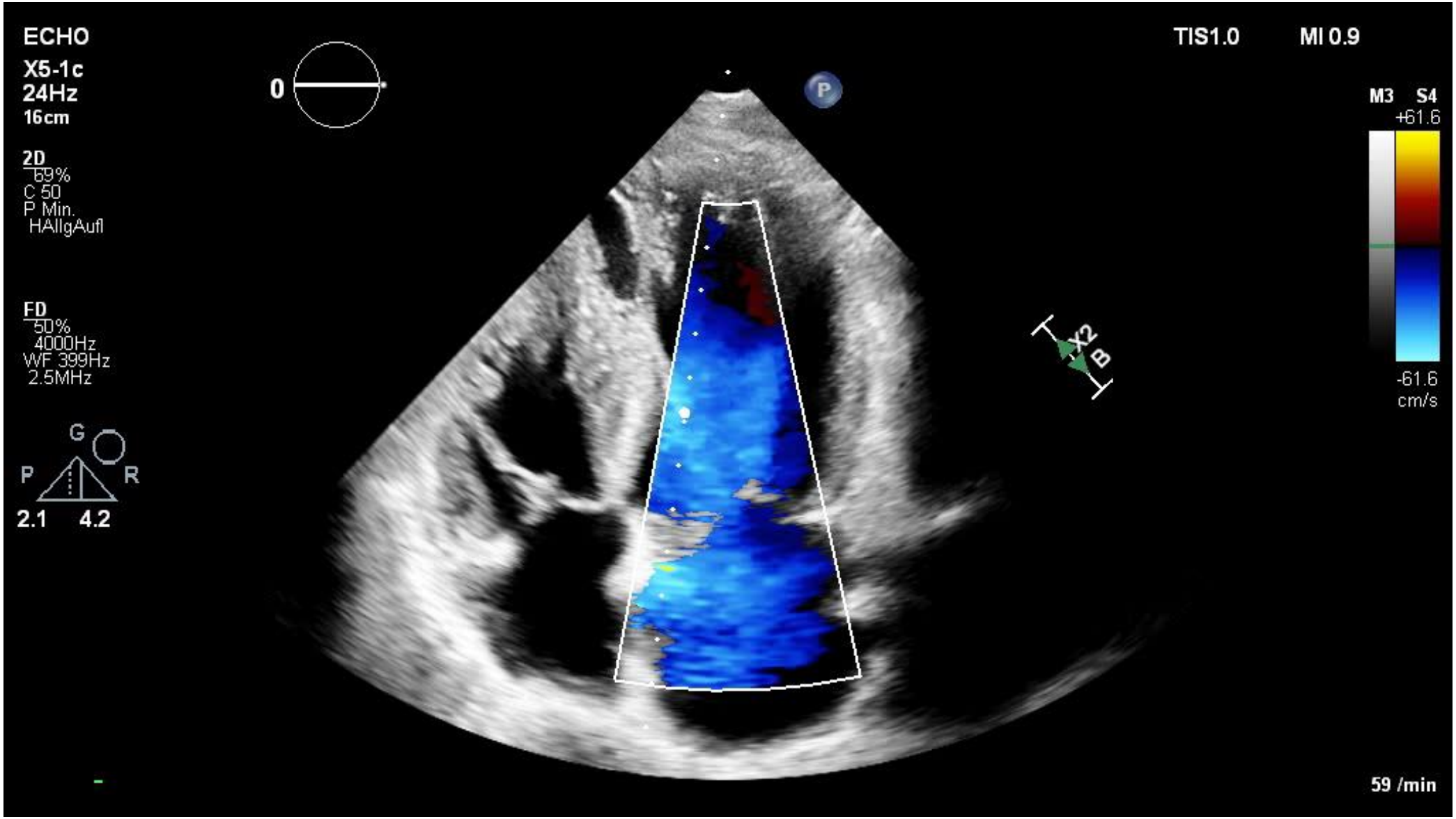
Mavacamten treatment and response

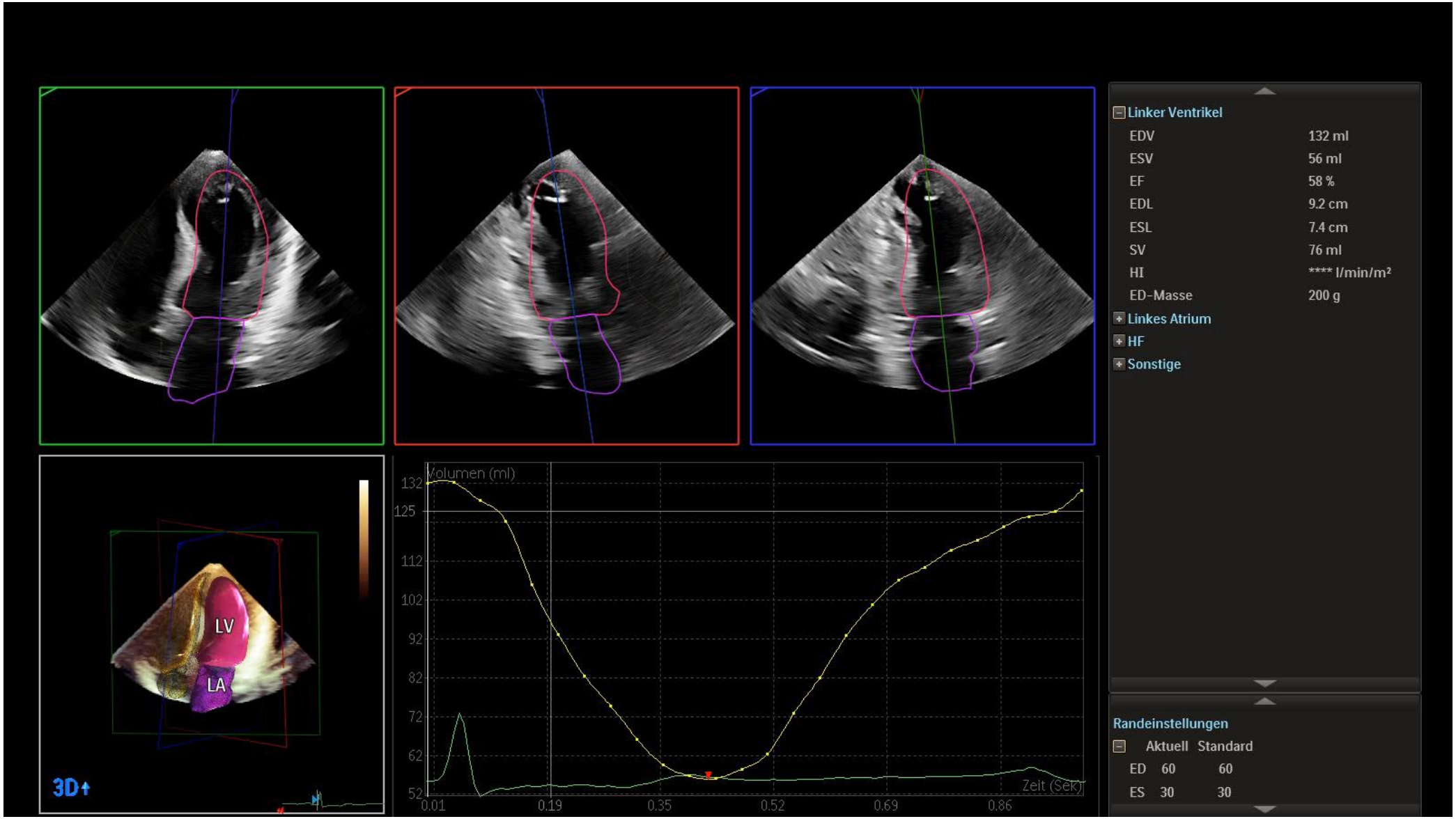
August 2023

February 2024

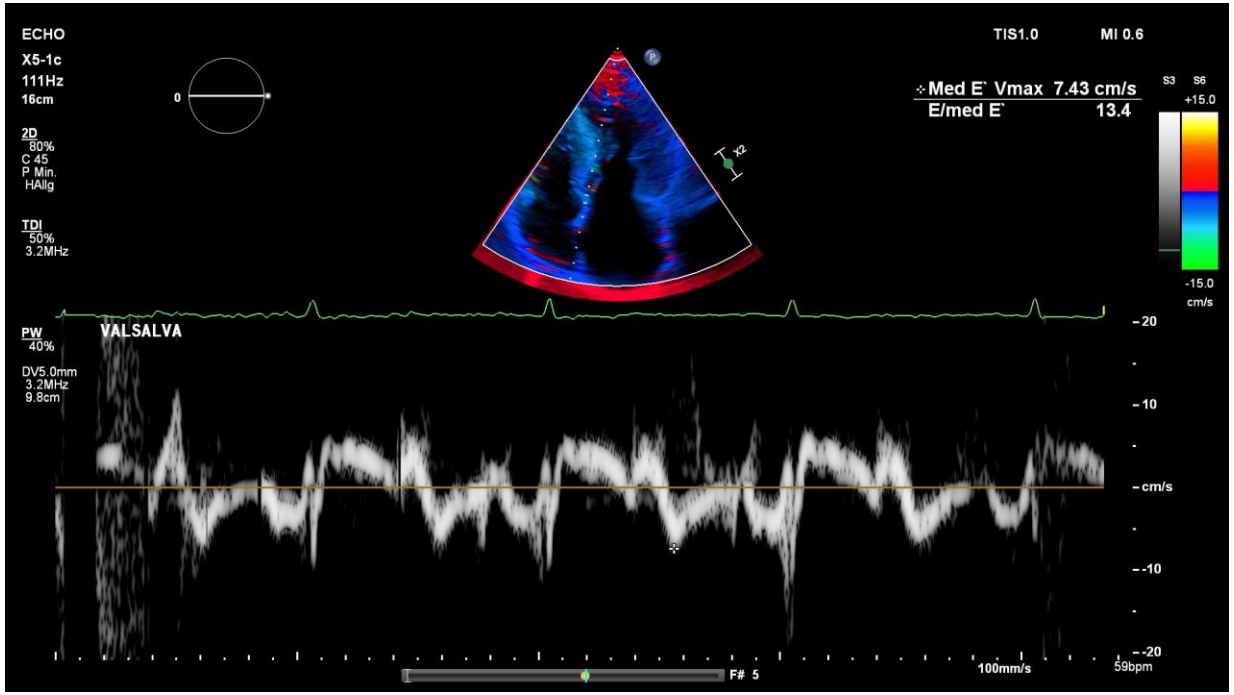
June 2024

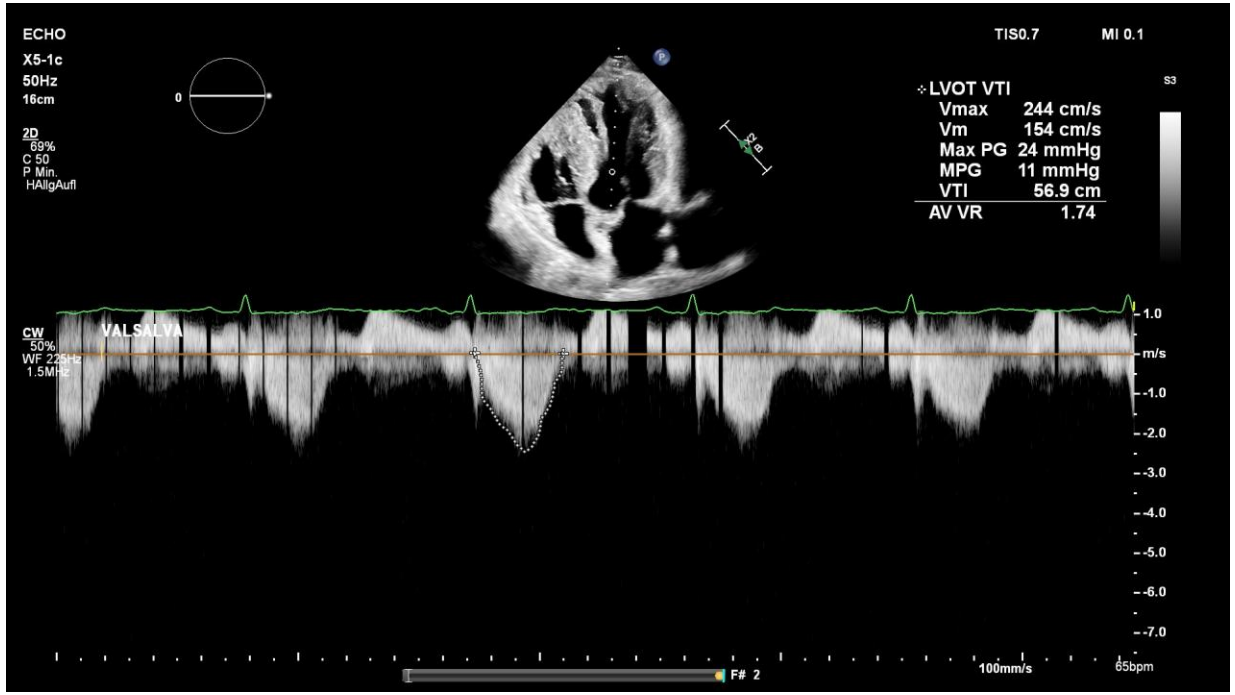

ECHO
X5-1c
50Hz
17cm
2D
70%
C 50
P Min.
HAllgAufl
0
TIS0.9
MI 1.2
M3
P
X2
B
G
P
R
2.1
4.2
58 /min


ECHO
X5-1c
24Hz
16cm
2D
69%
C 50
P Min.
HAllgAufl
FD
50%
4000Hz
WF 399Hz
2.5MHz
G
P
R
2.1
4.2
0
P
TIS1.0
MI 0.9
M3 S4
+61.6
-61.6
cm/s
X2
B
59 /min


Linker Ventrikel
EDV 132 ml
ESV 56 ml
EF 58 %
EDL 9.2 cm
ESL 7.4 cm
SV 76 ml
HI **** l/min/m²
ED-Masse 200 g
Linkes Atrium
HF
Sonstige
Volumen (ml)
132
125
112
102
92
82
72
62
52
0.01
0.19
0.35
0.52
0.69
0.86
Zeit (Sek)
LV
LA
3D
Randeinstellungen
Aktuell Standard
ED 60 60
ES 30 30

Follow-up


ECHO
X5-1c
111Hz
16cm
2D
80%
C 45
P Min.
HAllg
TDI
50%
3.2MHz
PW
40%
DV5.0mm
3.2MHz
9.8cm
VALSALVA
TIS1.0
MI 0.6
Med E` Vmax 7.43 cm/s
E/med E` 13.4
S3
S6
+15.0
-15.0
cm/s
20
10
cm/s
-10
-20
F# 5
100mm/s
59bpm


ECHO
X5-1c
50Hz
16cm
2D
69%
C 50
P Min.
HAllgAufl
CW
50%
WF 225Hz
1.5MHz
VALSALVA
TIS0.7
MI 0.1
LVOT VTI
Vmax 244 cm/s
Vm 154 cm/s
Max PG 24 mmHg
MPG 11 mmHg
VTI 56.9 cm
AV VR 1.74
S3
1.0
m/s
-1.0
-2.0
-3.0
-4.0
-5.0
-6.0
-7.0
F# 2
100mm/s
65bpm

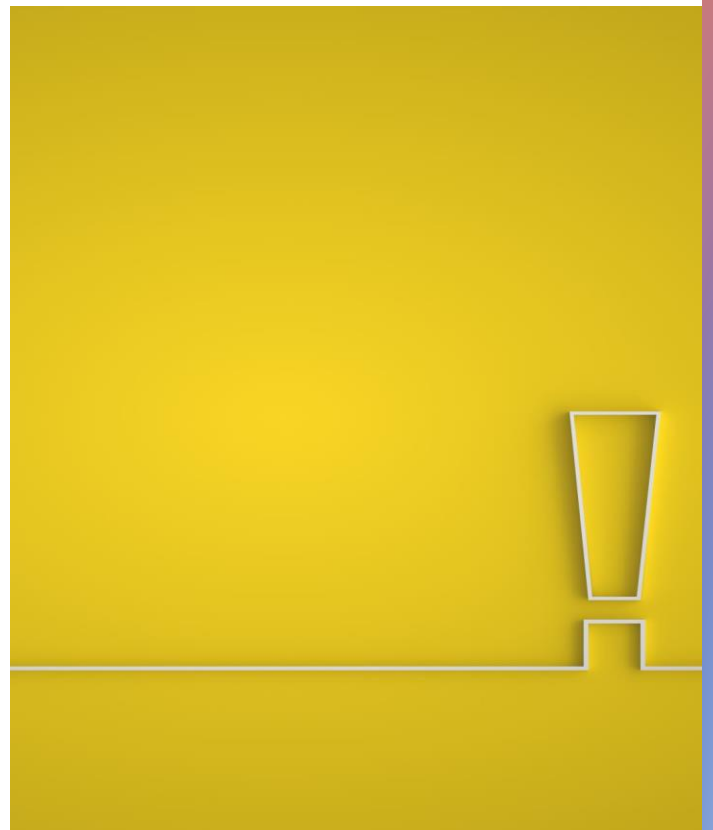
Lab

- NTproBNP: 2828pg/mL August 2023 Mavacamten 2,5mg
- NTproBNP 2700pg/mL February 2024 Mavacamten 10mg
- NTproBNP 1586pg/mL June 2024 Mavacamten 15mg

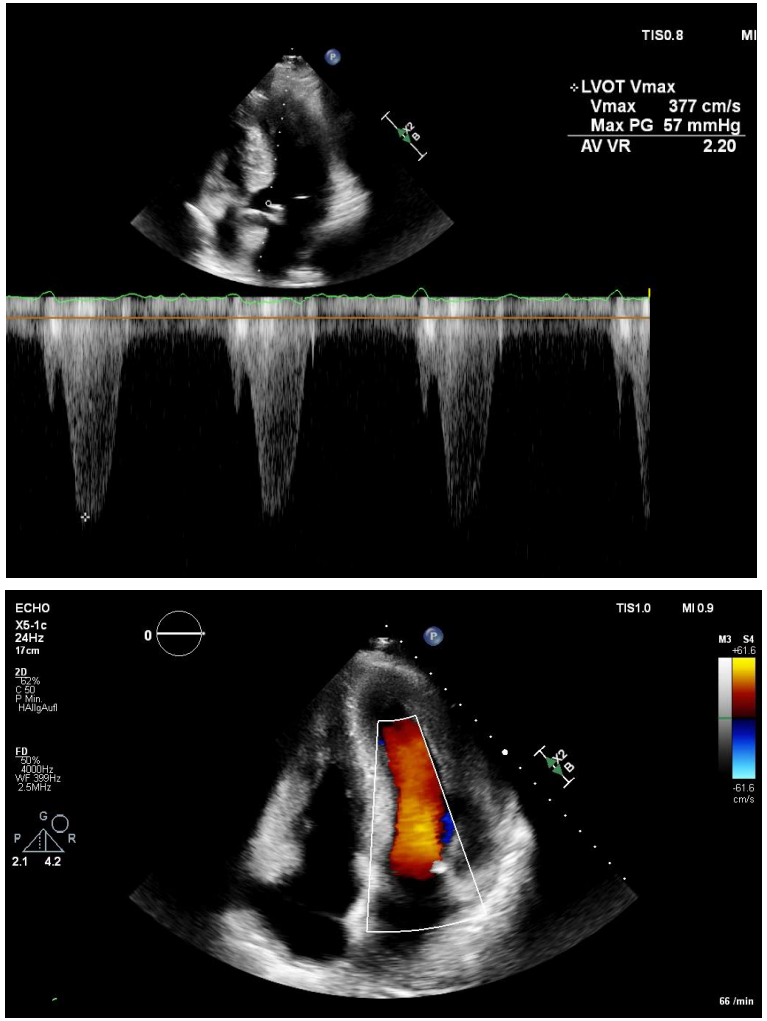
Follow-up CPET

Leistungsparameter:	Istwert	Referenzwert	% Referenz
Wmax	167	118 (99)	142
Wmax Normgewicht	167	118 (21)	141
VO2max, L/min	1,77	1,58 (21)	112
VO2max Normg., L/min	1,77	1,58 (21)	112
VO2max, ml/kg/min	29,5	26,4 (9)	112
VO2/W, ml/W	9,1	>= 9	
VT1, %VO2max Soll	80	40 - 70	
HF an VT1	127		
Watt an VT1	105		
VT2, %VO2max Soll	100		
HF an VT2	145		
Watt an VT2	139		

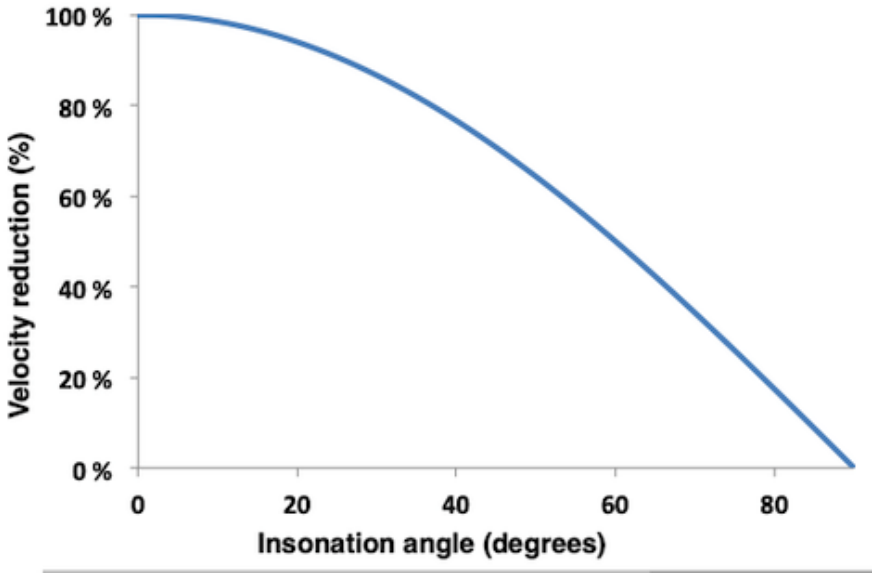
Lessons learned



Pitfalls im TTE

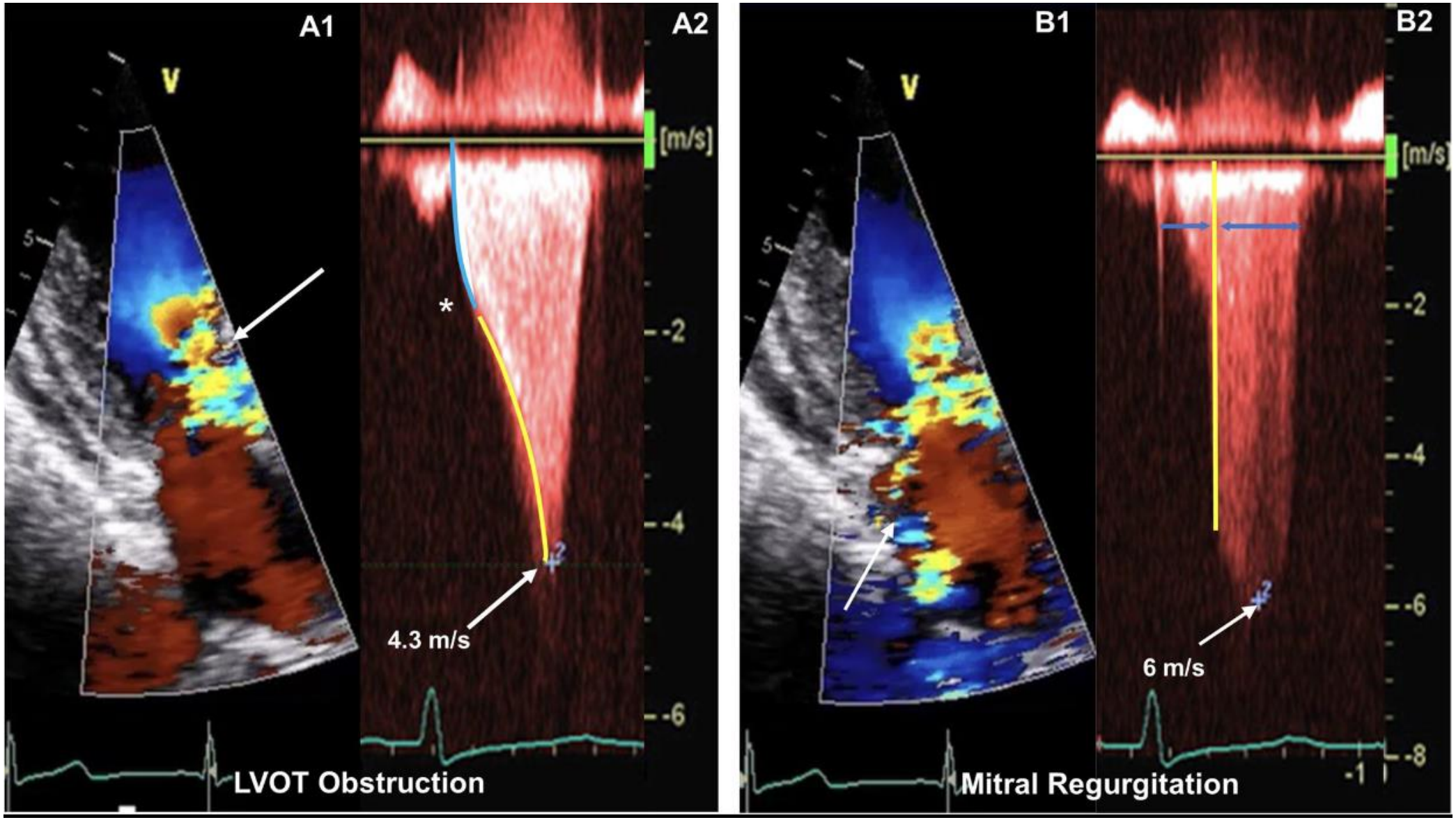


LVOTO als pathognomonisch für eine HCM interpretieren



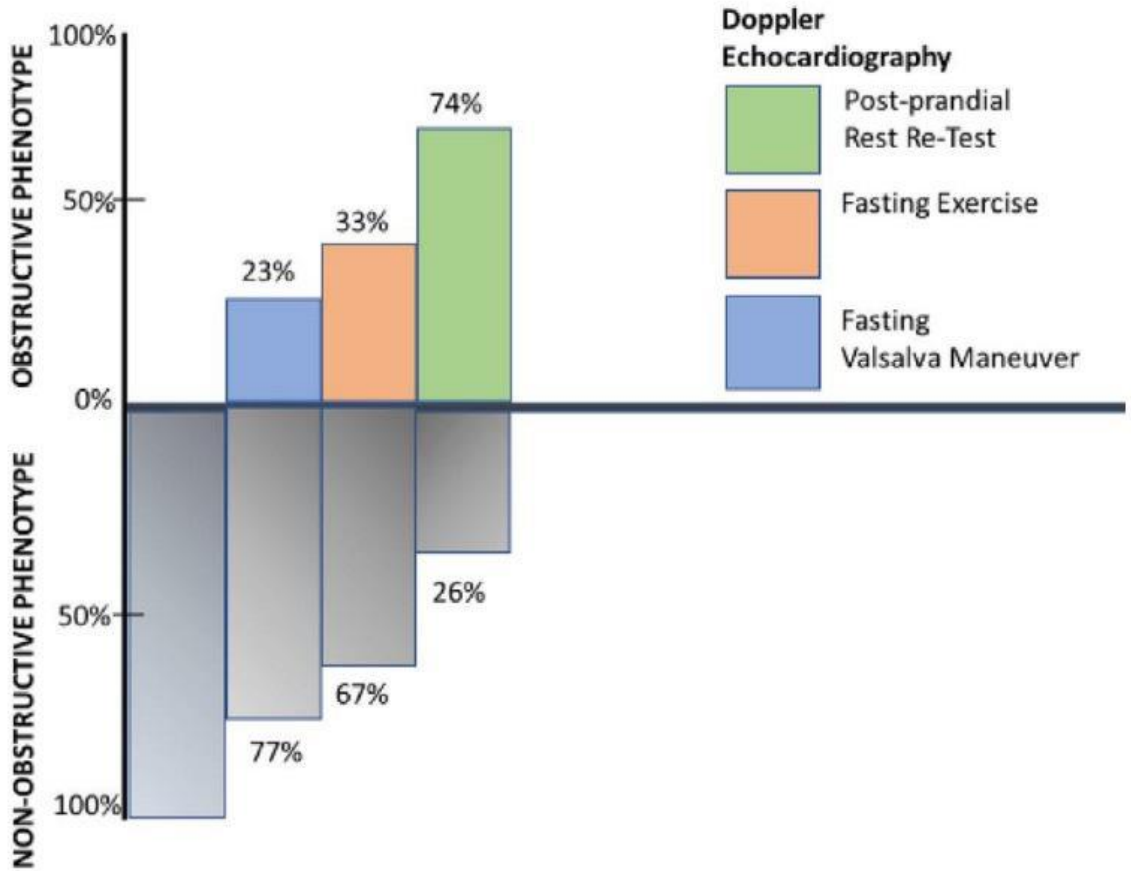
Angulation CW Doppler / MI Signal

LVOTO ist Dynamisch!

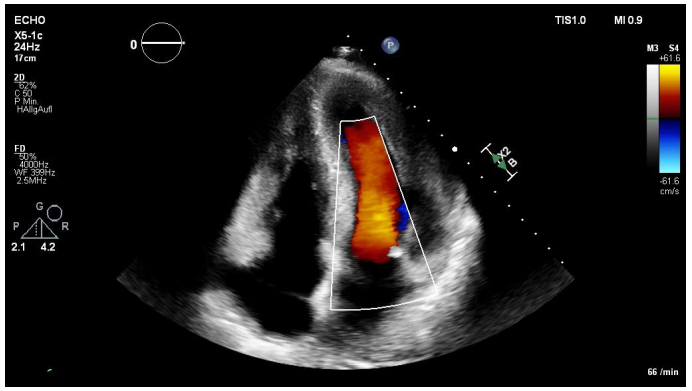


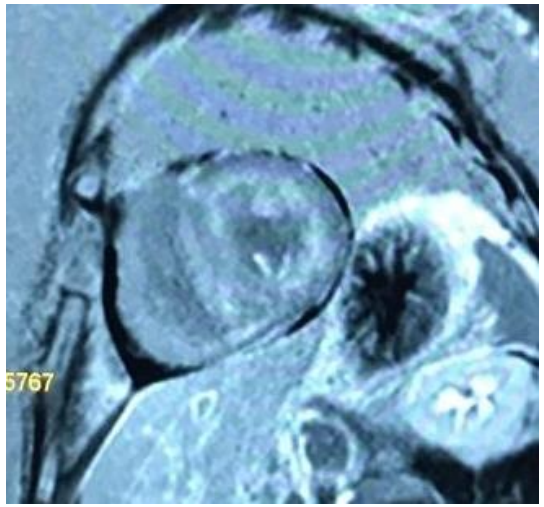
Abbasi et al. JASE 2024

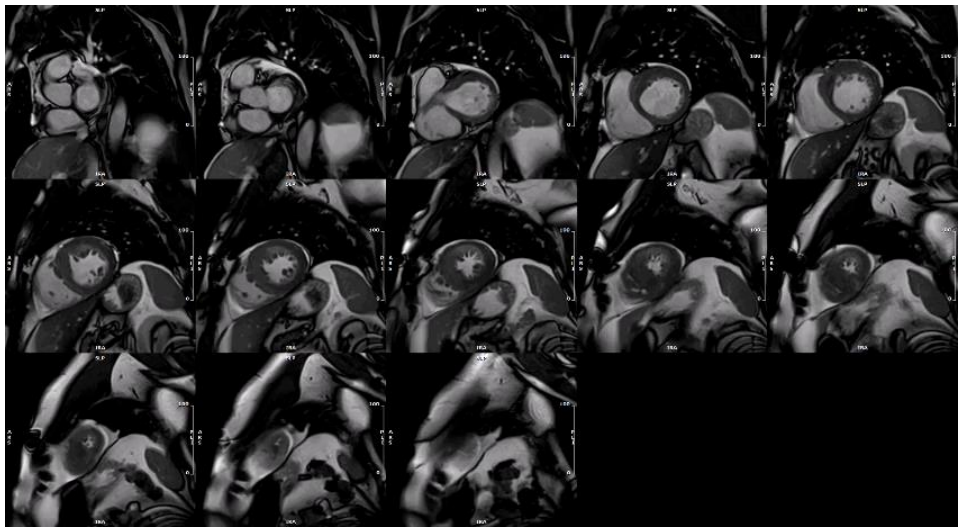
Post-prandial LVOT obstruction provocation

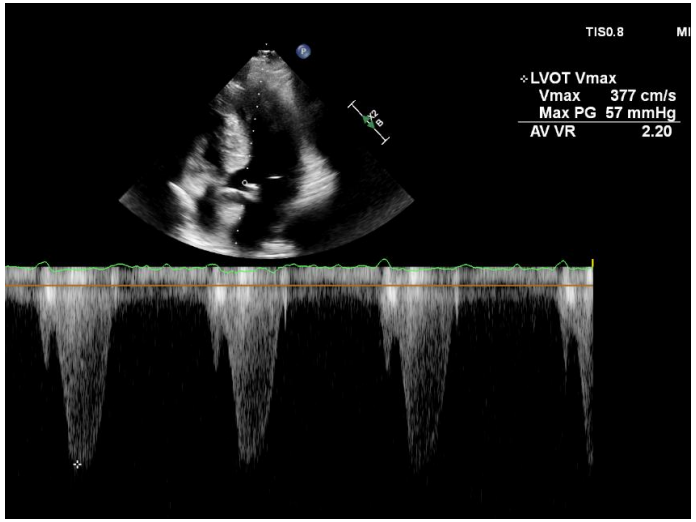


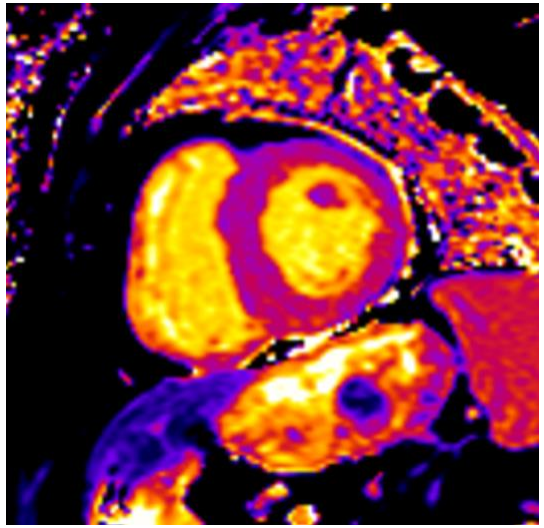
La Canna et al. Am J Cardiol 2020;125(11):1688-1693



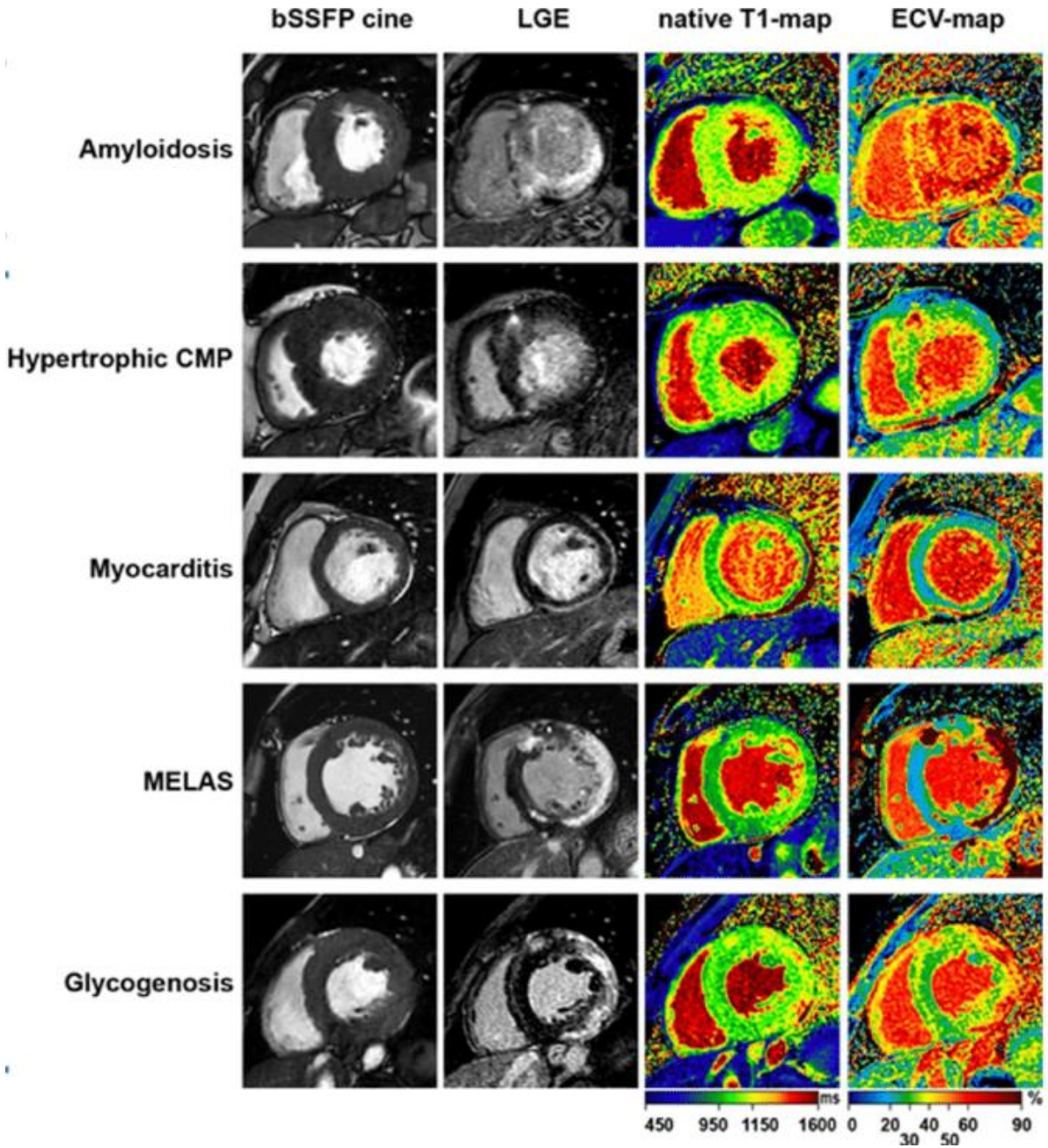








© Martin Grübler, MD
Under preperation for publication

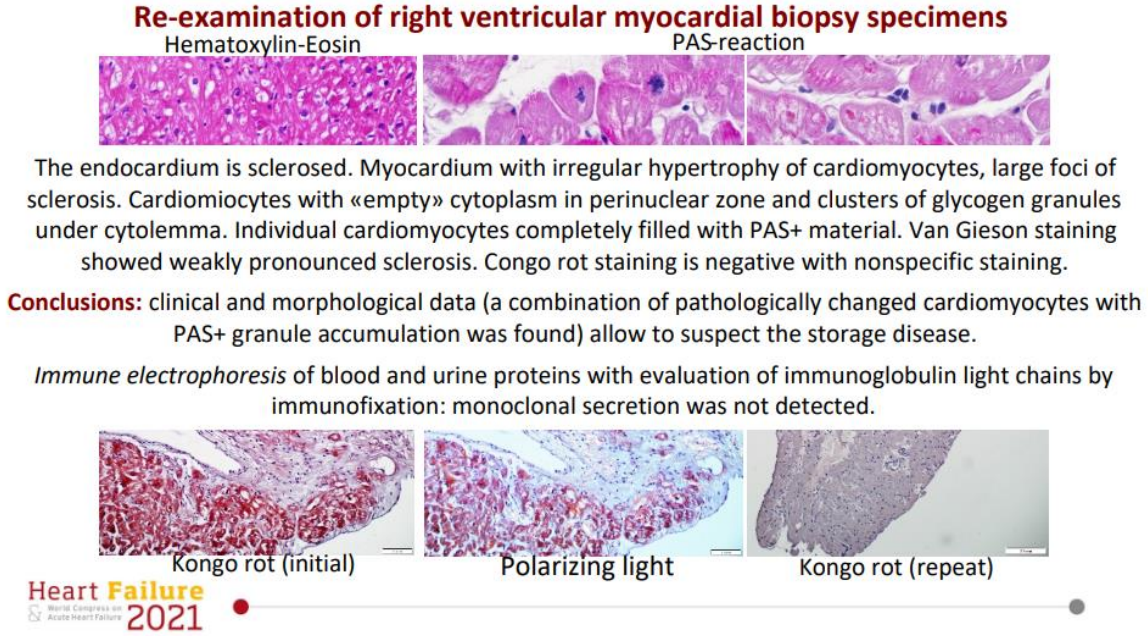


Marholdt et al. Clinical Research Cardiology, 2021

Ein Goldstandard der Irreführend sein kann:

Pitfalls Endomyokardbiopsie

Mitochondriopathien, **Dannon**, und andere noch **seltenere Speichererkrankungen** werden in der Regel in der EMB **<u>nicht erkannt</u>**!



© Prof. Blagova, HFA 2021

Danke!