Překvapivý MR nález u pacienta s HOKMP léčeného mavakamtenem

Júlia Borová, Martin Pleva, Jaroslav Januška

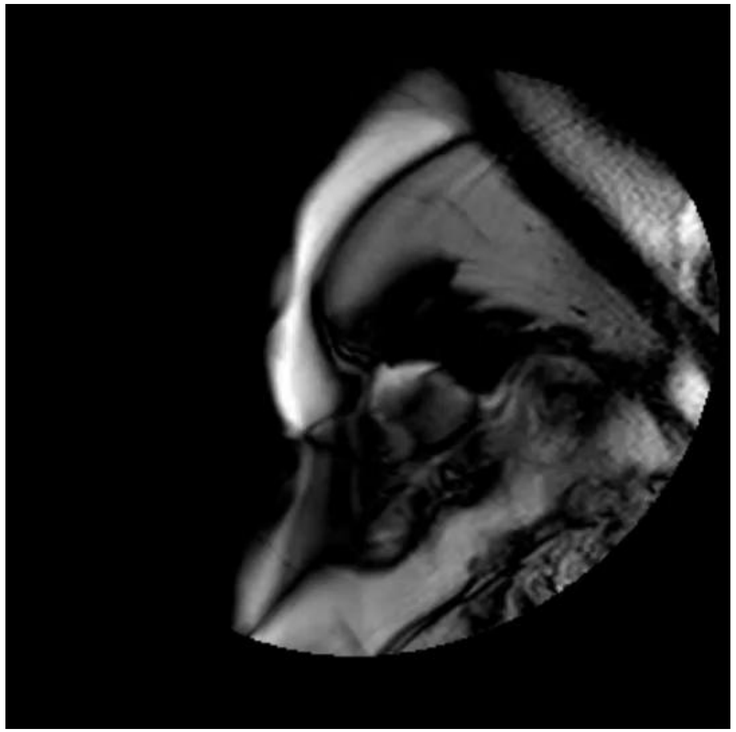
Popis případu

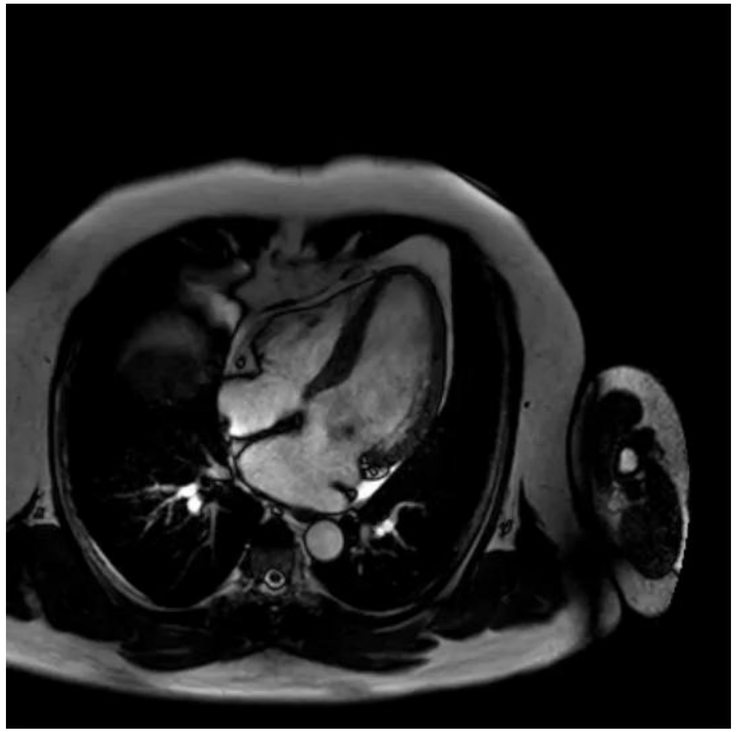
- muž nar. 1962, v roce 2010 diagnostikována HOCM
- OA: arteriální hypertenze, smíšená HLP, zvýšená glykémie nalačno, mírná obezita (BMI 33)
- RA: otec otce zemřel v 68 letech na srdeční selhání, rodiče bez výskytu KV onemocnění, 2 synové - jeden HCM (G+/F+)
- genetické vyšetření s nálezem PV c.3064C>T (p.(Arg1022Cys)) v genu MYBPC3

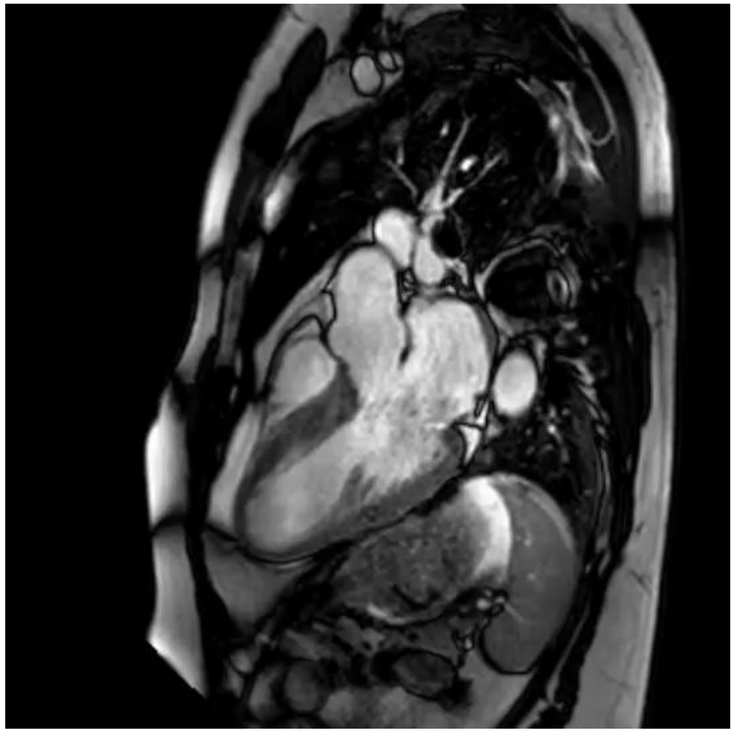
Popis případu

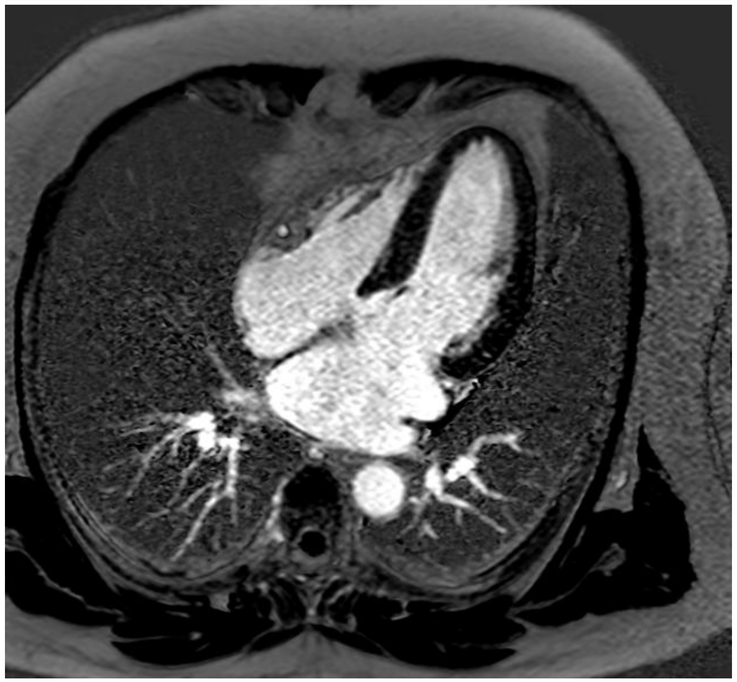
- asi od roku 2013 postupně rozvoj symptomatologie (námahová dušnost, zhoršená tolerance zátěže, oprese na hrudi)
- koronarogram negativní
- titrována dávka betablokátoru (bisoprolol 5….20 mg/denně)
- opakované EKG Holterovské monitorace oj. monotopní KES a kuplety KES, bez záchytu nsKT či jiných arytmií
- kalkulované riziko SCD nízké/střední

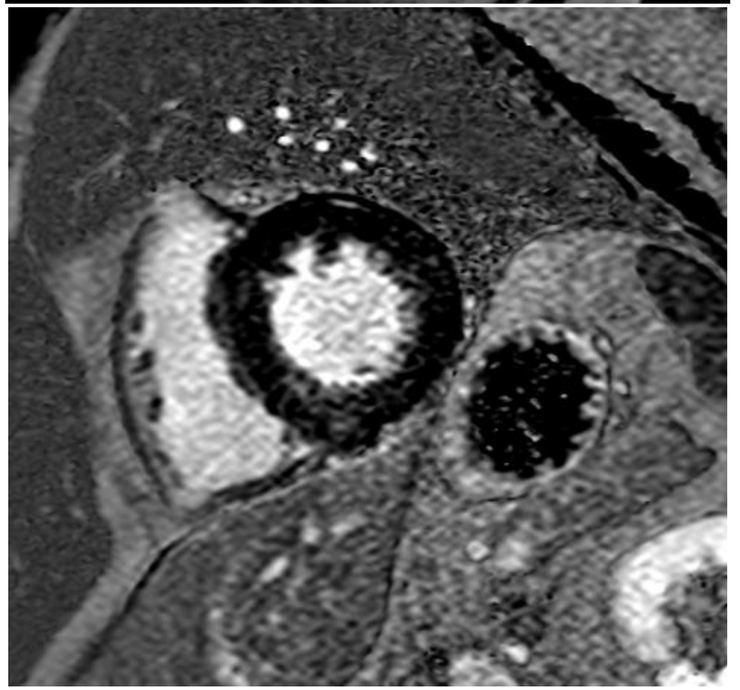
MR 2013







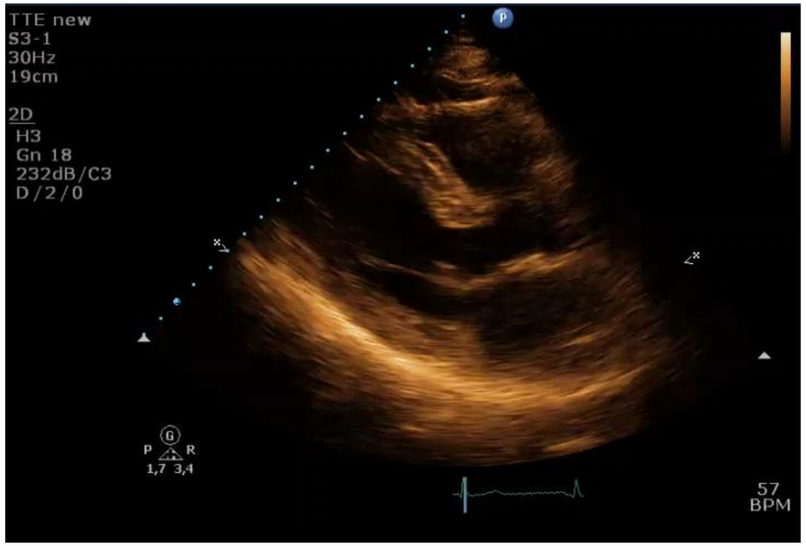


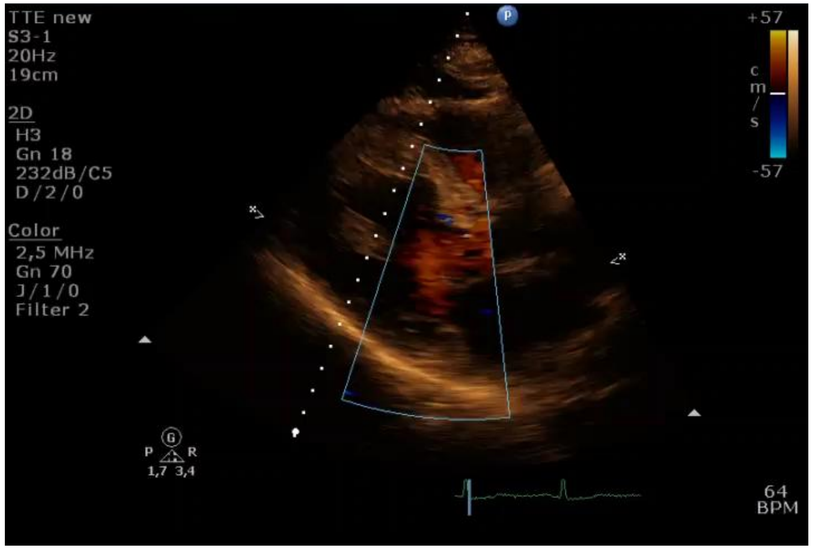


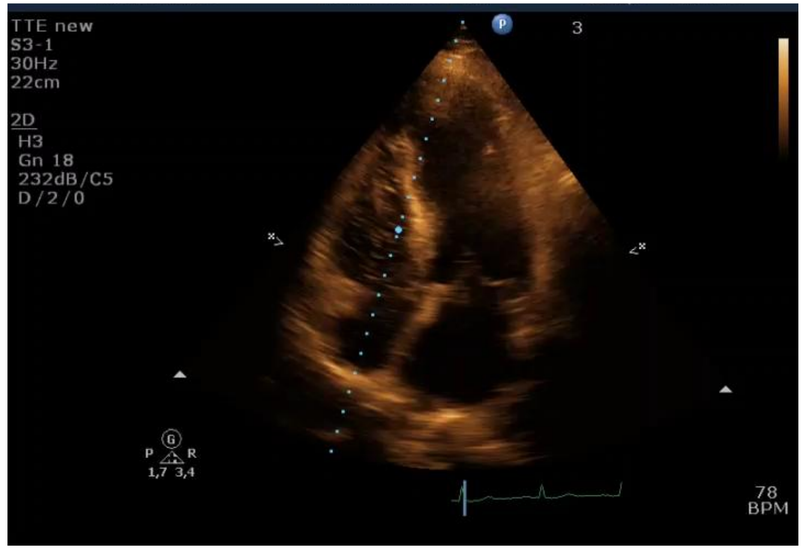
EF LK 70-80%

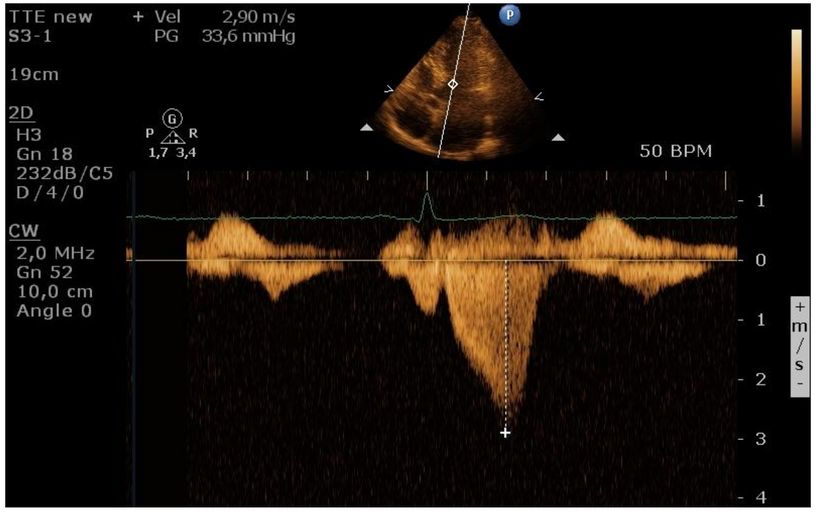
EDV 190 ml

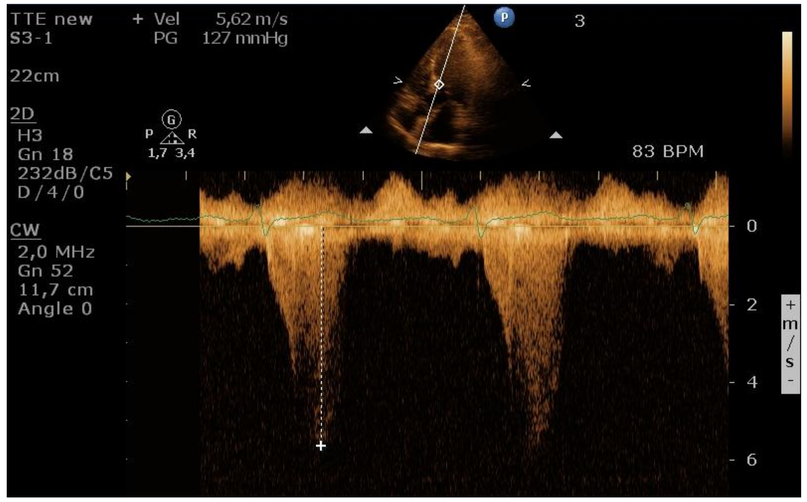
maxim.hypertrofie 18 mm





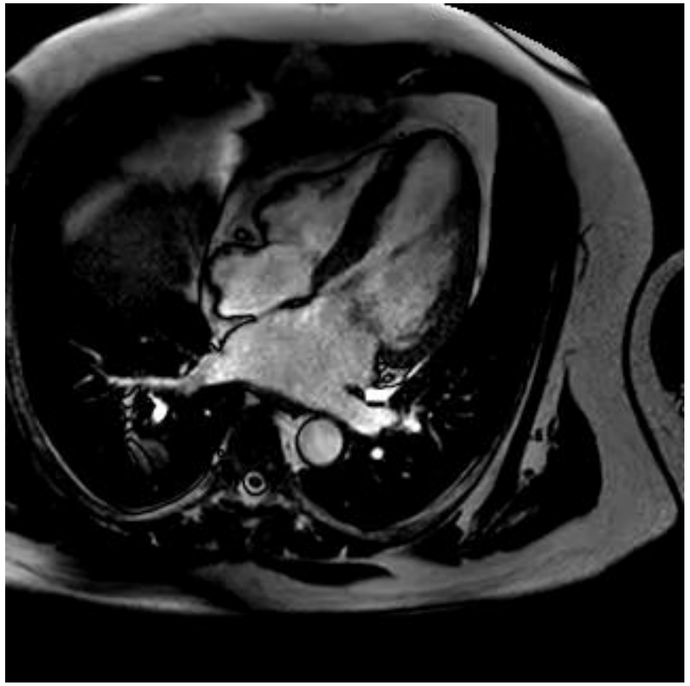


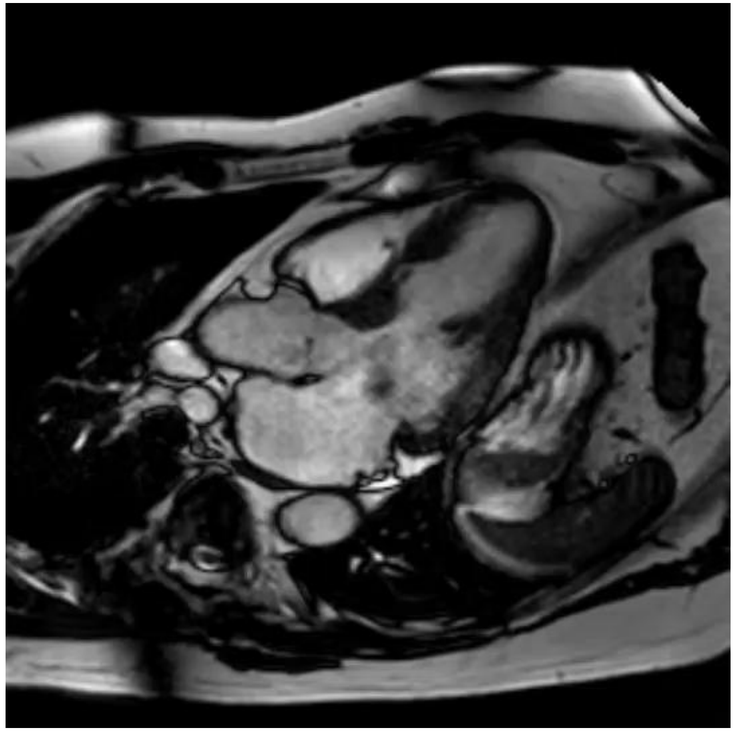


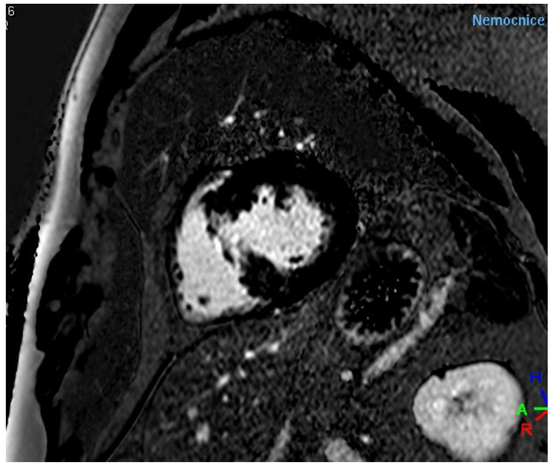


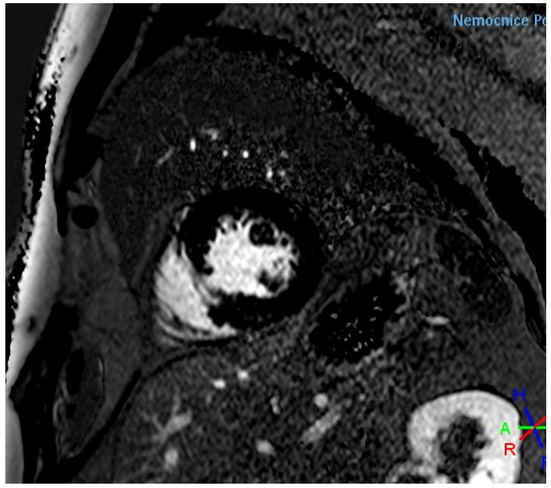
- 7/2013 provedena ASA 2. septální větve RIA

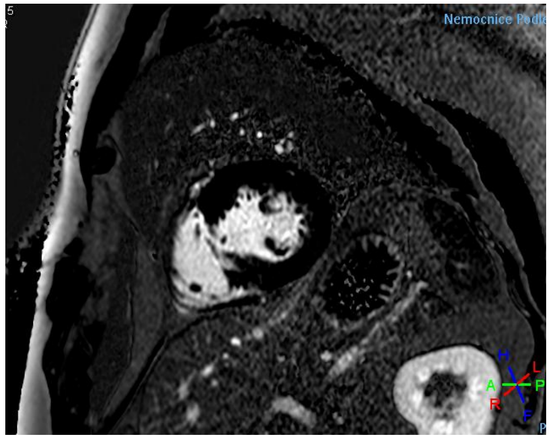
MR 2017











EF LK 76%

EDV 183 ml

Popis případu

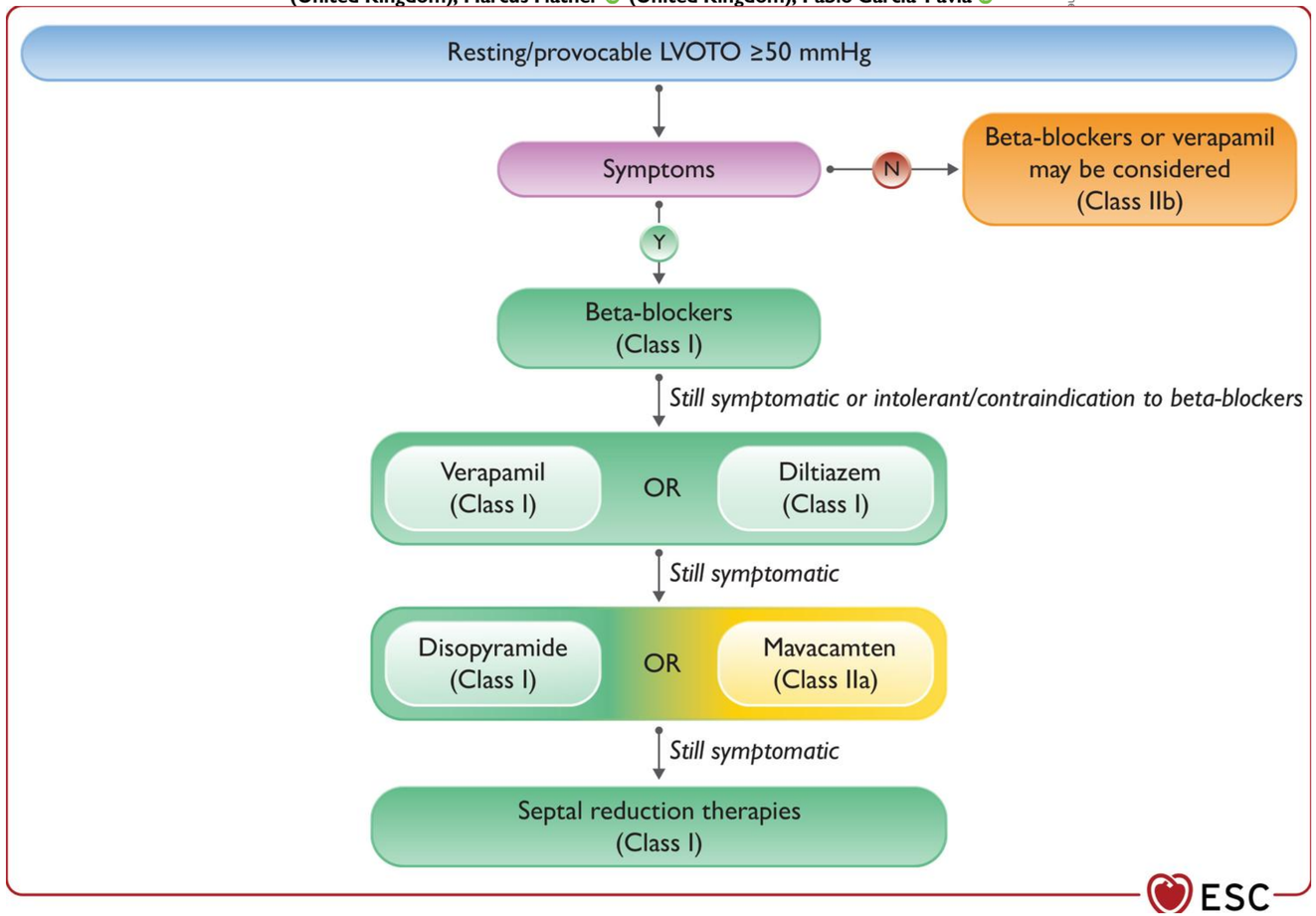
- pacient na maximální tolerované dávce betablokátoru (20 mg bisoprolol), symptomy NYHA II-III…indikován k terapii mavakamtenem
- genetické vyšetření na fenotyp CYP2C19 - středně rychlý metabolizátor
- 6/2024 zahájená terapie mavakamtenem 5MG denně
- ECHO kontroly 7, 8, 9, 10/2024… v 9/2024 navýšeno na 10 MG denně

ESC European Society of Cardiology
European Heart Journal (2023) **00**, 1–124
https://doi.org/10.1093/eurheartj/ehad194
ESC GUIDELINES

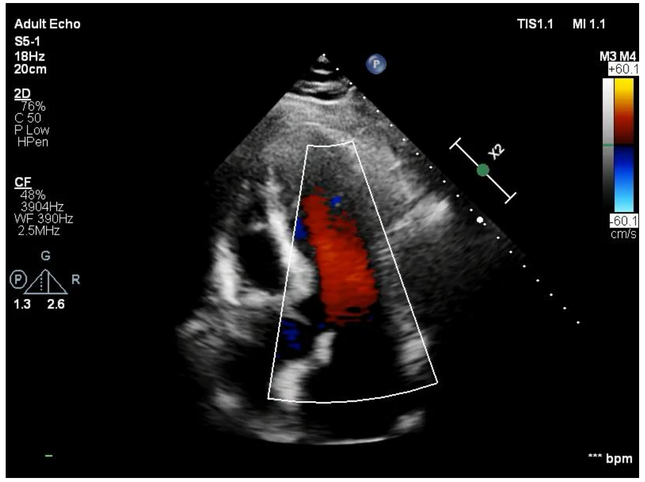
2023 ESC Guidelines for the management of cardiomyopathies

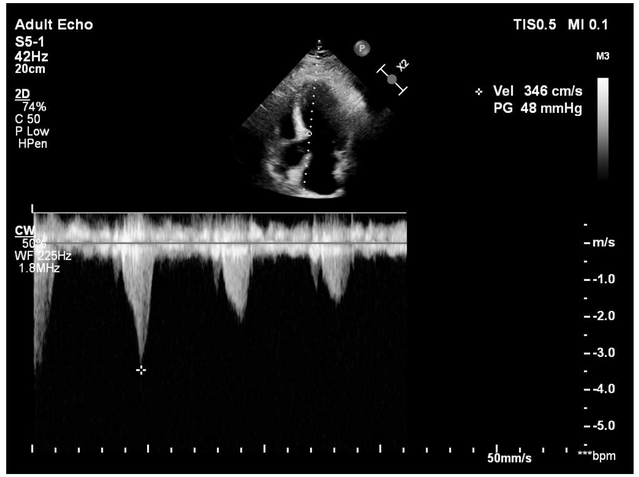
Developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC)

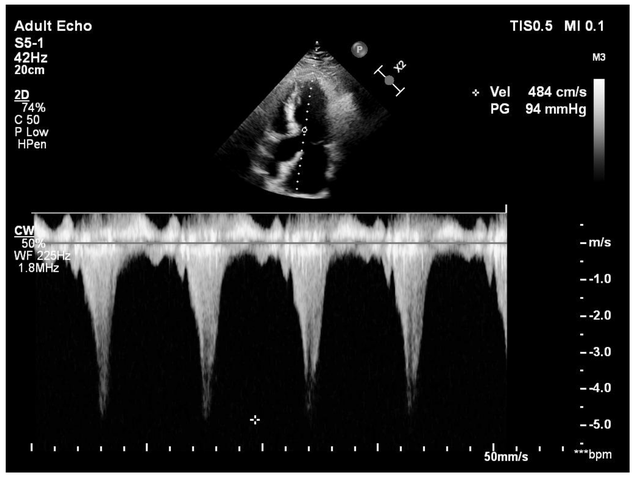
Authors/Task Force Members: Elena Arbelo *†, (Chairperson) (Spain), Alexandros Protonotarios ‡, (Task Force Co-ordinator) (United Kingdom), Juan R. Gimeno ‡, (Task Force Co-ordinator) (Spain), Eloisa Arbustini (Italy), Roberto Barriales-Villa (Spain), Cristina Basso (Italy), Connie R. Bezzina (Netherlands), Elena Biagini (Italy), Nico A. Blom[1] (Netherlands), Rudolf A. de Boer (Netherlands), Tim De Winter (Belgium), Perry M. Elliott (United Kingdom), Marcus Flather (United Kingdom), Pablo Garcia-Pavia



4TT
7/2025

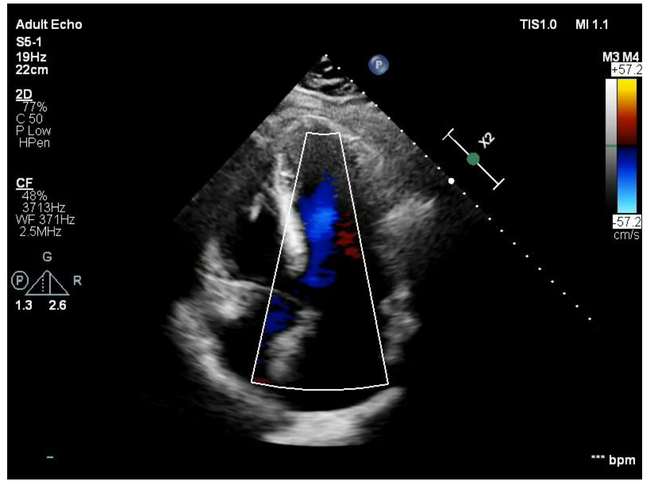


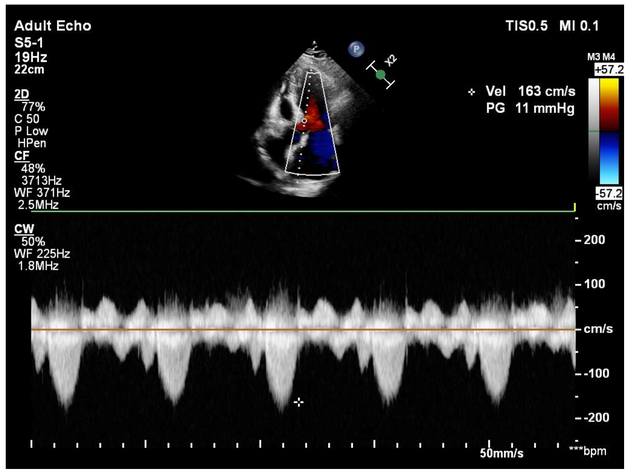


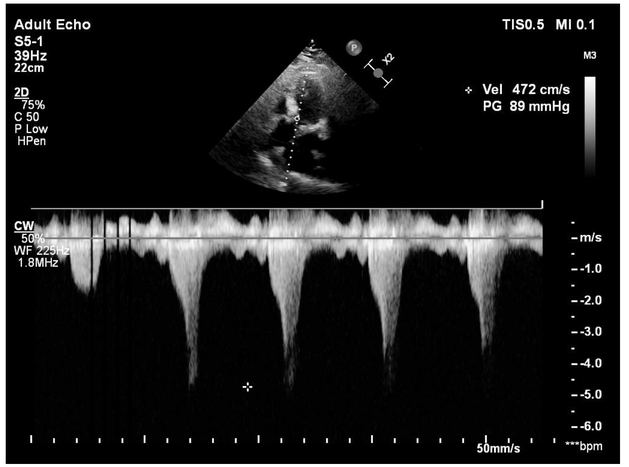


5MG

8TT
8/2025

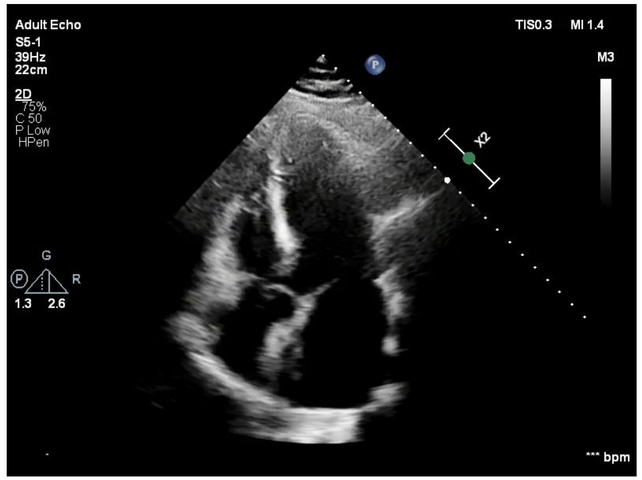


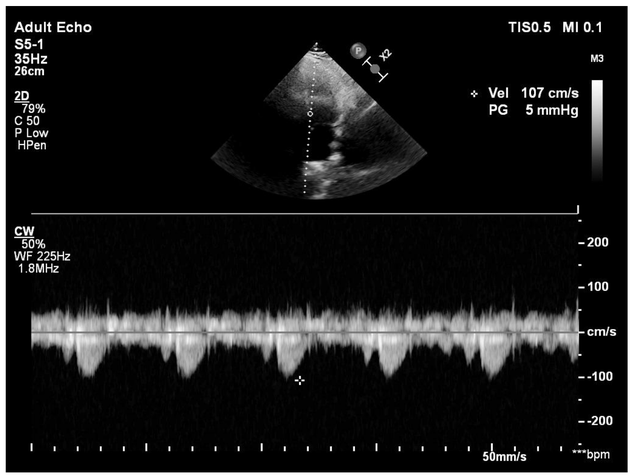


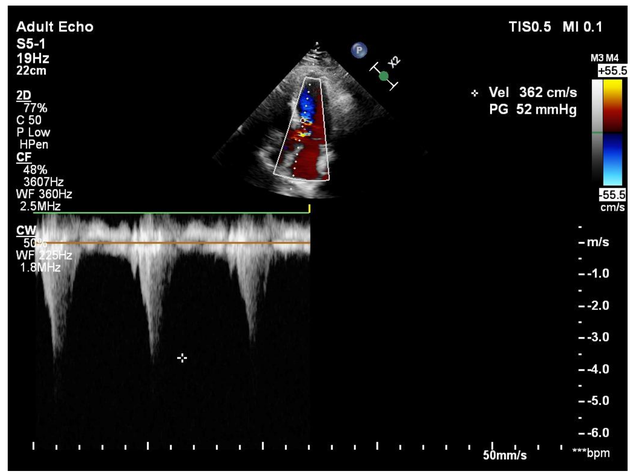


5MG

12TT
9/2025

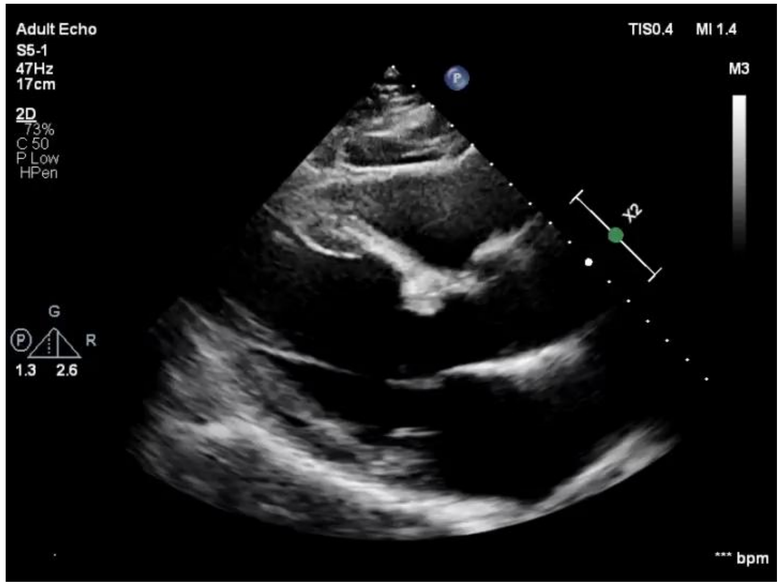


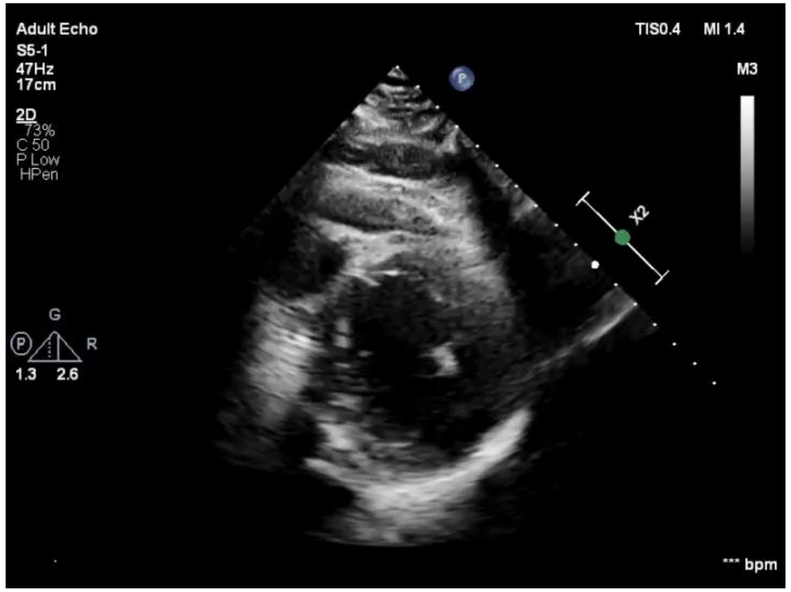


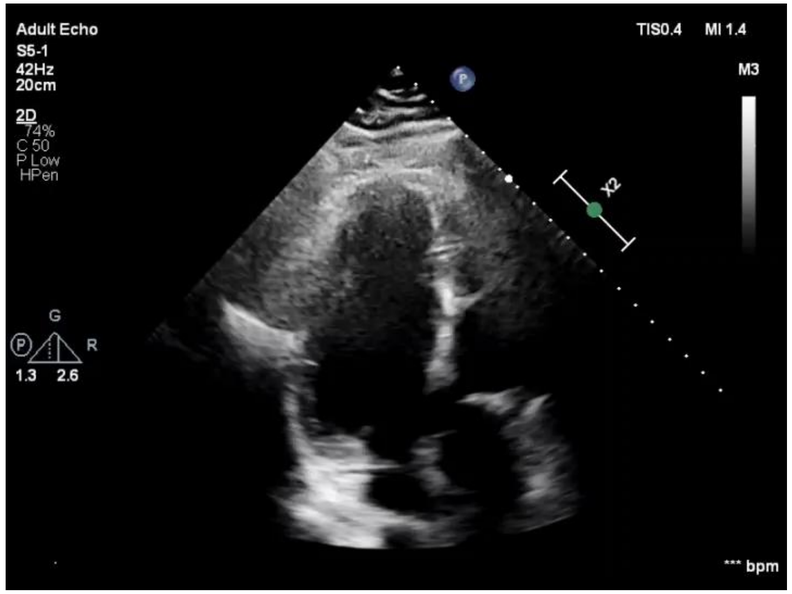


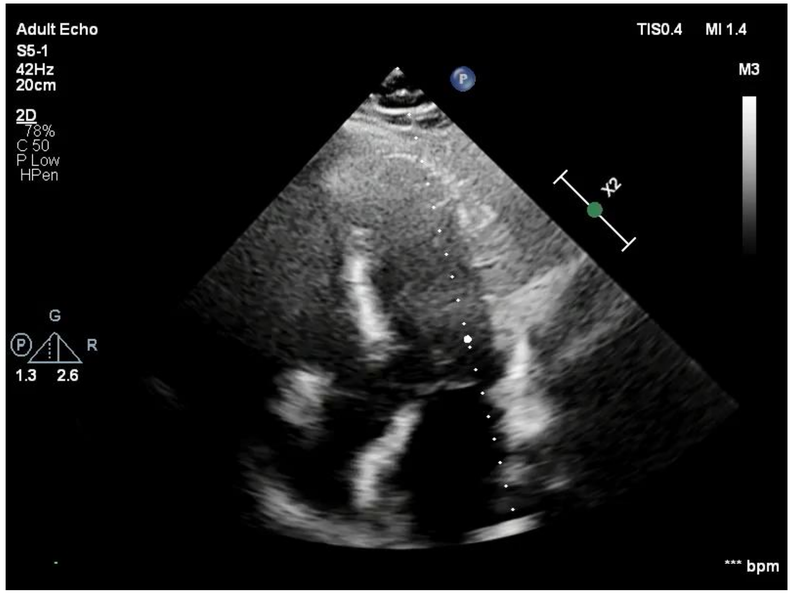
10MG

10/2025



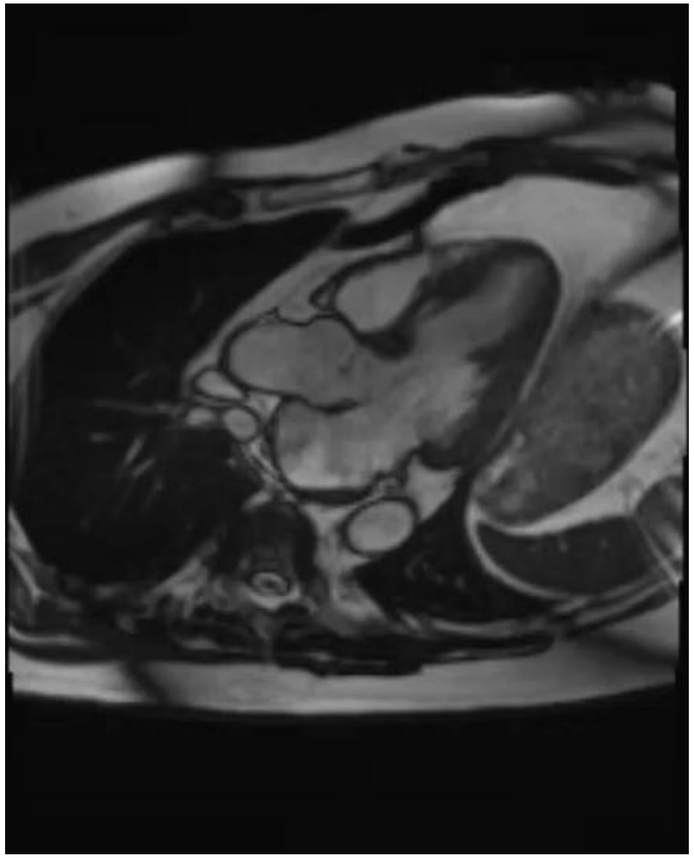


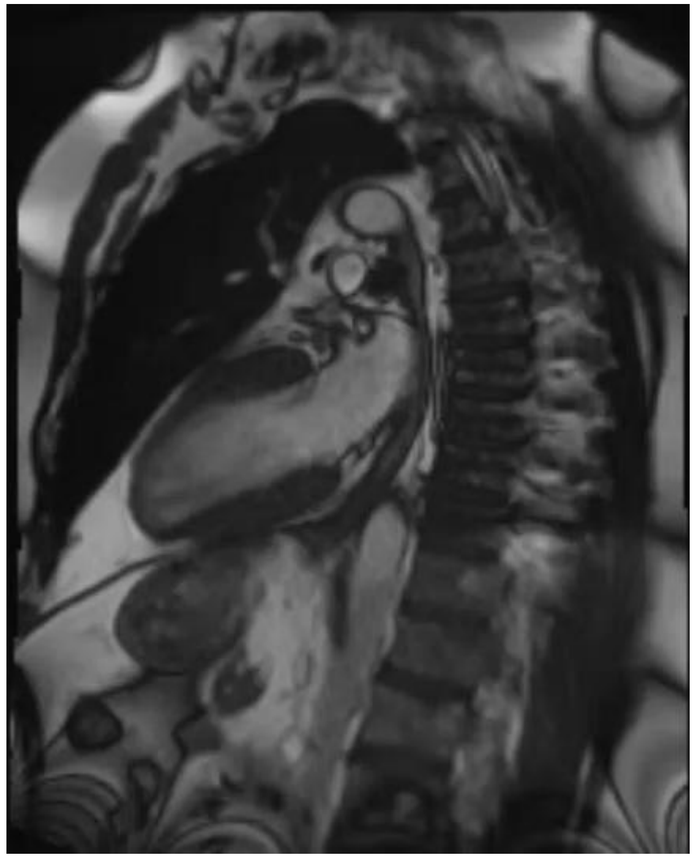


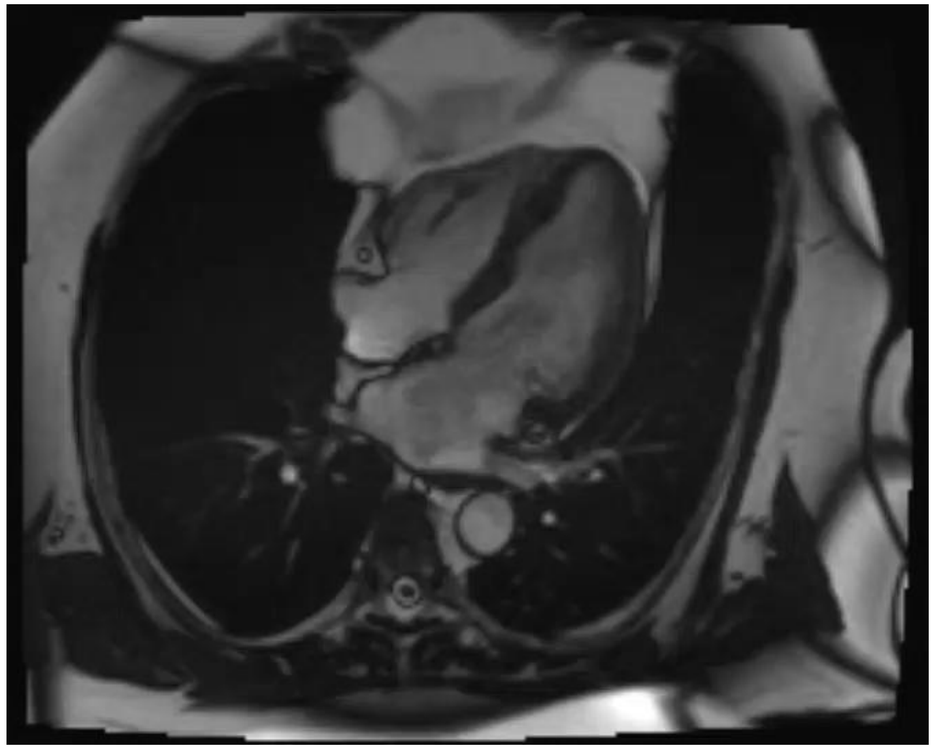


- asympt. pokles EF LK, pacient nadále NYHA I-II, lab. vzestup NT-proBNP 333 ng/L

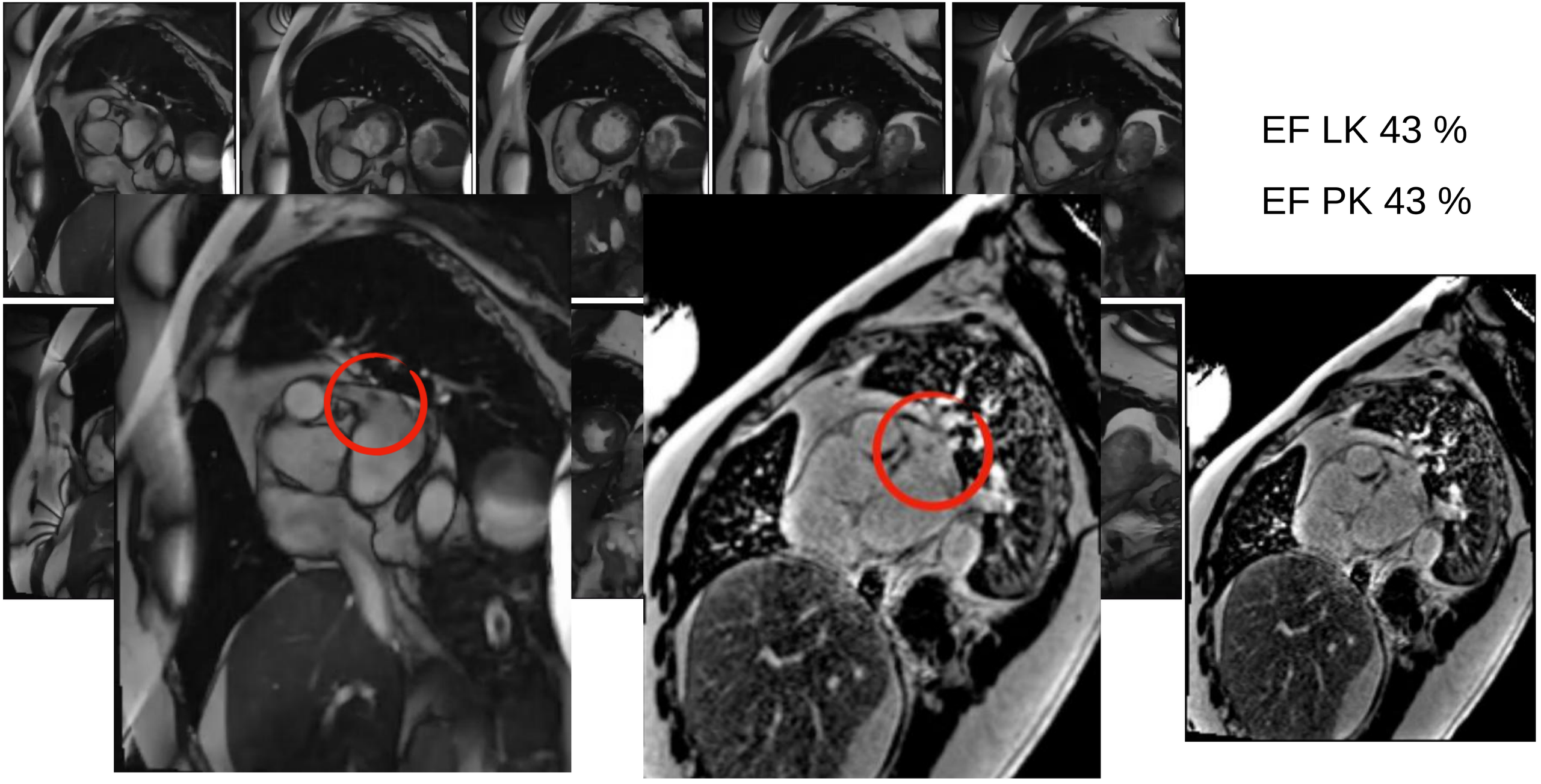
MR říjen 2024





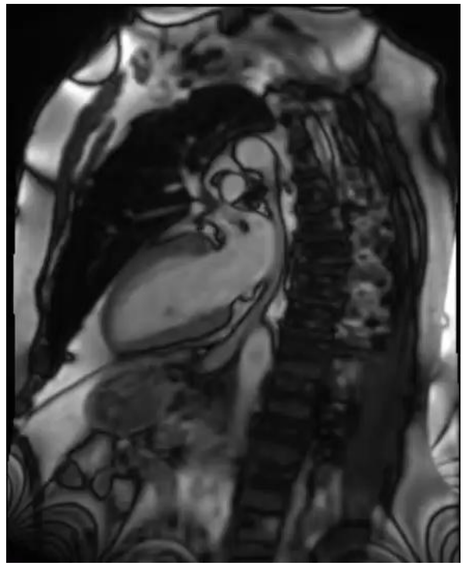
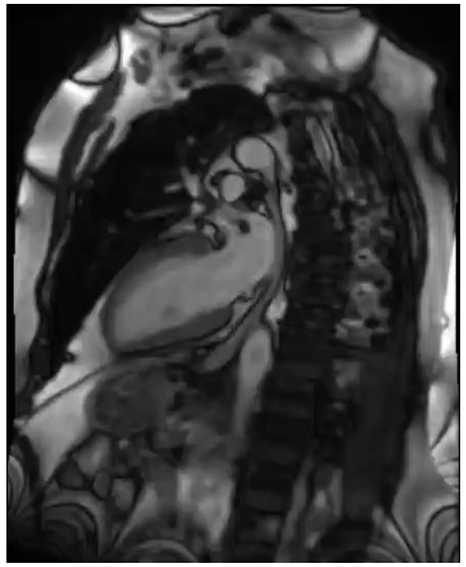
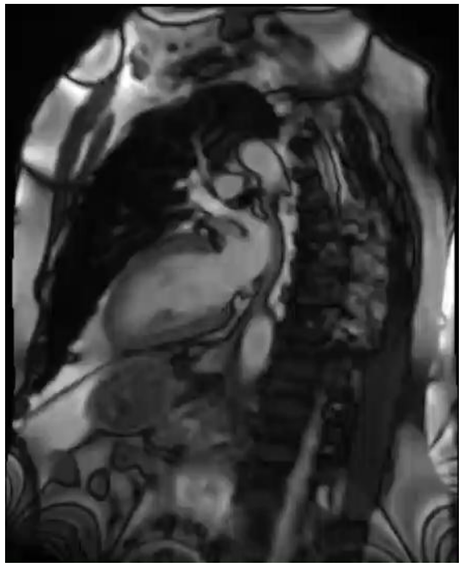
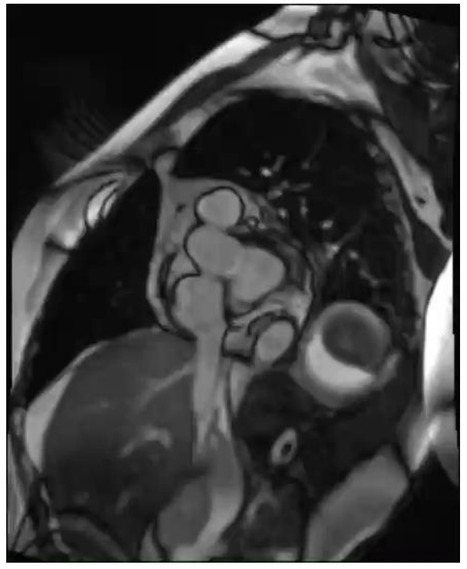
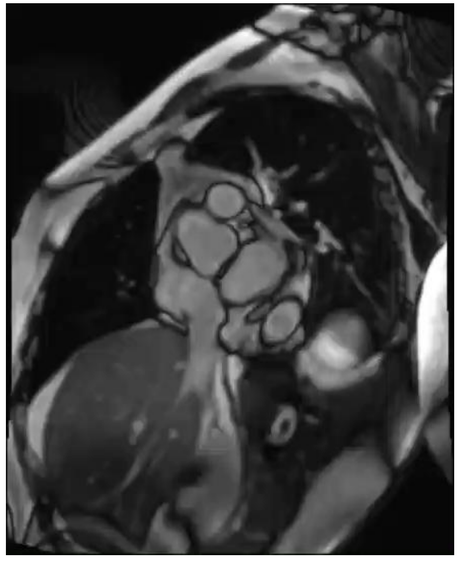
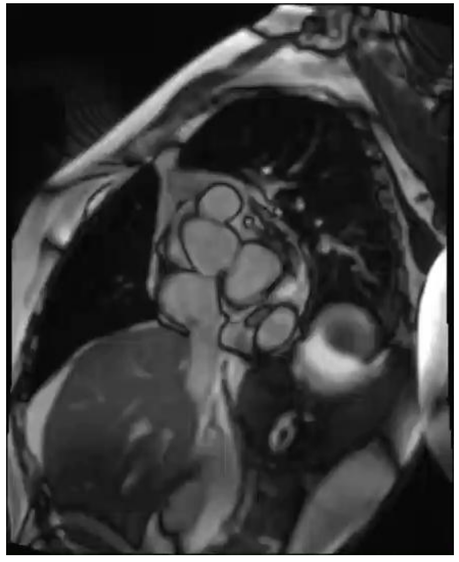


EF LK 47%, EDV 158 ml, GLS -11%



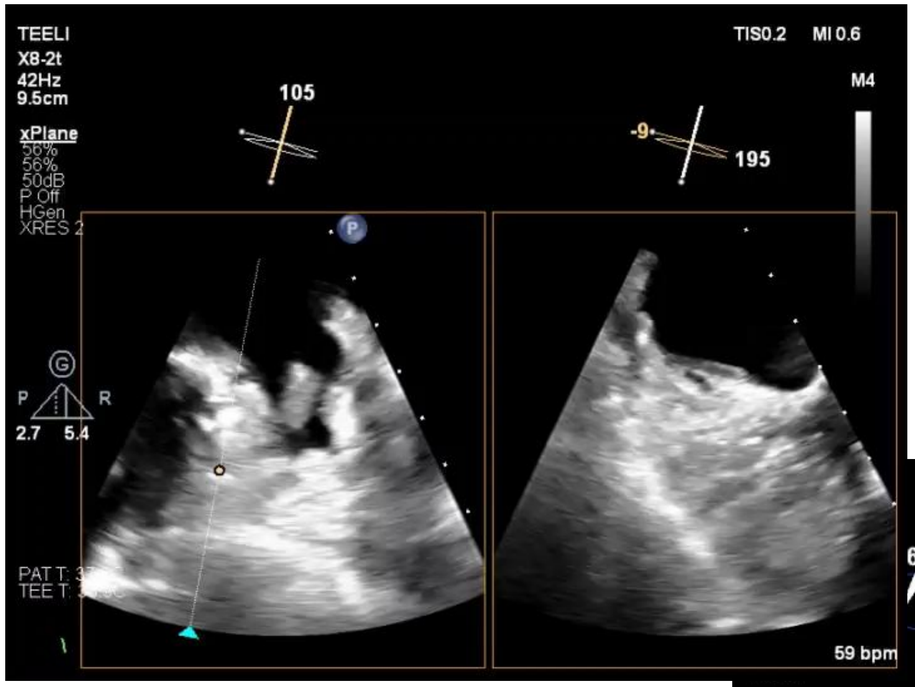
EF LK 43 %

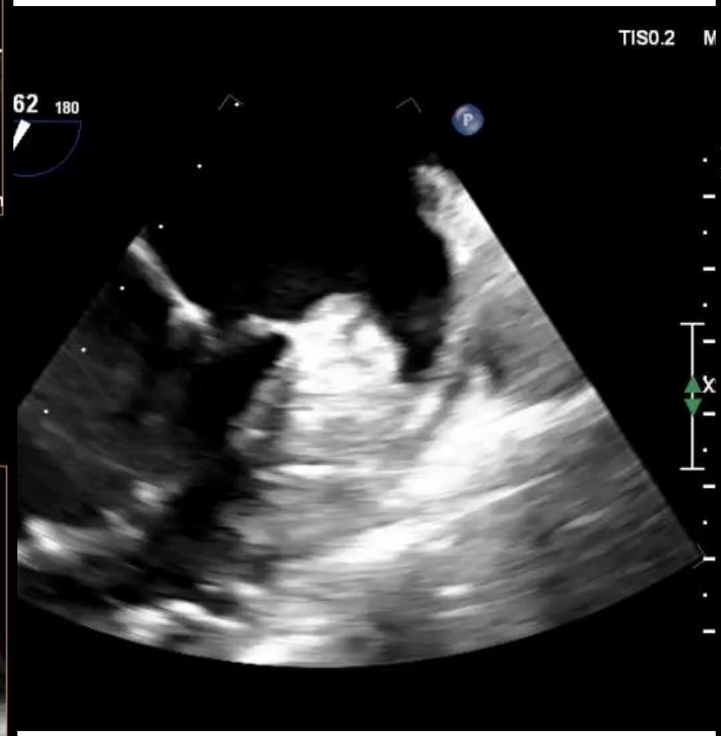
EF PK 43 %

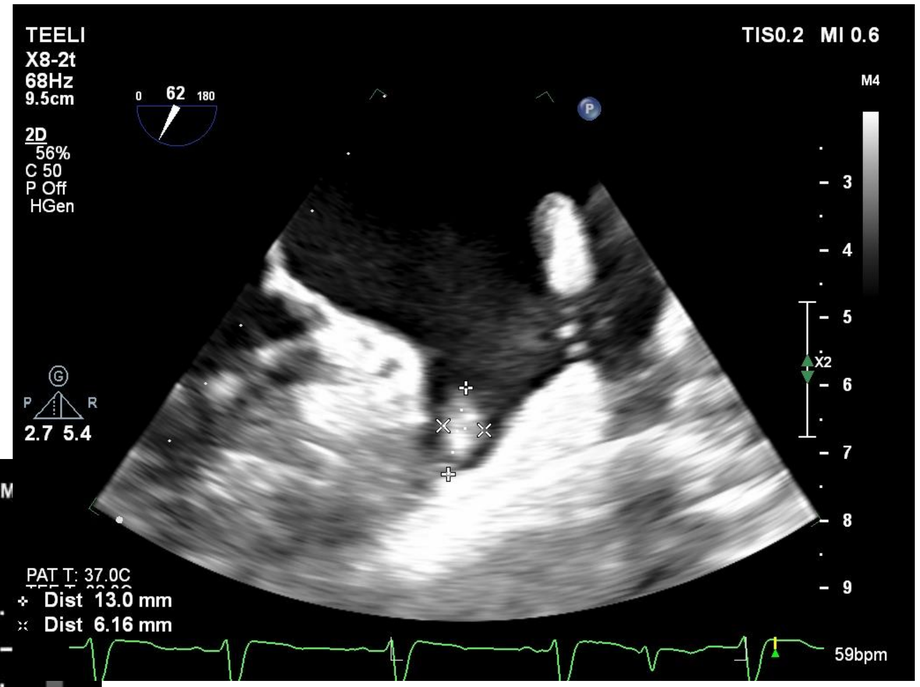







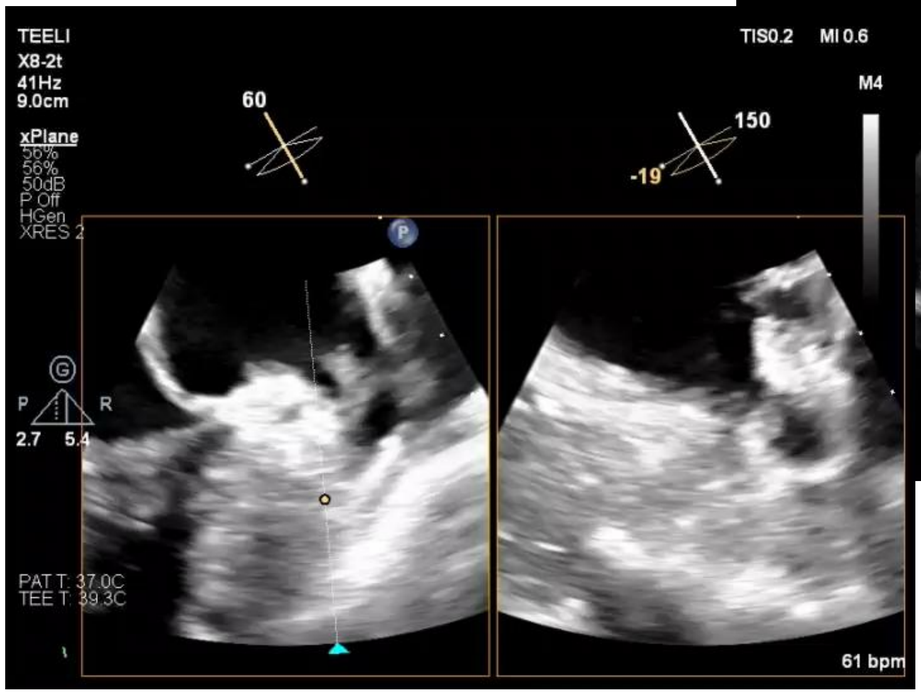
- Diagnostická rozvaha:
  - *jedná o artefakt?*
  - *trombus LAA? (ale normální kontraktilita LAA)*
  - *kontraktilita LAA je dobrá, pravděpodobnější je tumor LAA*
  - *z MR nevím, doplníme další vyšetření*

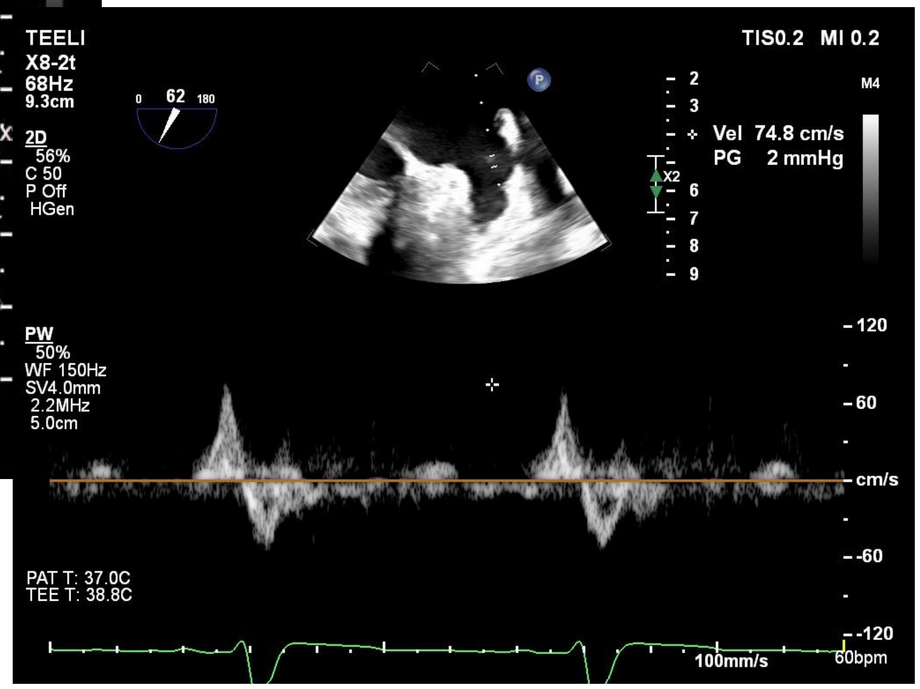
- přerušena terapie mavakamtenem
- antikoagulační léčba Xarelto 20 mg tbl. 1-0-0
- jícnové echo vyšetření
- týdenní holtrovská monitorace EKG


TEELI
X8-2t
42Hz
9.5cm
xPlane
56%
56%
50dB
P Off
HGen
XRES 2
TIS0.2 MI 0.6
M4
105
-9
195
2.7 5.4
59 bpm

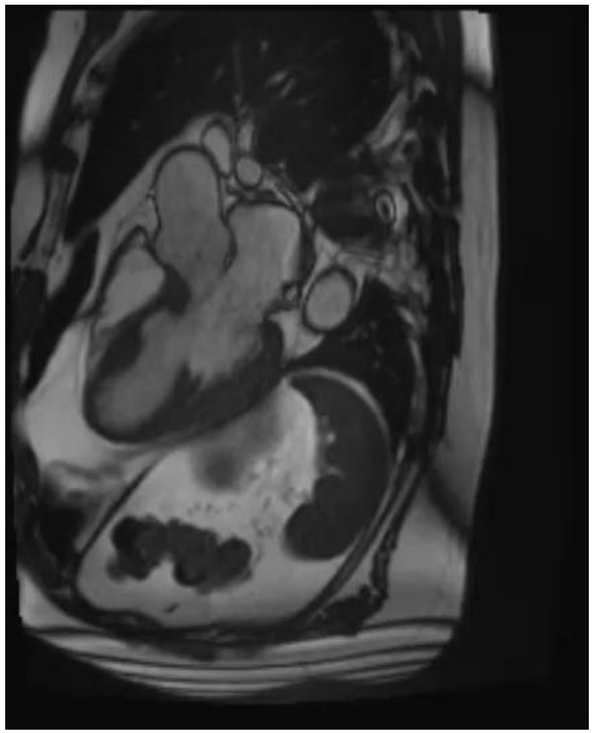

62 180

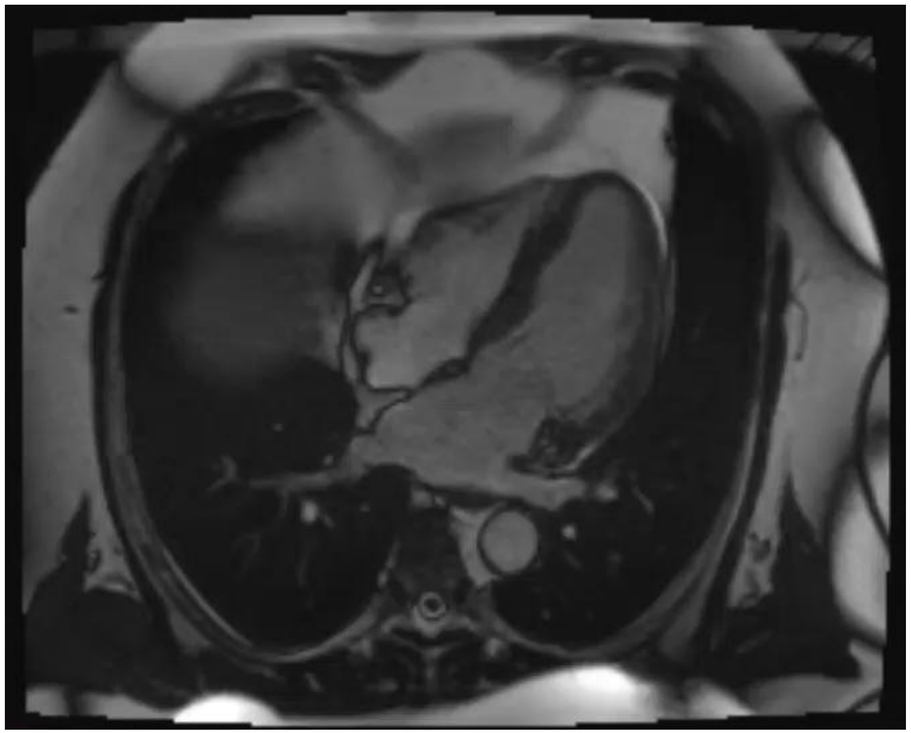

TEELI
X8-2t
68Hz
9.5cm
2D
56%
C 50
P Off
HGen
TIS0.2 MI 0.6
M4
62 180
2.7 5.4
PAT T: 37.0C
Dist 13.0 mm
Dist 6.16 mm
59bpm

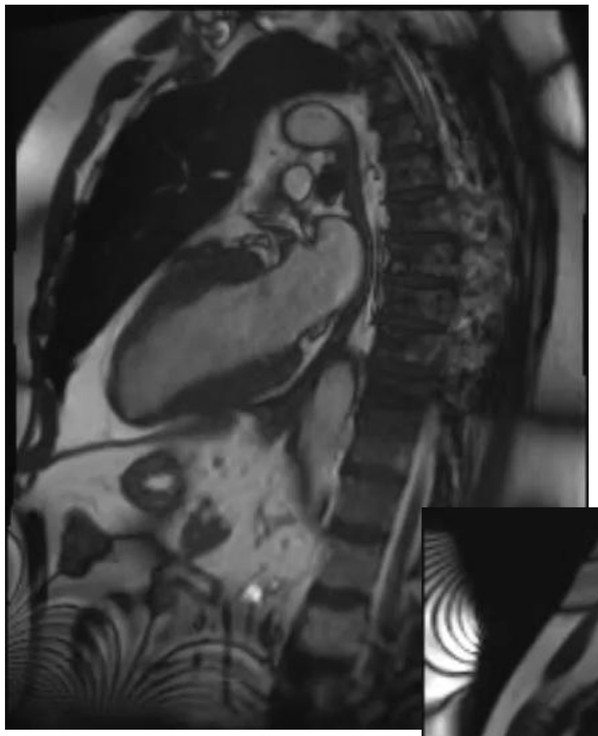

TEELI
X8-2t
41Hz
9.0cm
xPlane
56%
56%
50dB
P Off
HGen
XRES 2
TIS0.2 MI 0.6
M4
60
150
-19
2.7 5.4
PAT T: 37.0C
TEE T: 39.3C
61 bpm

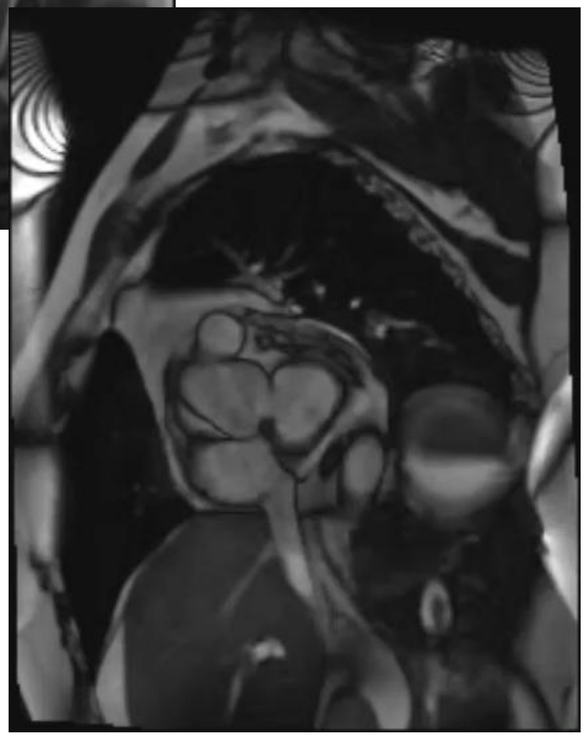

TEELI
X8-2t
68Hz
9.3cm
2D
56%
C 50
P Off
HGen
TIS0.2 MI 0.2
M4
62 180
Vel 74.8 cm/s
PG 2 mmHg
PW
50%
WF 150Hz
SV4.0mm
2.2MHz
5.0cm
cm/s
PAT T: 37.0C
TEE T: 38.8C
100mm/s
60bpm

MR 4.tt po vysazení mavakamtenu (bez k.l.)









EF LK 60 %

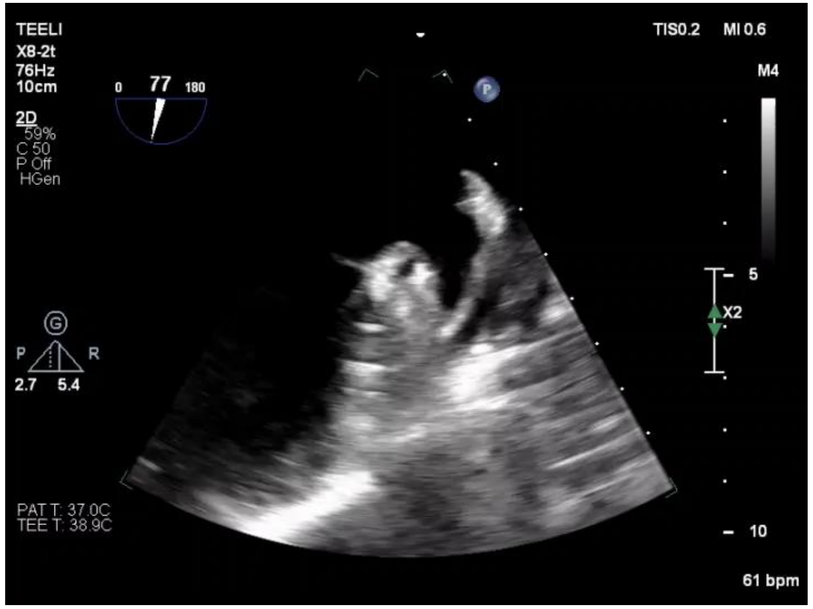
GLS -16%

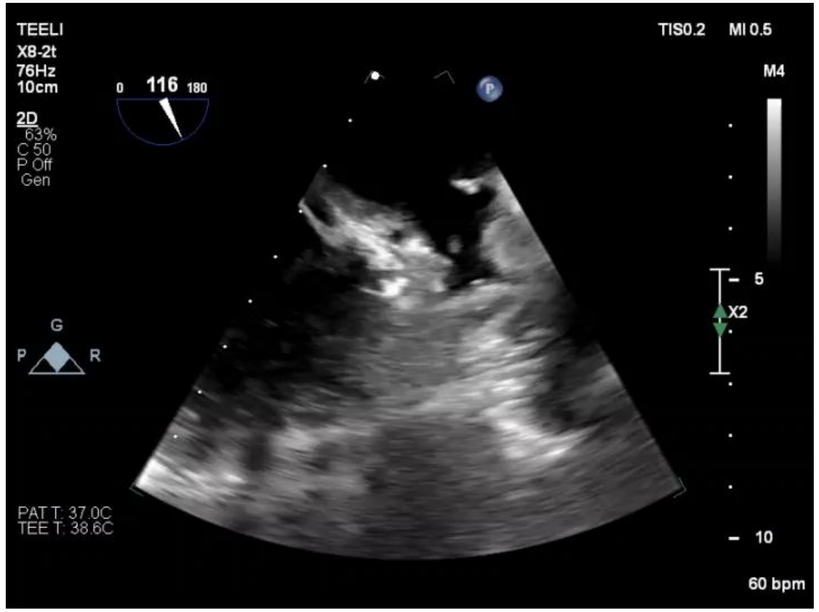
EF LS 47 %

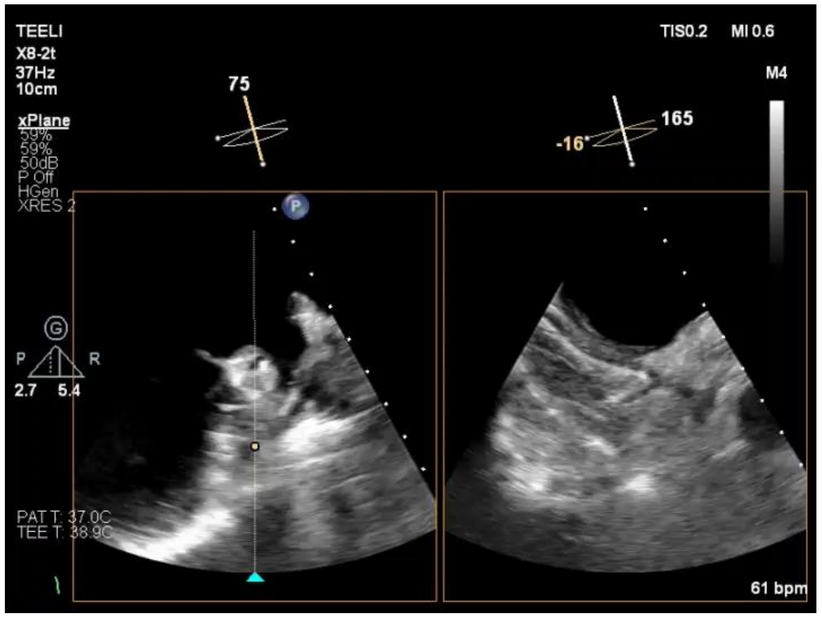
EF LK 47 %

GLS -11%

EF LS 37 %

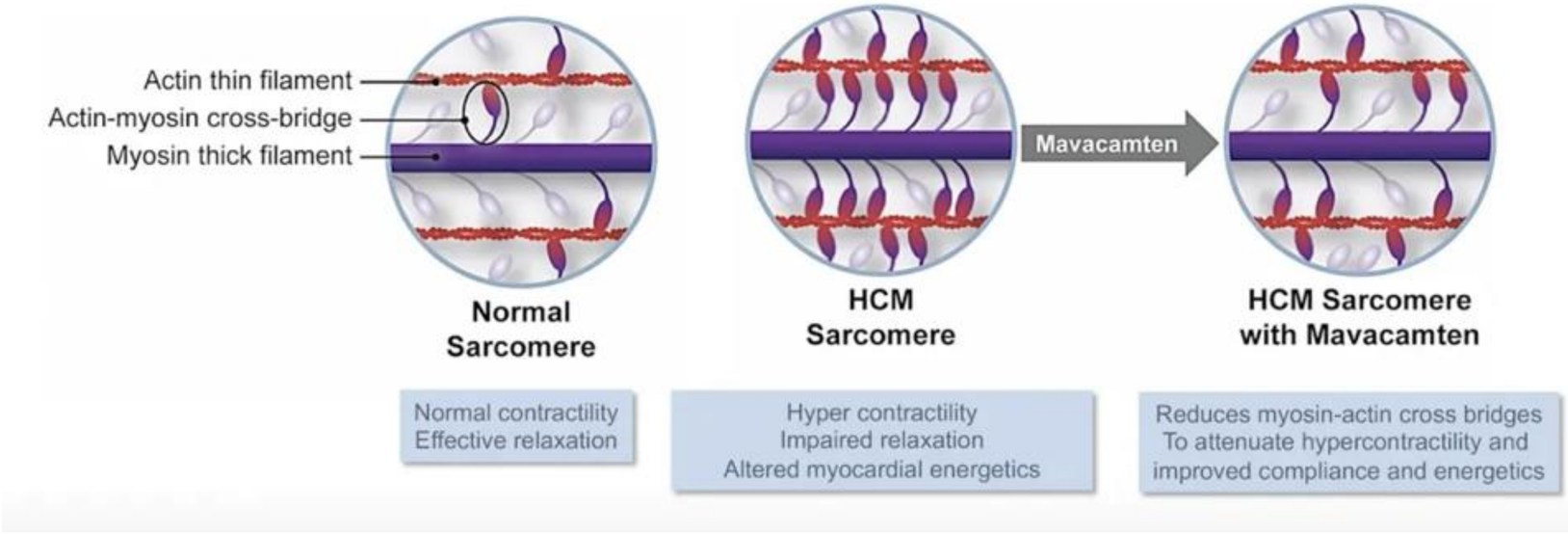






- po vysazení mavakamtenu subj. opět progrese potíží, nárůst gradientů v LVOT+ SAM
- po úpravě EF LK v 11/2025 znovu nasazen mavacamten 5 MG denně
- pacient subjektivně zlepšen NYHA I-II, NT-proBNP 94 ng/L
- holtrovská monitorace včetně týdení bez průkazu FS, antikoagulační léčba ponechána

Mavakamten



- reverzibilní inhibitor srdečního beta- myozinu
- v RCTs významně redukoval symptomy a LVOTO, zlepšoval toleranci zátěže a redukoval potřebu septální redukční terapie
- má prokazatelný vliv na pozitivní remodelaci LK
- dávkování a titrace se řídí fenotypem CYP2C19 a následnými ECHO kontrolami na funkci LK a klidové a provokované gradienty v LVOT (intervaly 4, 8, 12 tt.)
- při poklesu EF LK pod 50 % má být léčba přerušena

JACC: CARDIOVASCULAR IMAGING VOL. 18, NO. 3, 2025

ORIGINAL RESEARCH

Mavacamten-Associated Temporal Changes in Left Atrial Function in Obstructive HCM

Insights From the VALOR-HCM Trial

Milind Y. Desai, MD, MBA,[a,b,c] Yuichiro Okushi, MD,[a,b] Kathy Wolski, MPH,[c] Jeffrey B. Geske, MD,[d] Anjali Owens, MD,[e] Sara Saberi, MD, MS,[f] Andrew Wang, MD,[g] Paul C. Cremer, MD, MS,[c] Mark Sherrid, MD,[h] Neal K. Lakdawala, MD,[i] Albree Tower-Rader, MD,[i] David Fermin, MD,[j] Srihari S. Naidu, MD,[k] Kathy L. Lampl, MD,[l] Amy J. Sehnert, MD,[l] Steven E. Nissen, MD,[b,c] Zoran B. Popovic, MD, PhD,[a,b,c] the VALOR-HCM Investigators

ABSTRACT

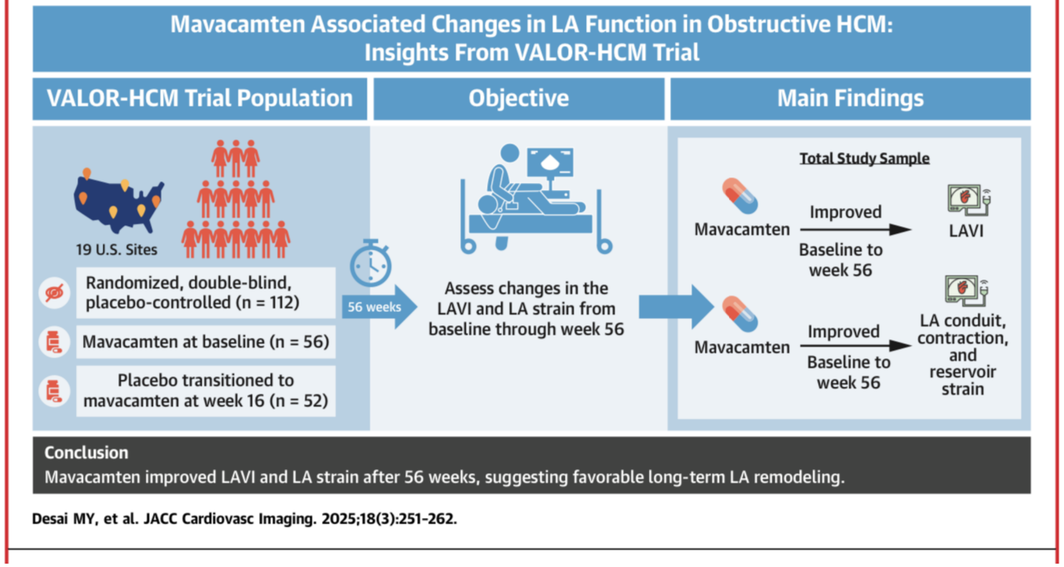
BACKGROUND In severely symptomatic patients with obstructive hypertrophic cardiomyopathy (HCM), the VALOR-HCM (A Study to Evaluate Mavacamten in Adults With Symptomatic Obstructive Hypertrophic Cardiomyopathy Who Are Eligible for Septal Reduction Therapy) trial showed that mavacamten reduced the eligibility for septal reduction therapy with sustained improvement in left ventricular outflow tract gradients. Mavacamten also resulted in favorable cardiac remodeling, including improvement in biomarkers (eg, N-terminal pro-B-type natriuretic peptide and troponin T). However, the impact of mavacamten on left atrial (LA) function is unknown.

OBJECTIVES The aim of this study was to assess serial changes in LA strain measures in patients enrolled in the VALOR-HCM trial.

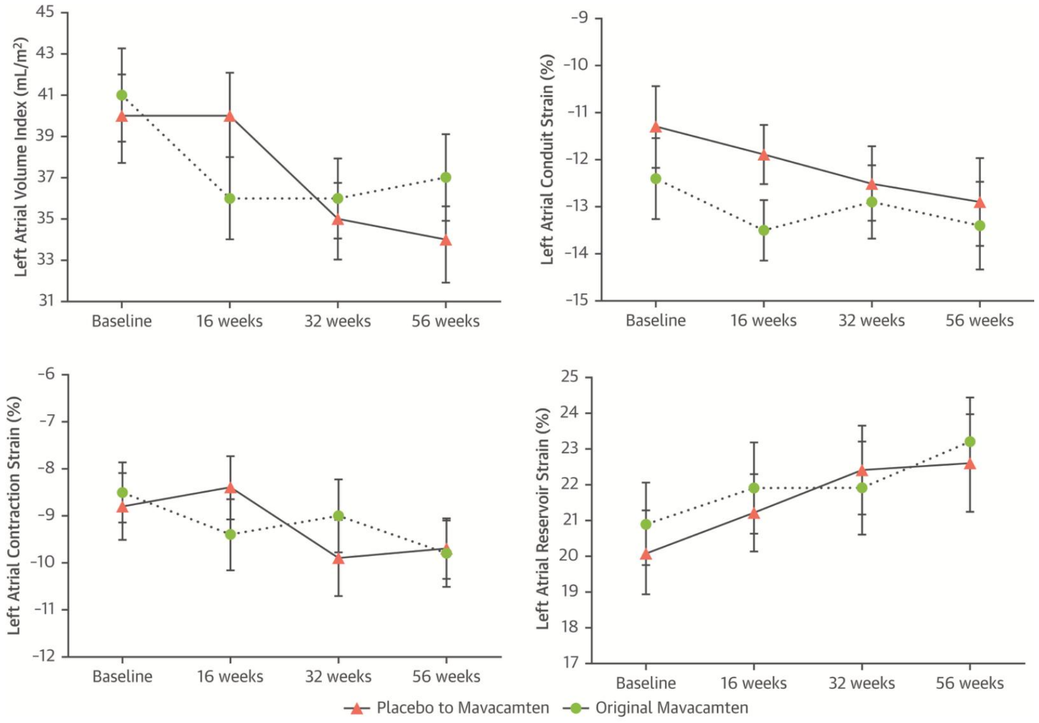
METHODS VALOR-HCM included 112 symptomatic patients with obstructive HCM (mean age 60 years; 51% male). Patients assigned to receive mavacamten at baseline (n = 56) continued therapy for 56 weeks and those assigned to placebo transitioned to mavacamten (n = 52) from week 16 to week 56. Echocardiographic LA strain (reservoir, conduit, and contraction) was measured by using a vendor-neutral postprocessing software.

RESULTS At baseline, the mean LA volume index (LAVI) and LA strain values (conduit, contraction, and reservoir) were 41.3 ± 16.5 mL/m^2, −11.8% ± 6.5%, −8.7% ± 5.0%, and 20.5% ± 8.7%, respectively (all worse than reported normal). LAVI significantly improved by −5.6 ± 9.7 mL/m^2 from baseline to week 56 ($P < 0.001$). There was a significant ($P < 0.05$) improvement in absolute LA strain values from baseline to week 56 (conduit [−1.7% ± 6%], contraction [−1.2% ± 4.5%], and reservoir [2.8% ± 7.7%]). Patients originally receiving placebo had no differences in LA measurements up to week 16. There was no significant improvement in LA strain values (conduit [−0.9% ± 3.8%], contraction [−0.4% ± 3.4%], and reservoir [1.4% ± 6.1%]; all; P = not significant) from baseline to week 56 in patients with history of atrial fibrillation.

CENTRAL ILLUSTRATION Graphical Details of the Current Study



Desai MY, et al. JACC Cardiovasc Imaging. 2025;18(3):251-262.



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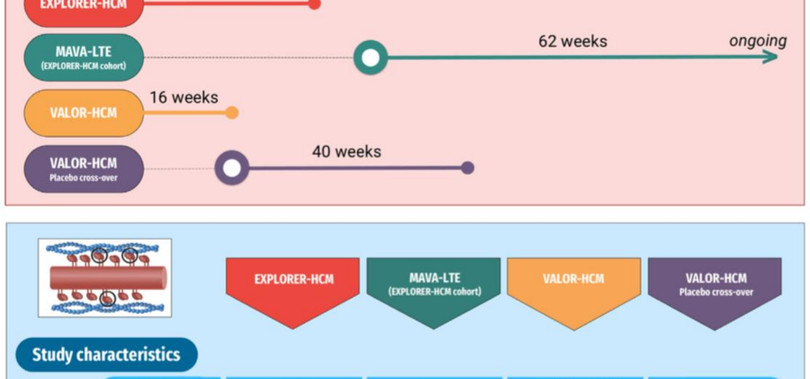
EDITORIAL COMMENT

Mavacamten

Practical Answers for the Clinician and New Questions From the MAVA–Long-Term Extension Study*

Enrico Ammirati, MD, PhD,[a,b] Guglielmo Gallone, MD[c,d]

FIGURE 1 Safety and Efficacy of Mavacamten in Obstructive Hypertrophic Cardiomyopathy



	EXPLORER-HCM	MAVA-LTE (EXPLORER-HCM cohort)	VALOR-HCM	VALOR-HCM Placebo cross-over
Study characteristics				
Population	NYHA II-III oHCM pts	EXPLORER-HCM pts	SRT guideline-eligible oHCM patients	VALOR-HCM pts
Design	Double-blind placebo-controlled RCT	Single-arm dose-blinded	Double-blind placebo-controlled RCT	Placebo cross-over to active treatment
N. of patients	n=251	n=231	n=112	n=108
Efficacy				
LVOT gradient*	Mava.: -47 ± 40 mmHg Placebo: -10 ± 30 mmHg	- 35.6 ± 32.6 mmHg	Mava.: - 39.1 ± 36.5 mmHg Placebo: -1.8 ± 28.8 mmHg	- 49.4 (-61.9, -36.9) mmHg
≥1 NYHA class reduction	Mava.: 65.0% Placebo: 31.1%	67.5%	Mava.: 62.5% Placebo: 21.4%	72.6%
SRT guideline-eligible	NA	NA	Mava.: 14.3% Placebo: 69.6%	19.2%
Safety				
LVEF <50%	Mava.: 5.7% Placebo: 1.6%	5.2%	Mava.: 3.6% Placebo: 0%	9.3%
Cardiac Failure	Mava.: 1.6% Placebo: 2.3%	3.5%	Mava.: 0% Placebo: 0%	0.9%
AF/flutter	Mava.: 6.5% Placebo: 7%	9.1%	Mava.: 3.6% Placebo: 0%	2.7%

Mavacamten and LVEF: Is the Devil in the Details?

Mavacamten, by targeting hypercontractility, causes a reduction in global LV systolic function, generally to the physiologic LVEF range. Several insights on the relationship between mavacamten and LVEF can be drawn from MAVA-LTE. First, mean LVEF reduction was 7%, and the drop was evident soon (4 weeks) after treatment initiation/titration and, at the cohort level, tended to remain stable up to 84 weeks. In MAVA-LTE, 12 (5.2%) patients experienced LVEF of <50%, and the drop occurred late (>4 weeks) after the drug dose optimization phase in 75% (9 of 12) of patients, supporting the hypothesis that, although cardiac myosin inhibition may represent a substratum for systolic function impairment, additional triggers are generally required for destabilization. In this concern, 5 of 12 patients had AF/flutter at the moment of LVEF <50% documentation, raising the hypothesis that cardiac myosin inhibition might predispose to tachycardiomyopathy, and 2 of 12 patients had drug plasma concentrations above 1,000 ng/mL, and they were at target at prior and subsequent assessments, with normal LVEF. Notably, only 1 of 12 with an LVEF of <50% had clinical manifestations of cardiac failure. If, on one side, this observation suggests that transient LVEF of <50% is clinically well tolerated in the majority of oHCM patients, on the other side, it brings to attention the fact that 7 of 8 cardiac failure events occurring in MAVA-LTE manifested among patients with preserved LVEF.

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Review

From Atrial Fibrillation Management to Atrial Myopathy Assessment: The Evolving Concept of Left Atrium Disease in Hypertrophic Cardiomyopathy

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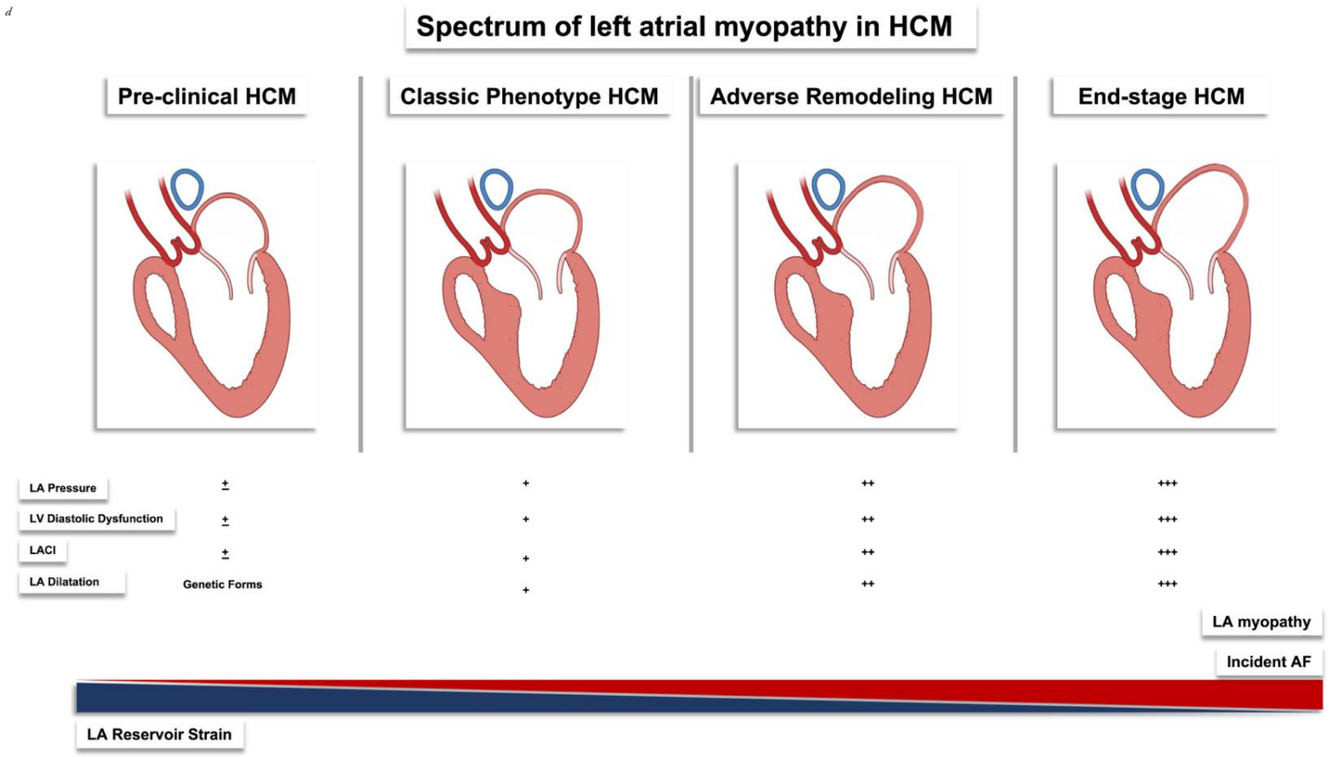
[c] *Cardiovascular Department, San Donato Hospital, Arezzo, Italy*



- incidence 2-4% ročně
- 20-25 % pacientů

HCM-AF score

Clinical variable	Range	Points
LA diameter, mm	24–29	+8
	30–35	+10
	36–41	+12
	42–47	+14
	48–53	+16
	54–59	+18
	60–65	+20
Age at clinical evaluation, y	10–19	+3
	20–29	+6
	30–39	+9
	40–49	+12
	50–59	+15
	60–69	+18
	70–79	+21
Age at HCM diagnosis, y	0–9	+0
	10–19	−2
	20–29	−4
	30–39	−6
	40–49	−8
	50–59	−10
	60–69	−12
	70–79	−14
Heart failure symptoms (Yes/no)*	Yes	+3
	No	+0

	HCM-AF score	Risk AF at 2 y, %	Risk AF at 5 y, %	No. of patients in cohort, %
Low risk (<1.0%/y)	8	0.4%	1.0%	1 (0.1%)
	9	0.5%	1.2%	14 (0.7%)
	10	0.6%	1.4%	12 (0.6%)
	11	0.7%	1.7%	22 (1.2%)
	12	0.9%	2.1%	26 (1.4%)
	13	1.0%	2.5%	42 (2.2%)
	14	1.3%	3.0%	43 (2.3%)
	15	1.5%	3.6%	80 (4.2%)
	16	1.8%	4.3%	94 (4.9%)
	17	2.2%	5.2%	108 (5.7%)
Intermediate risk (1.0%/y–2.0%/y)	18	2.6%	6.2%	181 (9.5%)
	19	3.1%	7.4%	191 (10.1%)
	20	3.8%	8.9%	186 (9.8%)
	21	4.5%	10.6%	213 (11.2%)
High risk (>2.0%/y)	22	5.4%	12.6%	169 (8.9%)
	23	6.5%	15.0%	169 (8.9%)
	24	7.8%	17.8%	99 (5.2%)
	25	9.3%	21.1%	81 (4.3%)
	26	11.1%	24.8%	51 (2.7%)
	27	13.3%	29.1%	51 (2.7%)
	28	15.7%	33.9%	29 (1.5%)
	29	18.7%	39.3%	15 (0.8%)
	30	22.0%	45.2%	11 (0.6%)
	31	25.9%	51.5%	5 (0.3%)

Carrick RT et al. Circ EP 2021

Kazuistika- závěry

- u pacienta s HOKMP jsme zaznamenali pokles EF obou komor při terapii mavakamtenem
- dokumentovali jsme přítomnost trombu v normokontraktilním oušku LS u pacienta se SR
- pokles EF LK byl asymptomatický
- na možnost trombu v LAA upozornila kontrolní MR srdce
- u pacienta dosud nebyla dokumentovaná žádná epizoda fibrilace síní

Děkuji za pozornost