Recognition and diagnosing heart failure in patients with HCM

Aleš Linhart

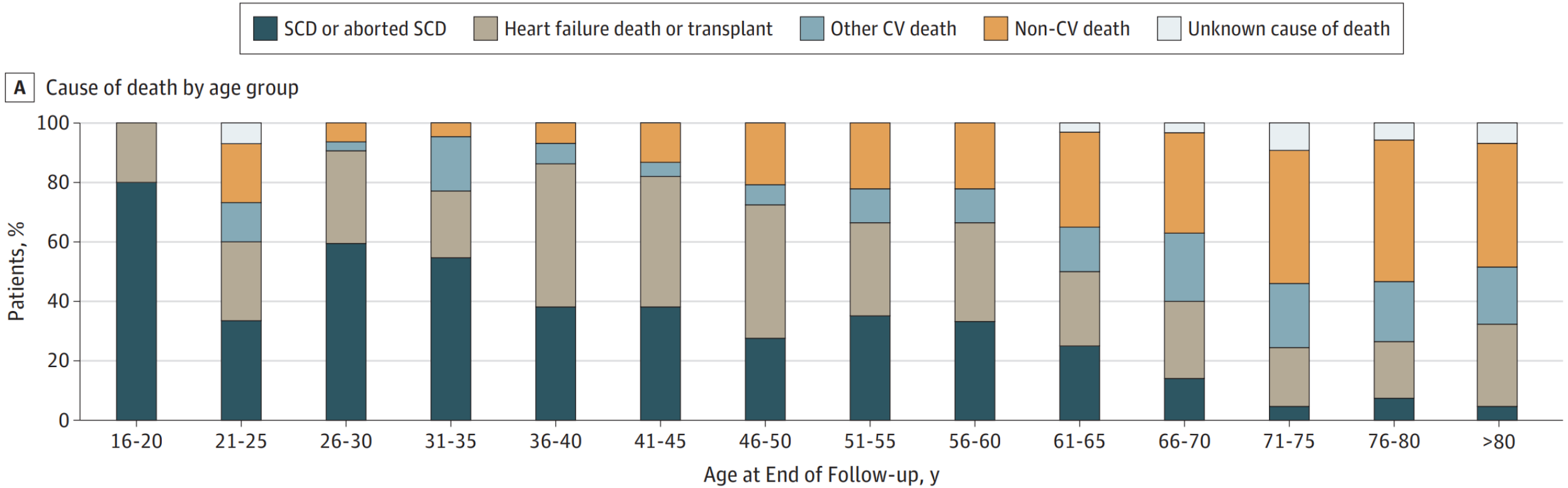
General University Hospital, Prague
First Faculty of Medicine
Charles University
Prague

Disclosures

- Consultancy and speaker´s honoraria: BMS, Chiesi, Sanofi, Novonordisk, Amicus Therapeutics, Roche

Cause of Death by Age Group

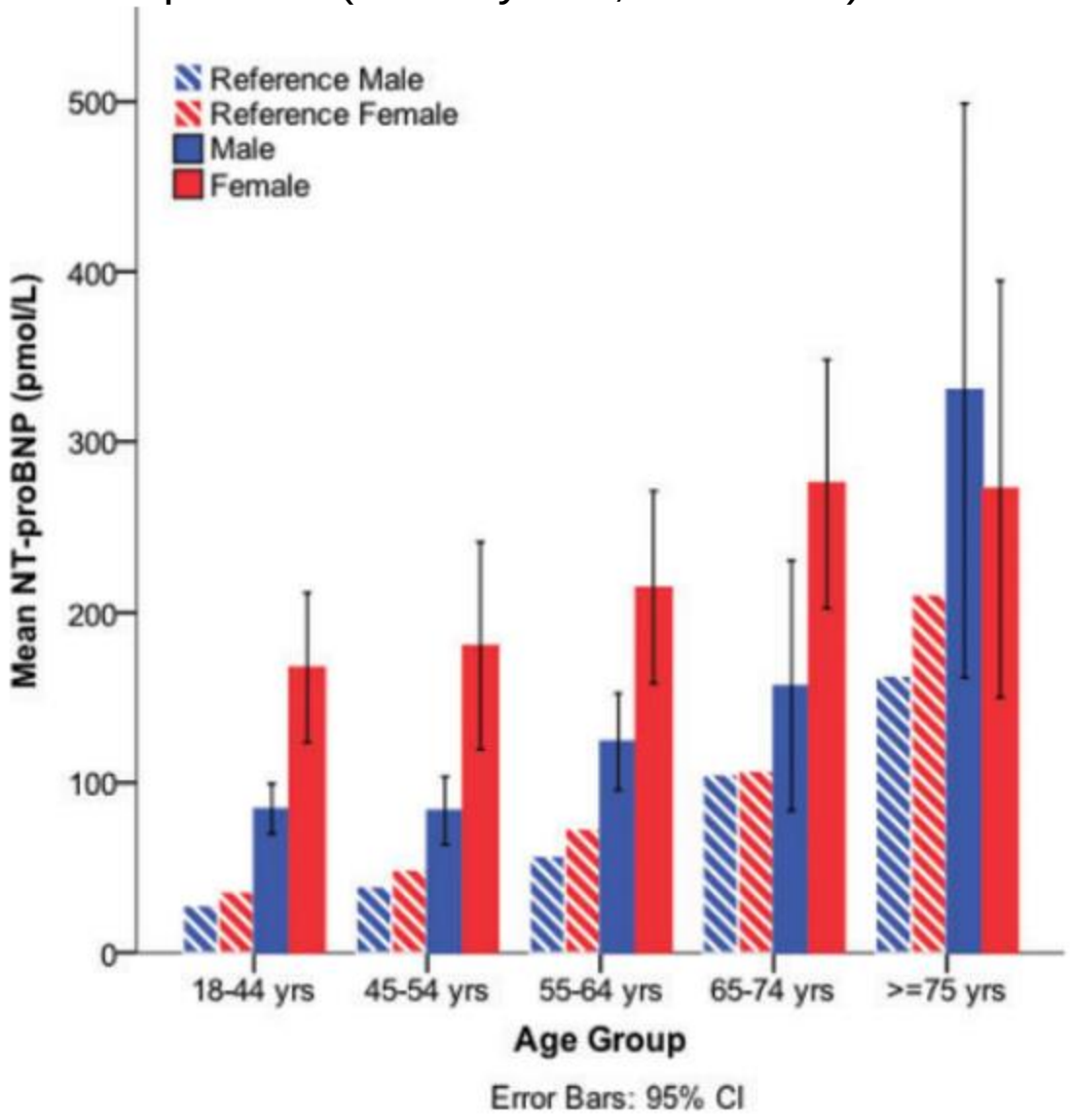
- 4893 patients with HCM, 3126 (63.9%) male,
- age at presentation was 49.2 (16.4) years
- LVOT gradient > 30 mmHg 1372/4238 (32.4)

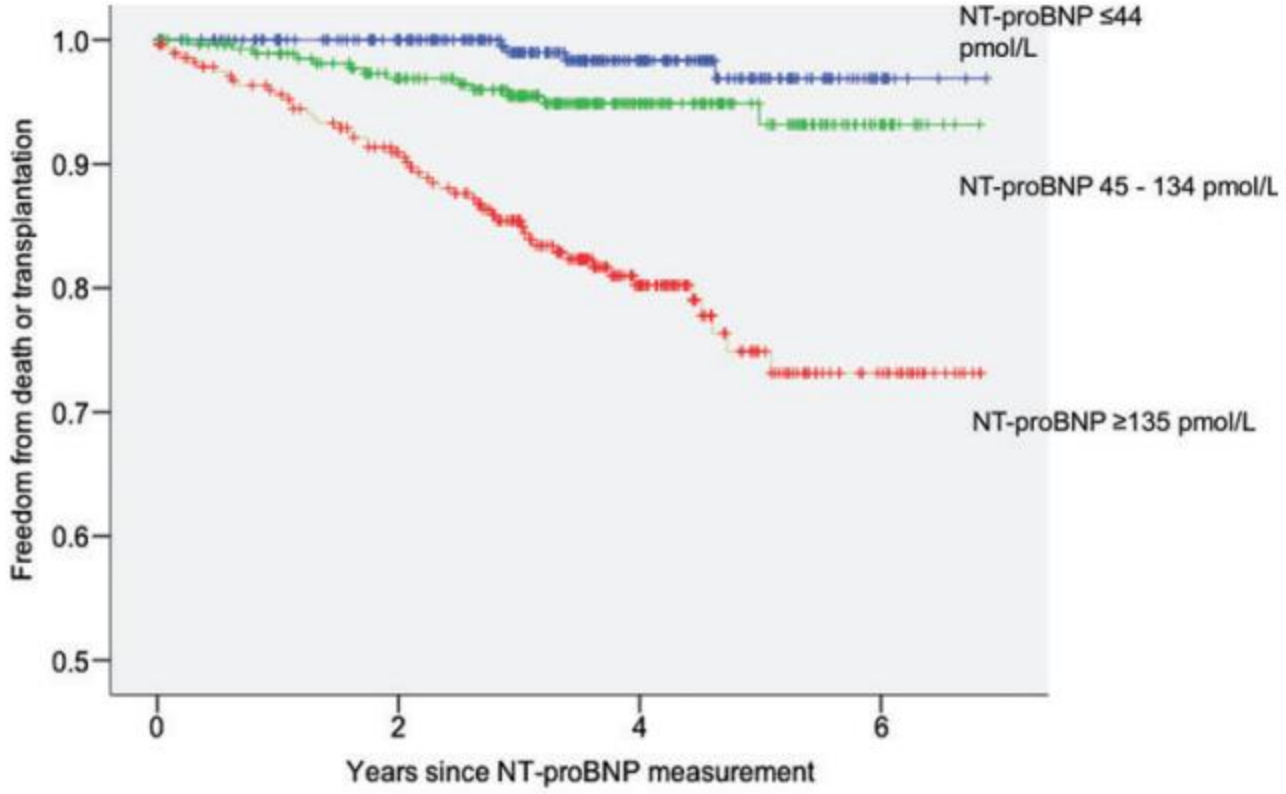


Lorenzini et al. JAMA Cardiol. 2020;5(1):73-80.

Prognostic implications of NT-proBNP in HCM

847 patients (53+15 years; 67% male) with HCM (28% with LVOTO≥30 mmHg at rest) followed for 3.5 years



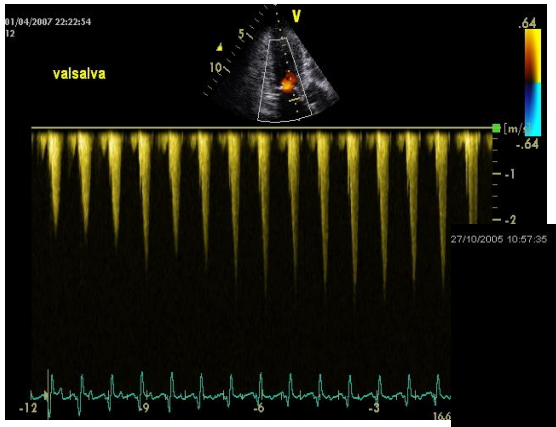


No. at risk				
NT-proBNP ≤44 pmol/L	284	238	106	11
NT-proBNP 45 - 134 pmol/L	281	229	96	16
NT-proBNP ≥135 pmol/L	282	225	100	21

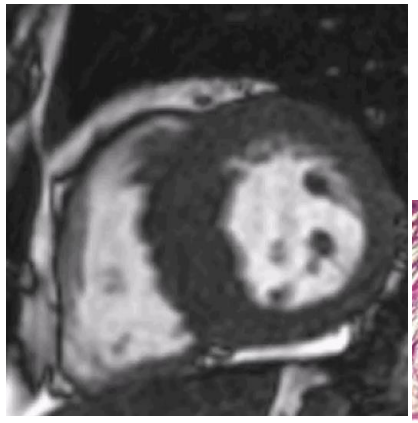
Coats C. et al. European Heart Journal (2013) 34, 2529–2537

Issues in HCM

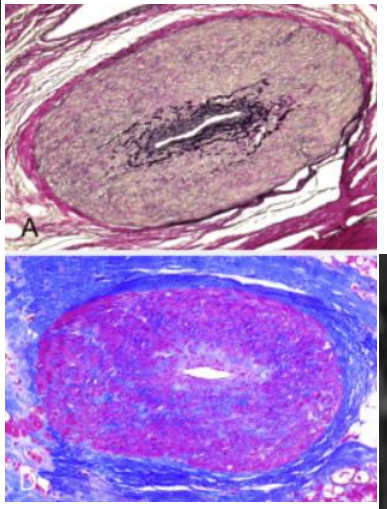
LVOTO



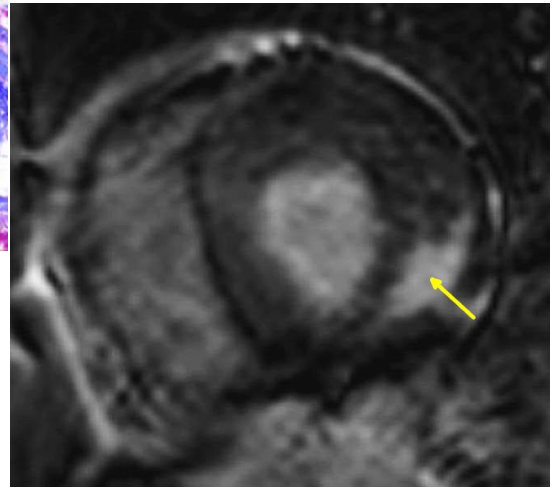
Hypertrophy



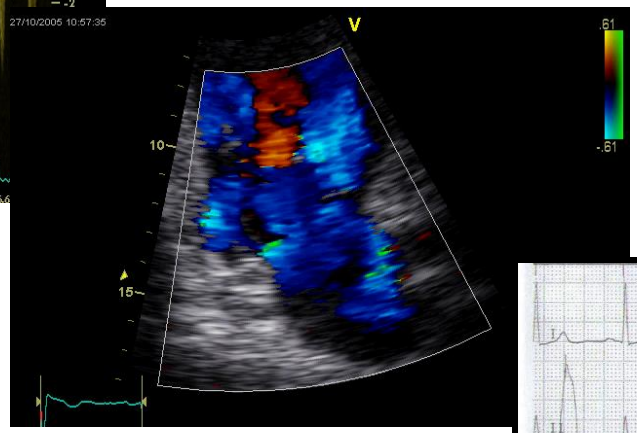
Vascular involvement



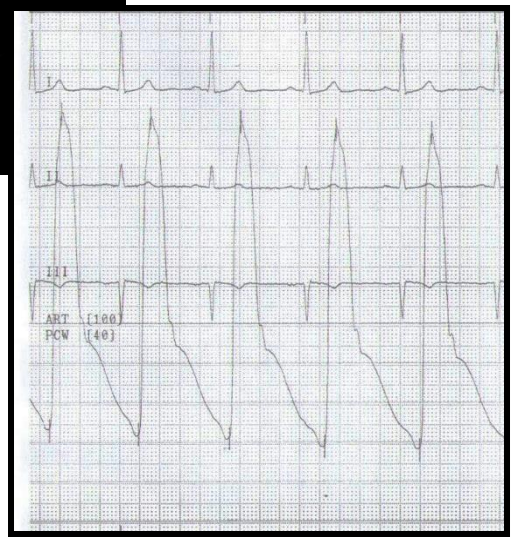
Fibrosis



Secondary mitral regurgitation



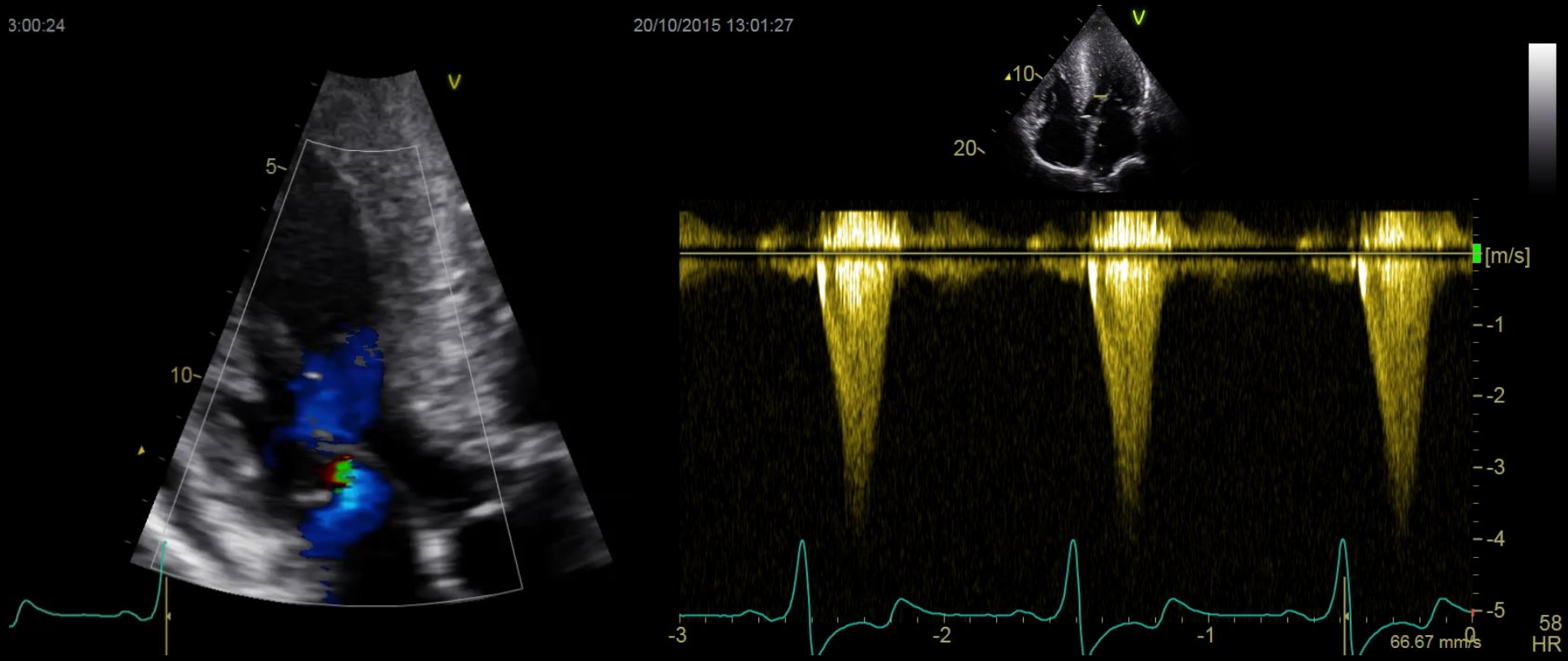
Pulmonary hypertension



Maron BJ et al. J Am Coll Cardiol HF 2018;6:353–63
Covella et al. Circ Heart Fail. 2017;10:e003689.
Foà et al. International Journal of Cardiology 291 (2019) 77–82

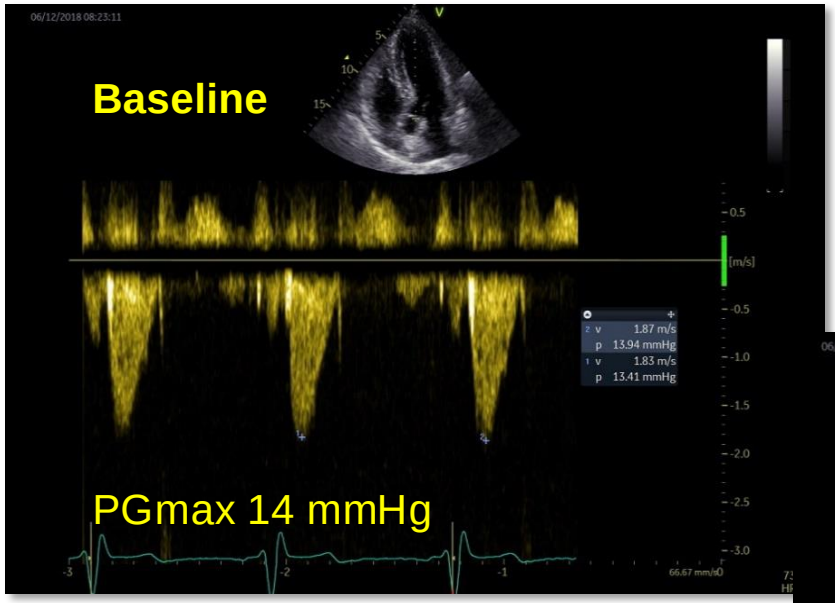
LVOT OBSTRUCTION

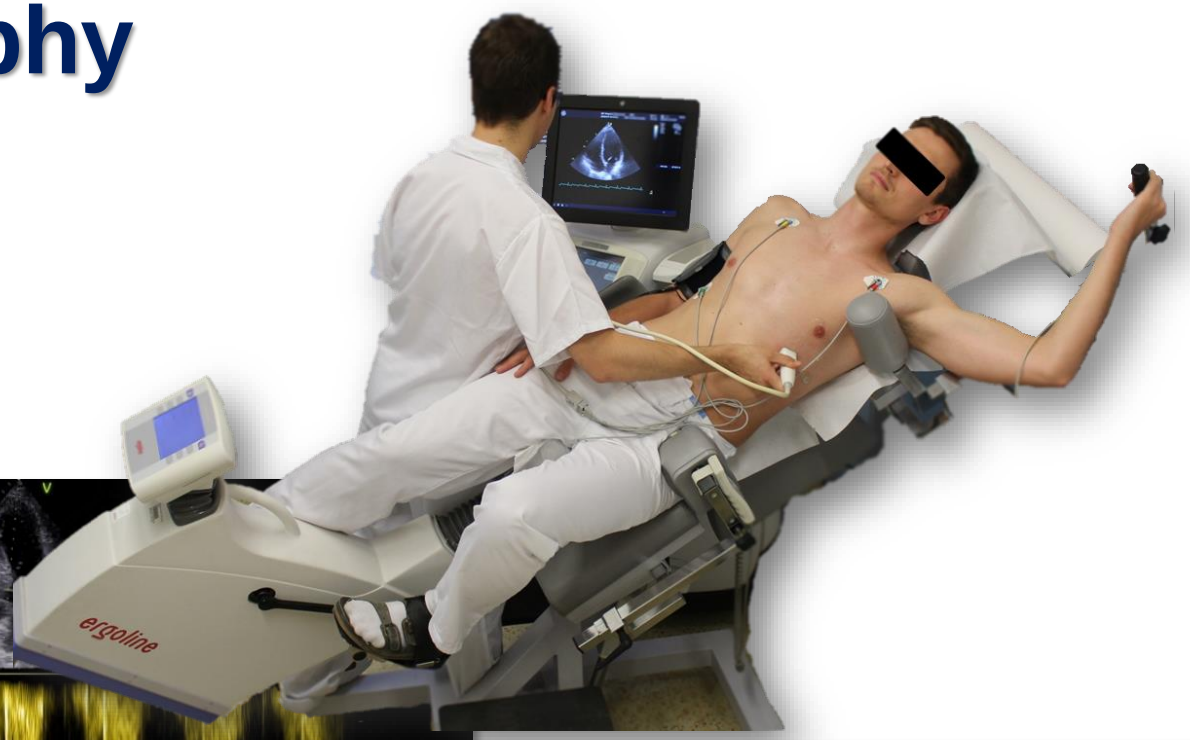
The issue of LVOTO

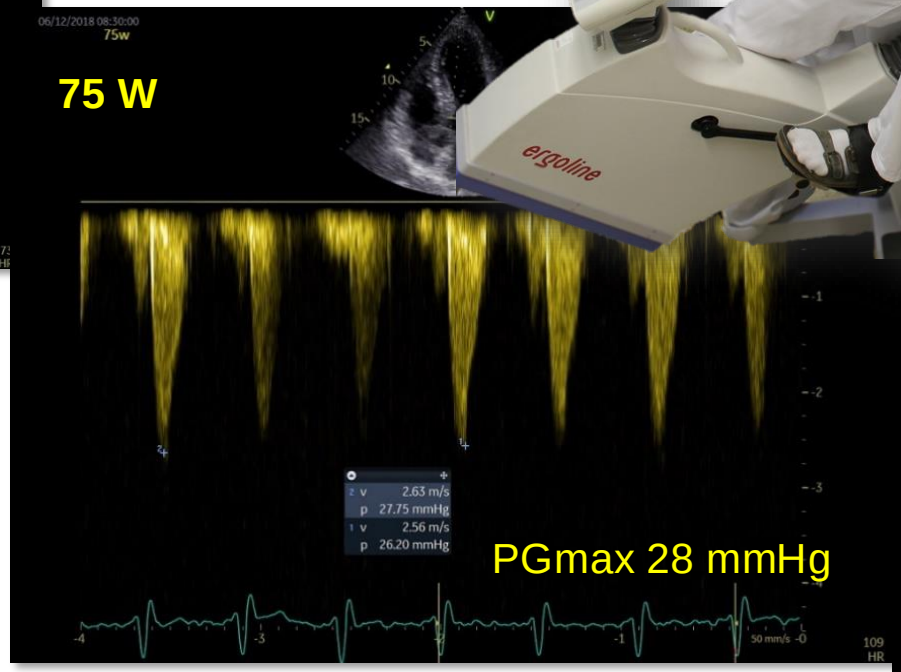


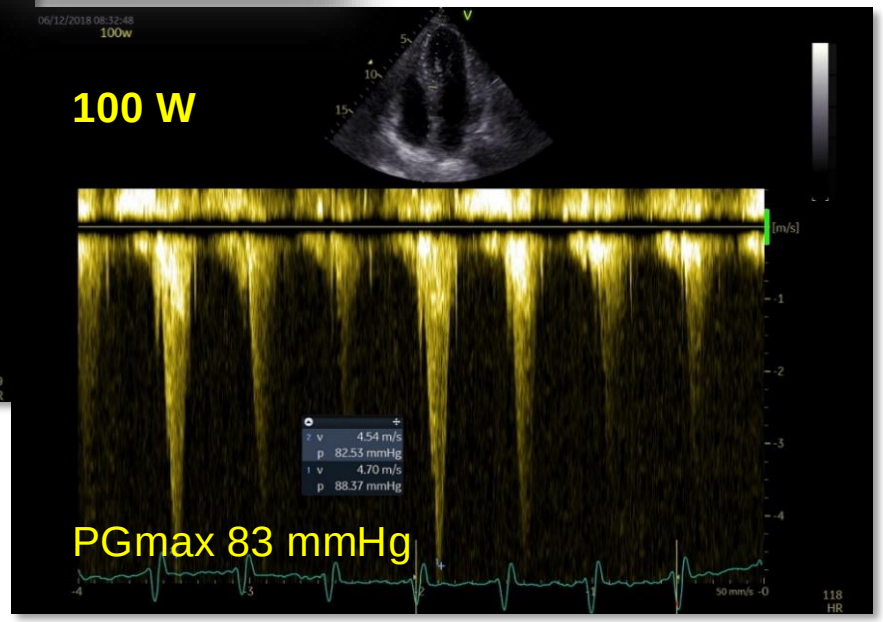
Imaging: General University Hospital, Prague, Czech Republic

Exercise echocardiography







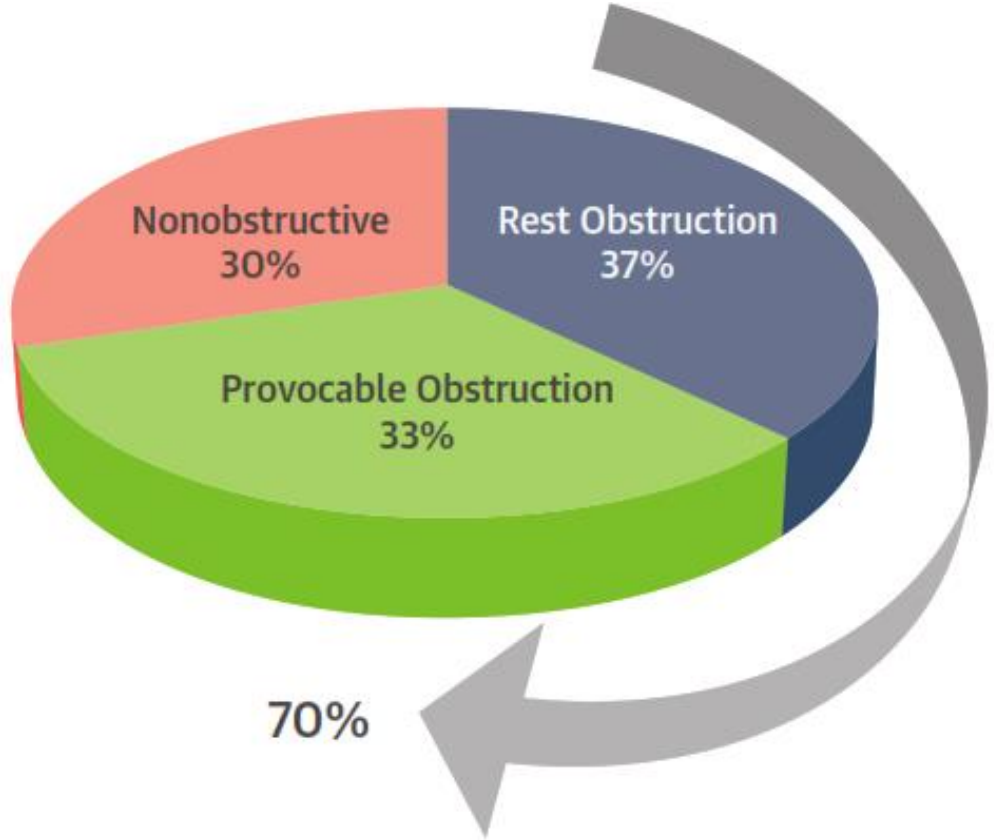


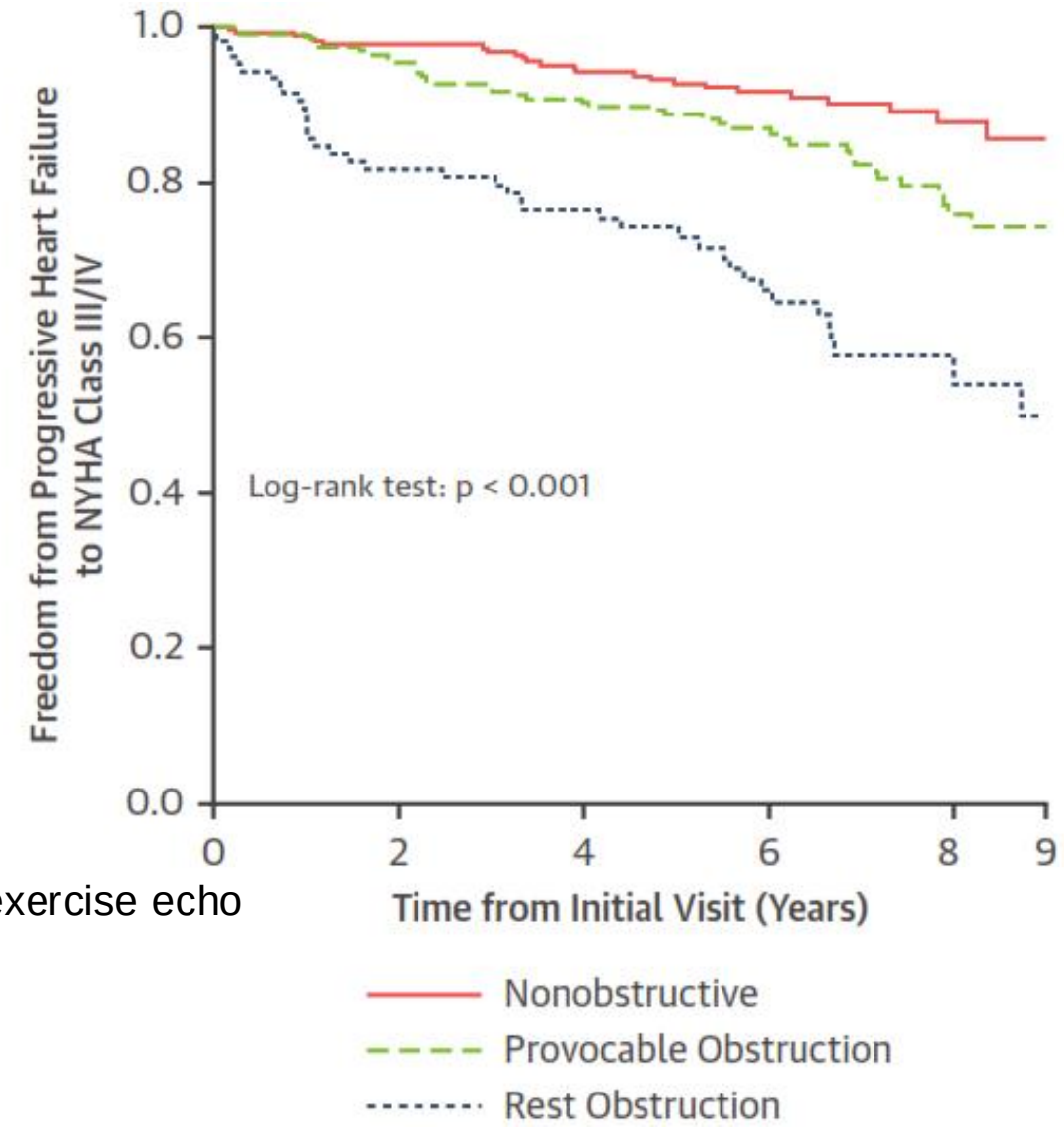
37% - obstruction at rest
33% - provoked obstruction

1. Maron MS, et al. *Circulation.* 2006;114:2232-2239.2. Maron MS, et al. *J Am Coll Cardiol.* 2016;67:1399-1409.
3. Rowin EJ, et al. *JACC Cardiovasc Imaging.* 2017;10:1374-1386. 4. Elliott PM, et al. *Eur Heart J.* 2006;27:1933-41.

Imaging: General University Hospital, Prague, Czech Republic

Significance of LVOT gradient in HCM



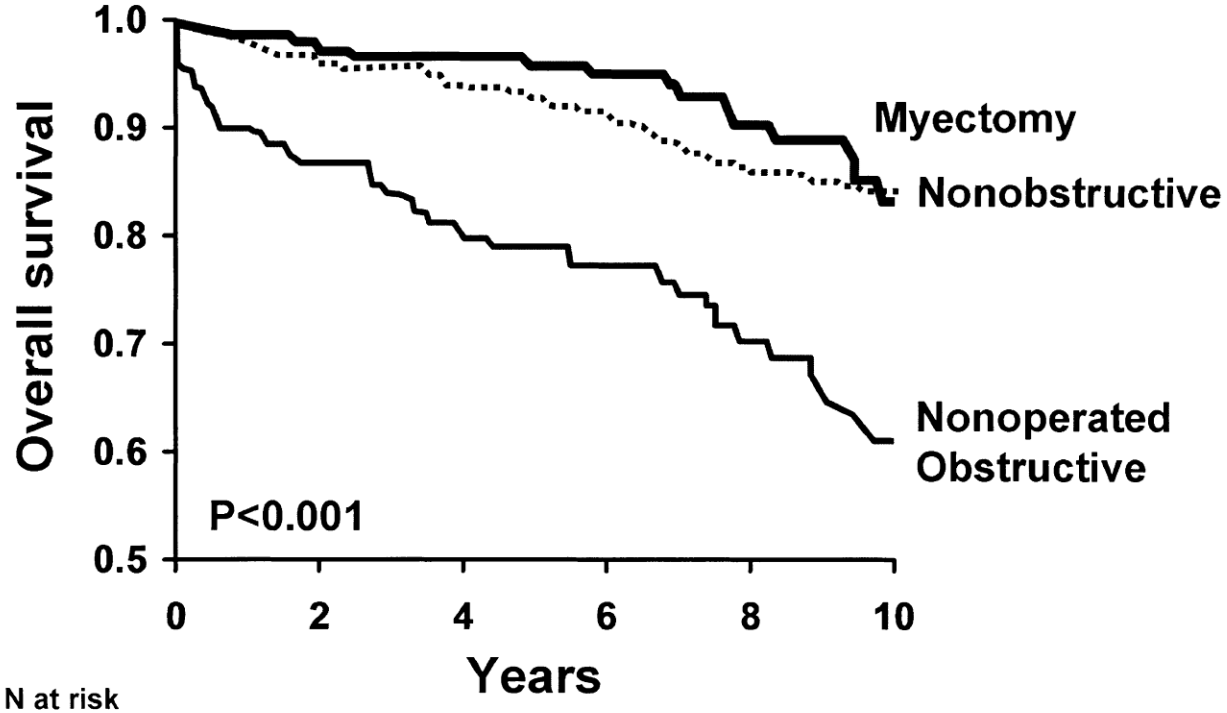


320 consecutive HCM patients (age, 47±17 years),
measuring LVOT gradient at rest, with Valsalva maneuver, and with exercise echo
119 had rest gradients ≥50 mm Hg and were not exercised.

Maron MS, Circulation 2006;114:2232–9.
Maron MS, J Am Coll Cardiol 2016;67:1399–409.
Rowin, E.J. et al. J Am Coll Cardiol Img. 2017;10:1374–86.

Is then septal reduction therapy a solution to prevent severe heart failure?

- 1,337 consecutive HCM patients at Mayo clinic
- LVOTO ≥50 mm Hg at rest or with provocative maneuvers
- NYHA III – IV
- Age 45 +/- 20 years
- Procedural risk <1%

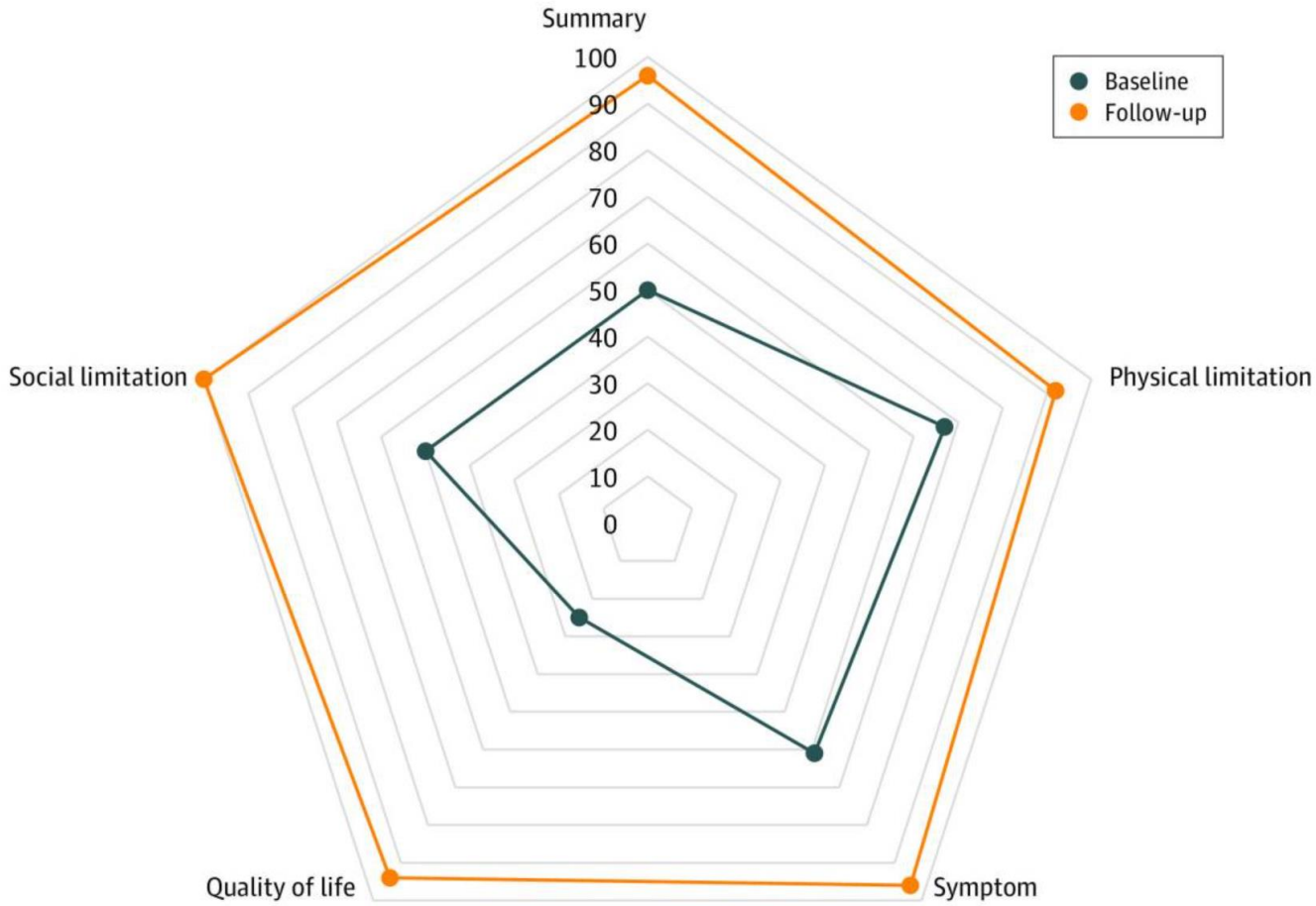


N at risk						
Myectomy	289	249	179	108	66	39
Nonobstructive	820	587	490	355	244	201
Nonoperated obstructive	228	146	106	69	42	28

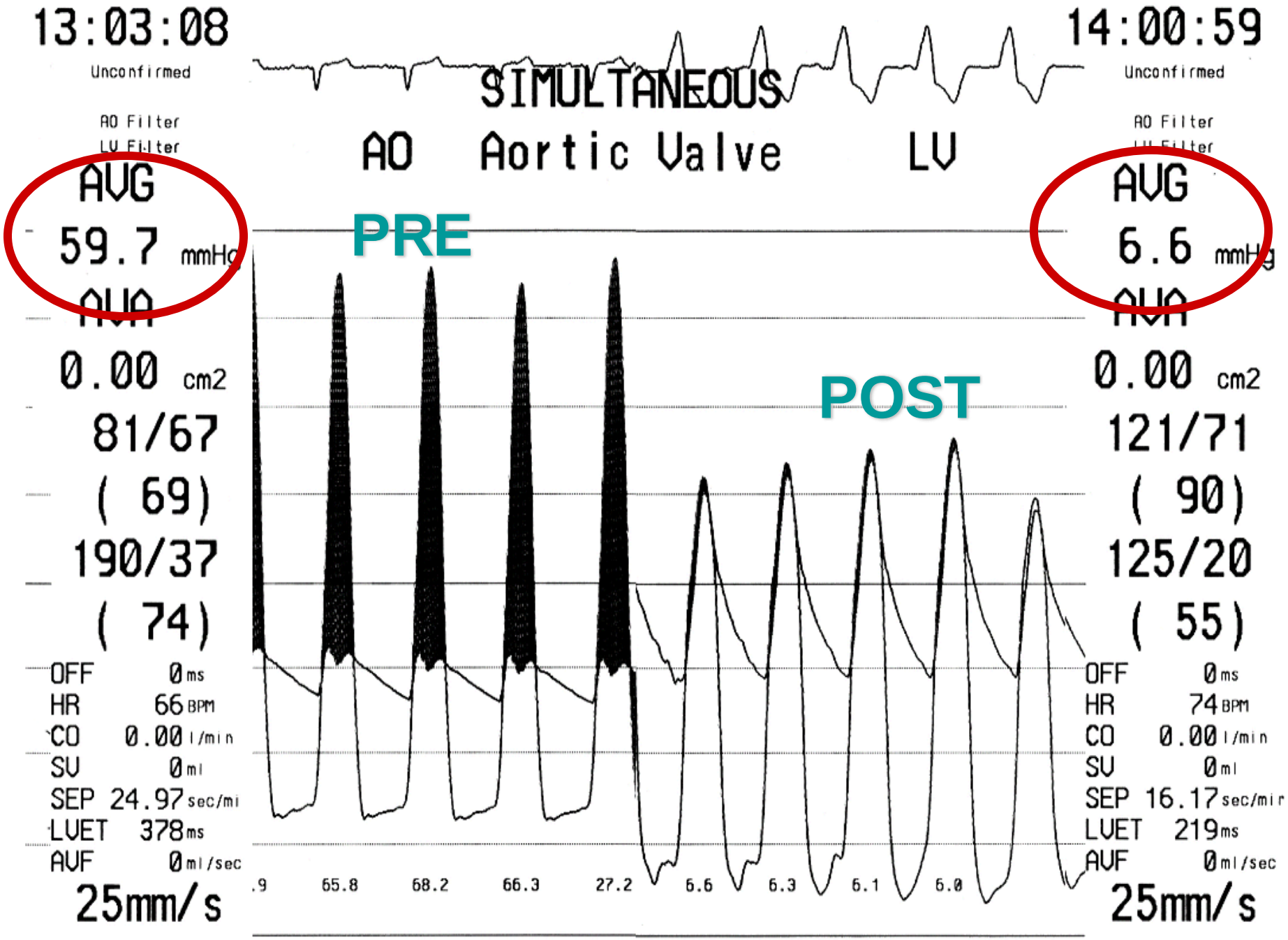
Ommen et al. J Am Coll Cardiol 2005;46:470 – 6

QoL after septal myectomy

NYHA class	Before myectomy	After myectomy
I	0	91 (67)
II	62 (46)	41 (30)
III/IV	74 (54)	4 (3)

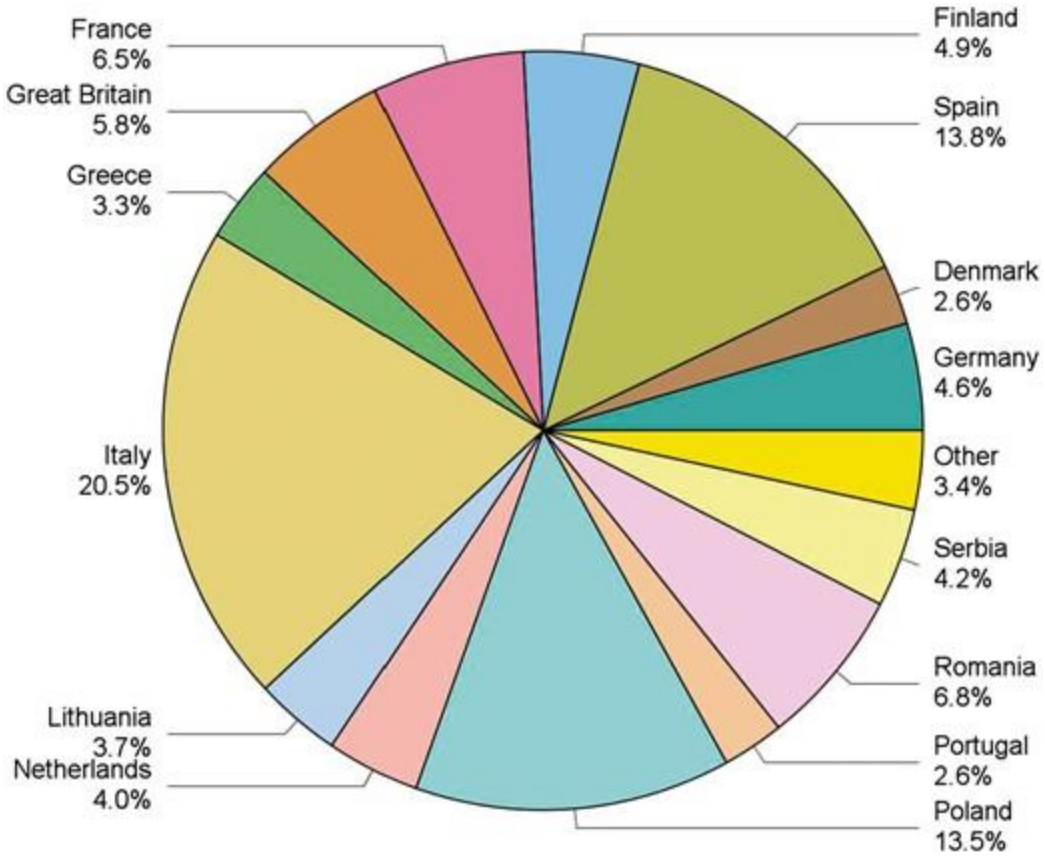


Desai MY et al. JAMA Netw Open. 2022 Apr; 5(4): e227293.


13:03:08
Unconfirmed
AO Filter
LV Filter
AVG
59.7 mmHg
AVA
0.00 cm2
81/67
(69)
190/37
(74)
OFF 0 ms
HR 66 BPM
CO 0.00 l/min
SU 0 ml
SEP 24.97 sec/mi
LVET 378 ms
AVF 0 ml/sec
25mm/s
SIMULTANEOUS
AO Aortic Valve LV
PRE
POST
.9 65.8 68.2 66.3 27.2 6.6 6.3 6.1 6.0
14:00:59
Unconfirmed
AO Filter
AVG
6.6 mmHg
AVA
0.00 cm2
121/71
(90)
125/20
(55)
OFF 0 ms
HR 74 BPM
CO 0.00 l/min
SU 0 ml
SEP 16.17 sec/mir
LVET 219 ms
AVF 0 ml/sec
25mm/s

Magage et al.

European Experience – EORP registry



- 1739 patients (59.1% males)
- Mean age 55 years

- ICD implantation 19.9%

- Class NYHA II or higher 77.3%
- Symptomatic 84.8%
- Exercise test 39.5%

- Betablockers 74.4%
- **Septal myectomy 4.9%**
- **Alcohol septal ablation 4.0%**

Charron P et al. *European Heart Journal*, Volume 39, Issue 20, 21 May 2018, Pages 1784–1793,

GAPS IN CLINICAL CARE

Who are those „non-operated“ ?

Parameter	All Patients (n = 1,337)	Myectomy (n = 289)	Nonoperated Obstructive* (n = 228)	Nonobstructive (n = 820)	ANOVA p Value
Age (yrs)	45.3 ± 20	45.3 ± 19‡	**50.0 ± 22**	44.0 ± 19	<0.001
Male gender	779 (58)	148 (51)	106 (46)	525 (64)	<0.001
NYHA functional class (at entry)					
Mean	1.83 ± 0.9	2.89 ± 0.7‡	1.74 ± 0.8	1.49 ± 0.6	<0.001
I	608 (45)	22 (7)‡	98 (43)	488 (60)	—
II	380 (28)	11 (4)‡	**95 (42)**	274 (33)	—
III to IV	348 (26)	256 (89)‡	**34 (15)**	58 (7)	—
LV outflow gradient (at rest) (mm Hg)	29.2 ± 39	67.3 ± 41	68.0 ± 31	5.1 ± 7	—
Severe MR	71 (5)	21 (7)	**24 (8)**	26 (3)	<0.001

*Obstruction defined as peak instantaneous left ventricular (LV) outflow gradient ≥30 mm Hg under resting conditions.

Ommen et al. J Am Coll Cardiol 2005;46:470 – 6

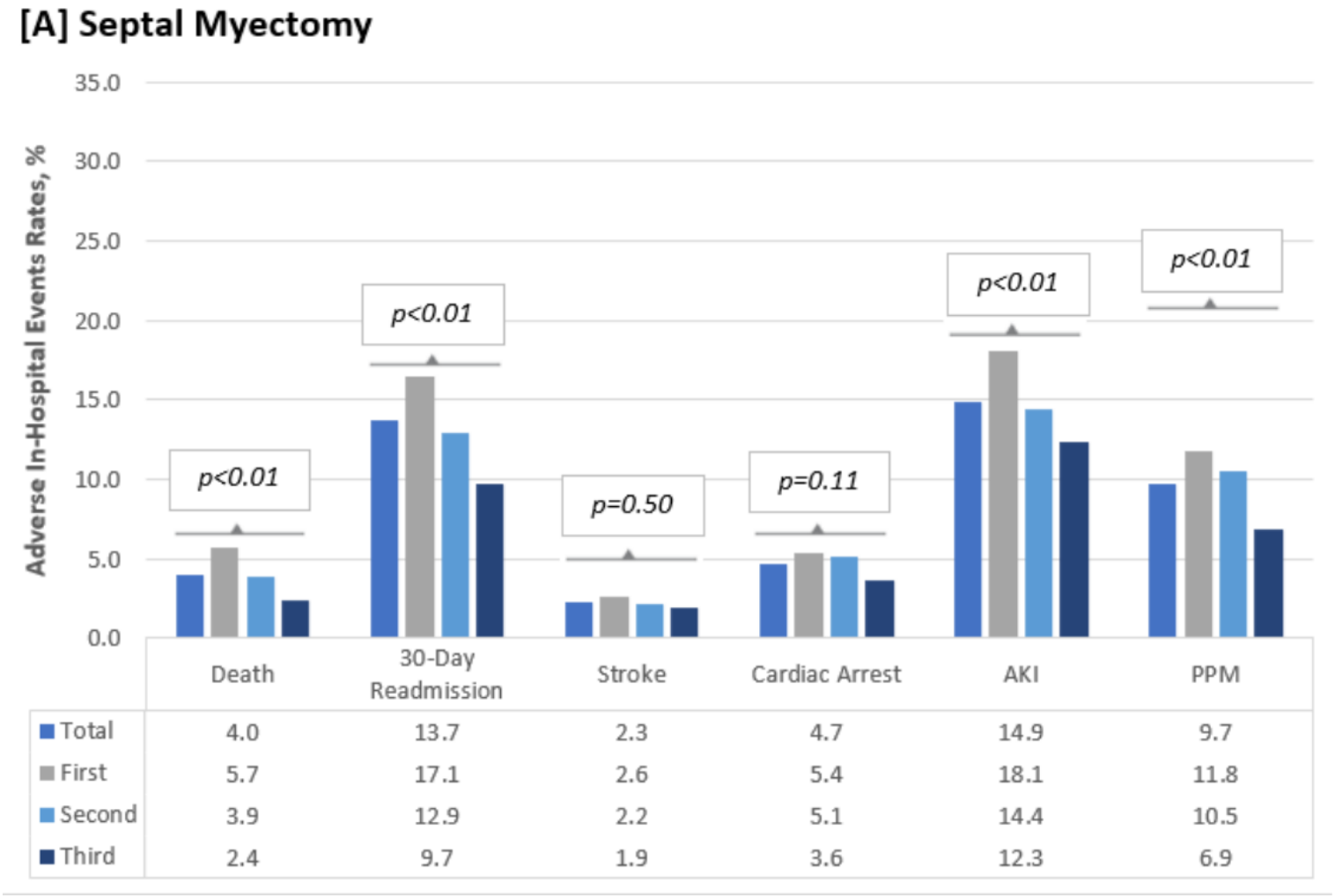
Who should be in charge of septal myectomy?

12 065 (63%) had SM

There were 63 (3.7%) hospitals (averaging 2.2 SM cases/year) with 100% in-hospital mortality.

The median number of SM :

- **low- volume, 2.2 (IQR, 1.6–4.0),**
- **medium- volume, 12.1 (IQR, 9.9–17.6)**
- **high-volume 47.0 (IQR, 34.9–63.5)**

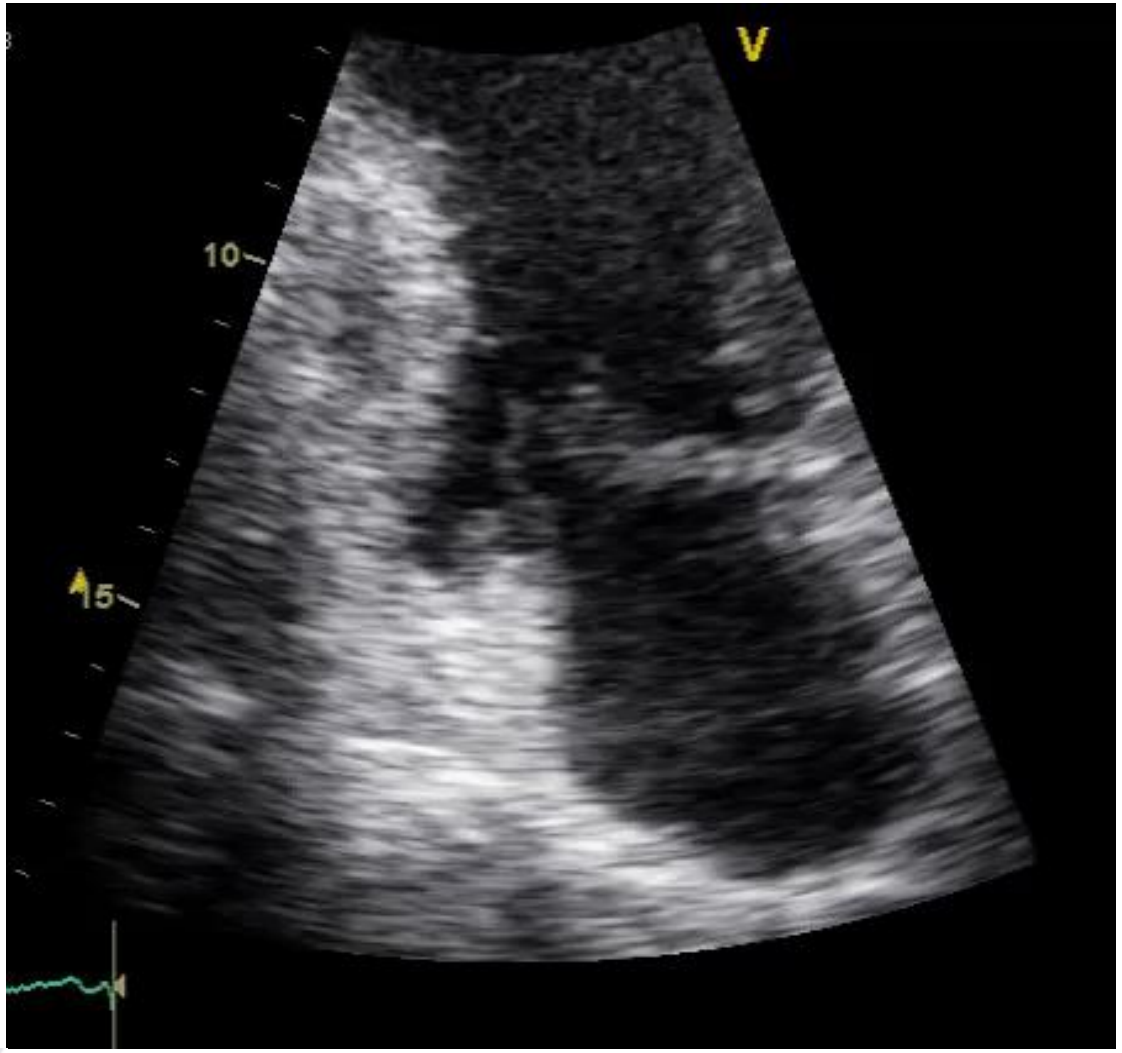


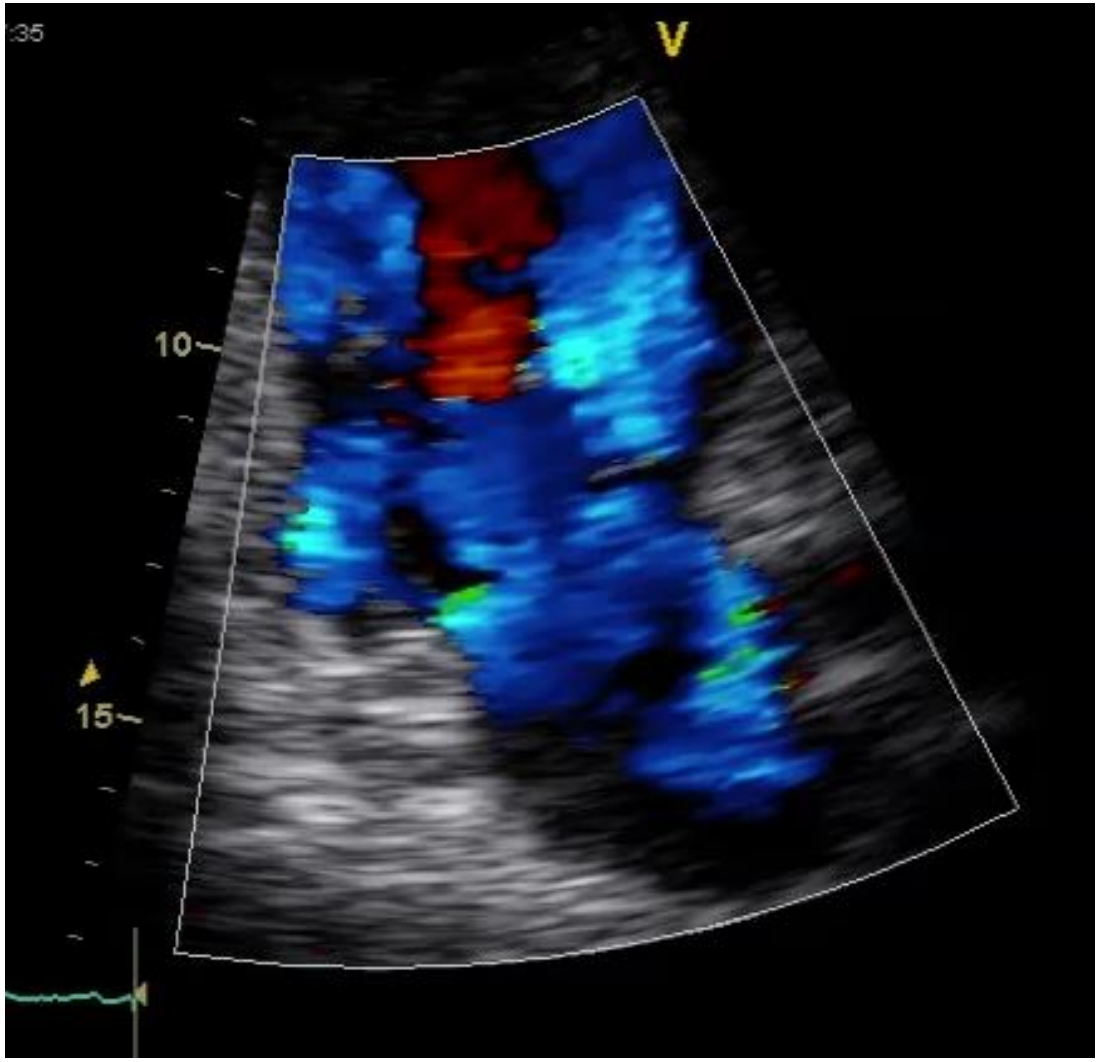
	Death	30-Day Readmission	Stroke	Cardiac Arrest	AKI	PPM
Total	4.0	13.7	2.3	4.7	14.9	9.7
First	5.7	17.1	2.6	5.4	18.1	11.8
Second	3.9	12.9	2.2	5.1	14.4	10.5
Third	2.4	9.7	1.9	3.6	12.3	6.9

Altibi et al. J Am Heart Assoc. 2023 May 16; 12(10): e028693

MITRAL VALVE IN HYPERTROPHIC CARDIOMYOPATHY

Mitral regurgitation in HCM





Imaging: General University Hospital, Prague, CZ

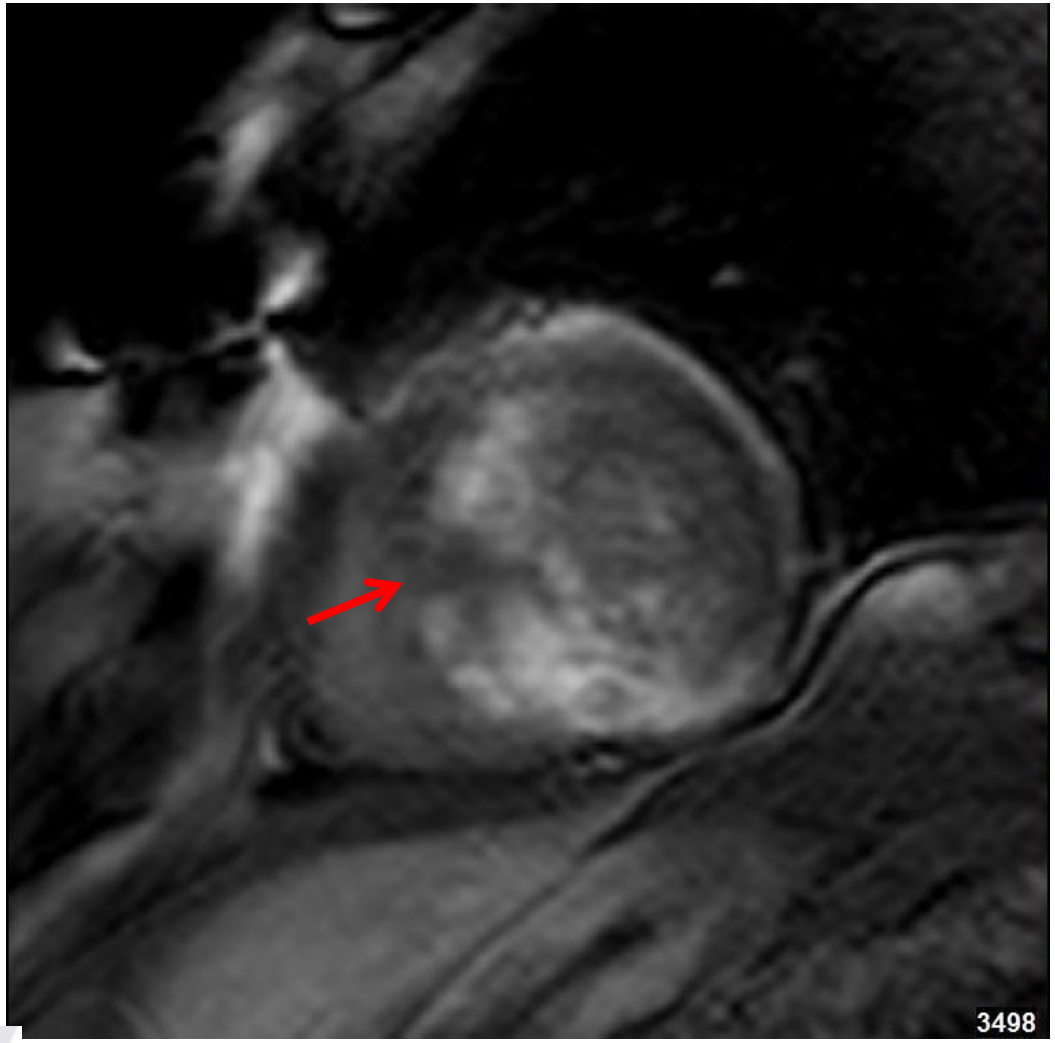
Need for MV surgery

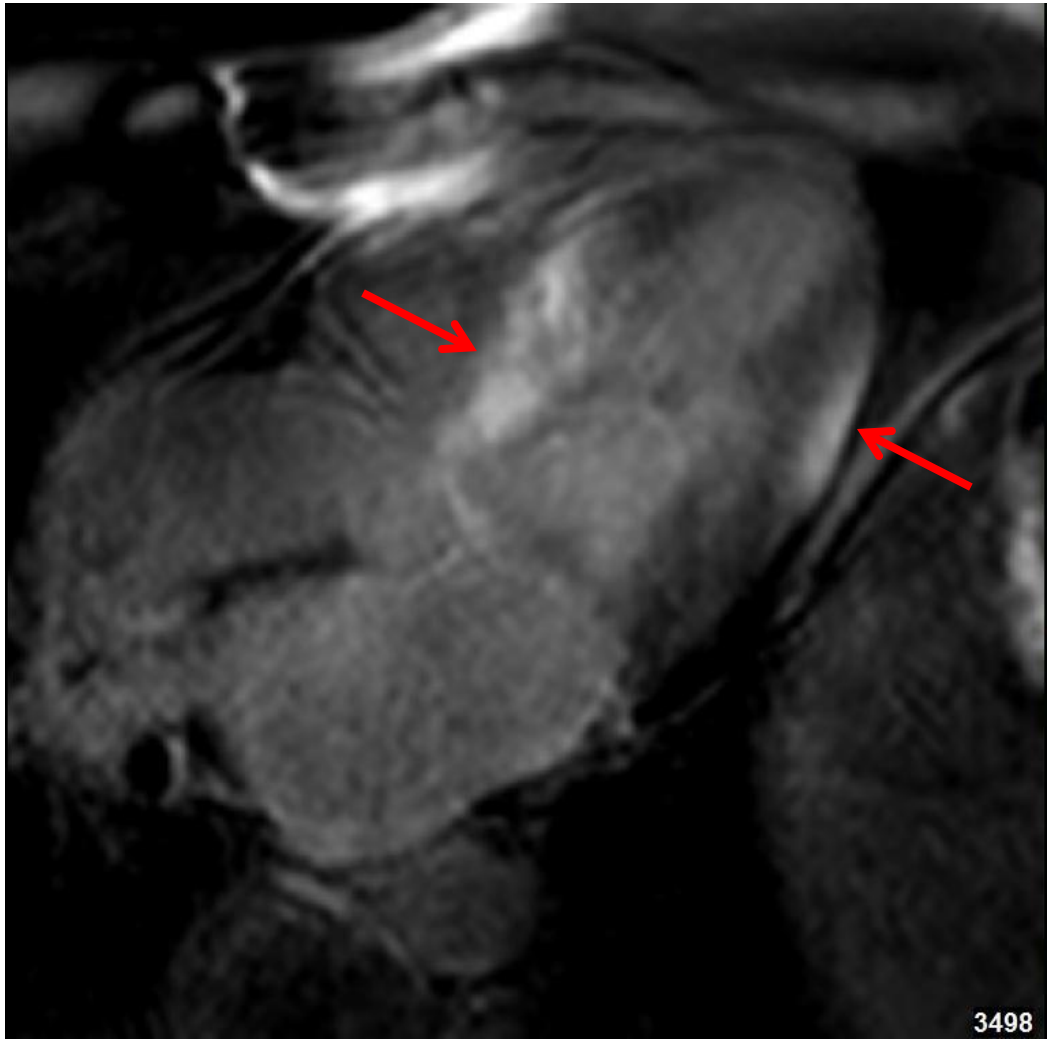
First Author (Location)	Year	N	MV Surgery (%)	MV Repair (%)	MV Replacement (%)
Mohr (Rochester, MN)	1989	115	**5.2**	**0**	**5.2**
Heric (Cleveland, OH; Tacoma, WA; Buffalo, NY)	1995	178	11.9	2.3	9.6
Schönbeck (Zurich, Switzerland)	1998	110	10.9	9.1	1.8
Kaple (Cleveland, OH)	2008	851	13.5	7.9	5.6
Iacovoni (Bergamo, Italy)	2012	124	7.2	5.6	1.6
Balaram (New York, NY)	2012	132	**76.0**	**65.0**	**11.0**
Wang (Beijing, China)	2013	93	20.4	9.7	10.7
Desai (Cleveland, OH)	2015	990	24.2	20.4	3.8
Hong (Rochester, MN)	2016	1,993	8.8	6.7	2.1
Ralph-Edwards (Toronto, Canada)	2016	577	5.7	4.2	1.5

Teekakirikul and Wang JACC 2018

FIBROSIS

Replacement fibrosis in hypertrophic cardiomyopathy

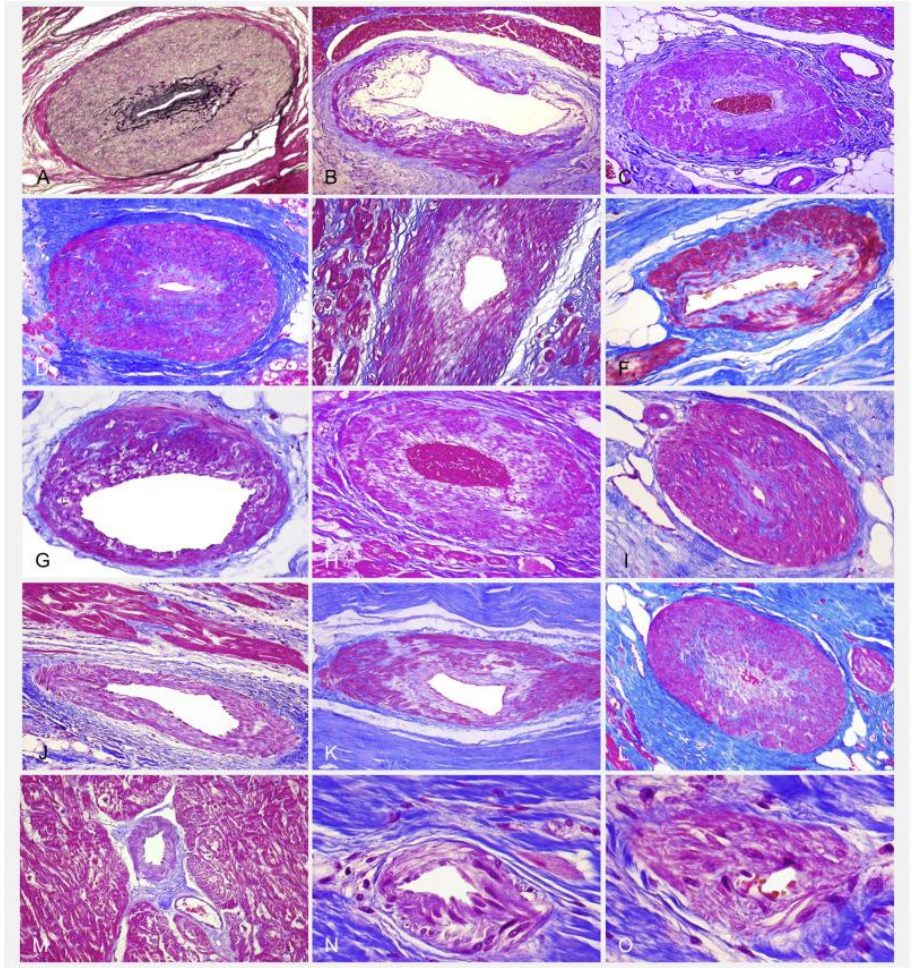


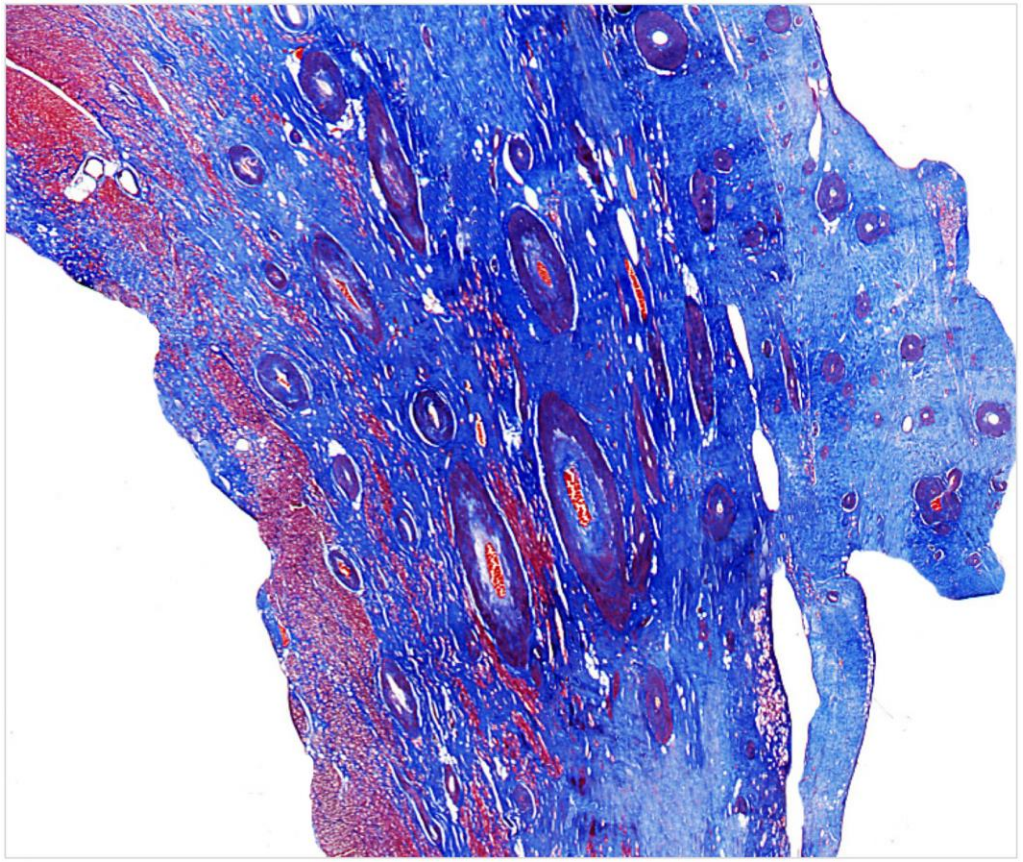


Imaging: General University Hospital, Prague, CZ

End-stage HCM is associated with extensive fibrosis and arteriolar dysplasia

27 myectomy specimens of obstructive HCM patients and 30 ES-HCM explanted hearts
Replacement fibrosis more frequent in end-stage hearts
Vasculopathy present in both subgroups





Example of severe and extensive microvasculopathy topographically associated with marked scar-like fibrosis in an end-stage HCM specimen."

Foà et al. International Journal of Cardiology 291 (2019) 77–82

Replacement fibrosis and mitral regurgitation as predictor of heart failure

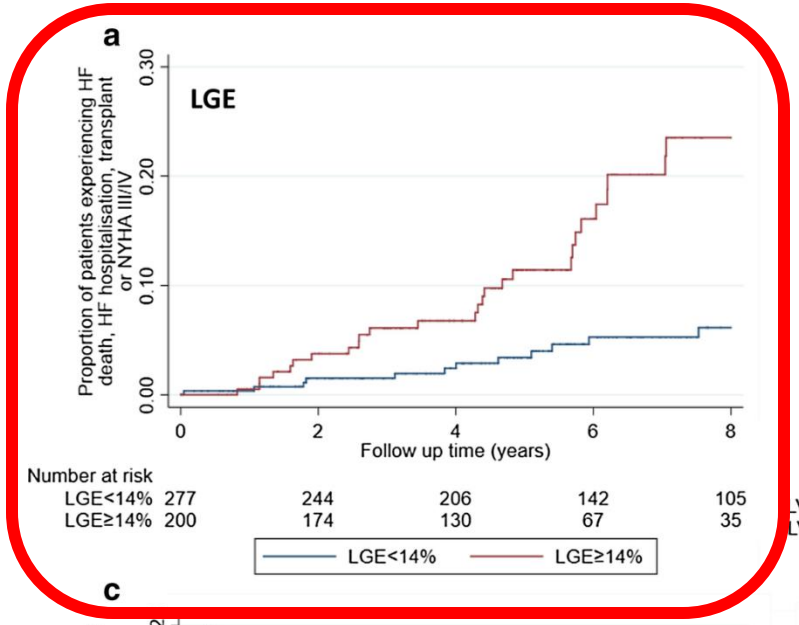
543 patients with HCM underwent CMR,

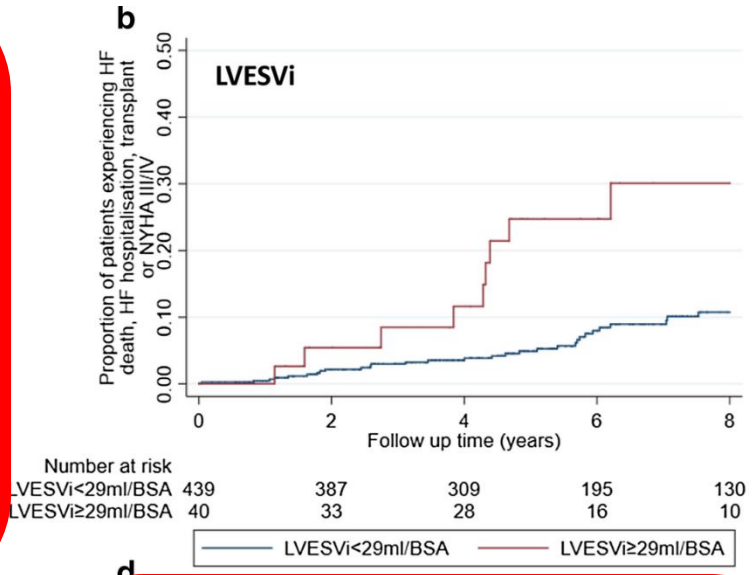
94 - composite endpoint at baseline.

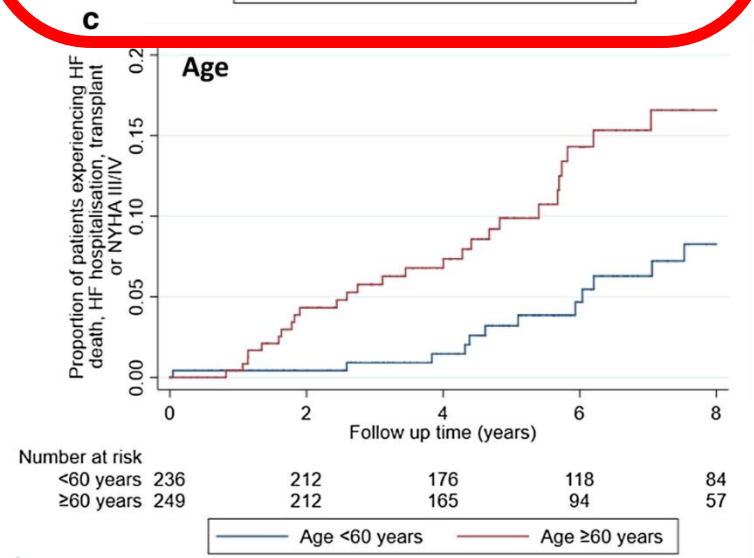
449 patients followed for 5.6 years.

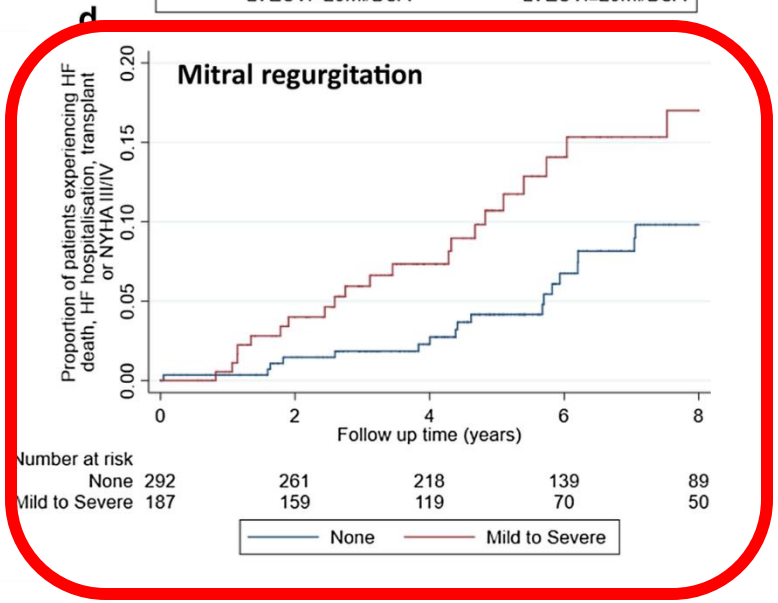
39 (8.7%) reached the composite endpoint

- **HF death (n = 7),**
- **cardiac transplantation (n = 2)**
- **progression to NYHA III/IV (n = 20)**







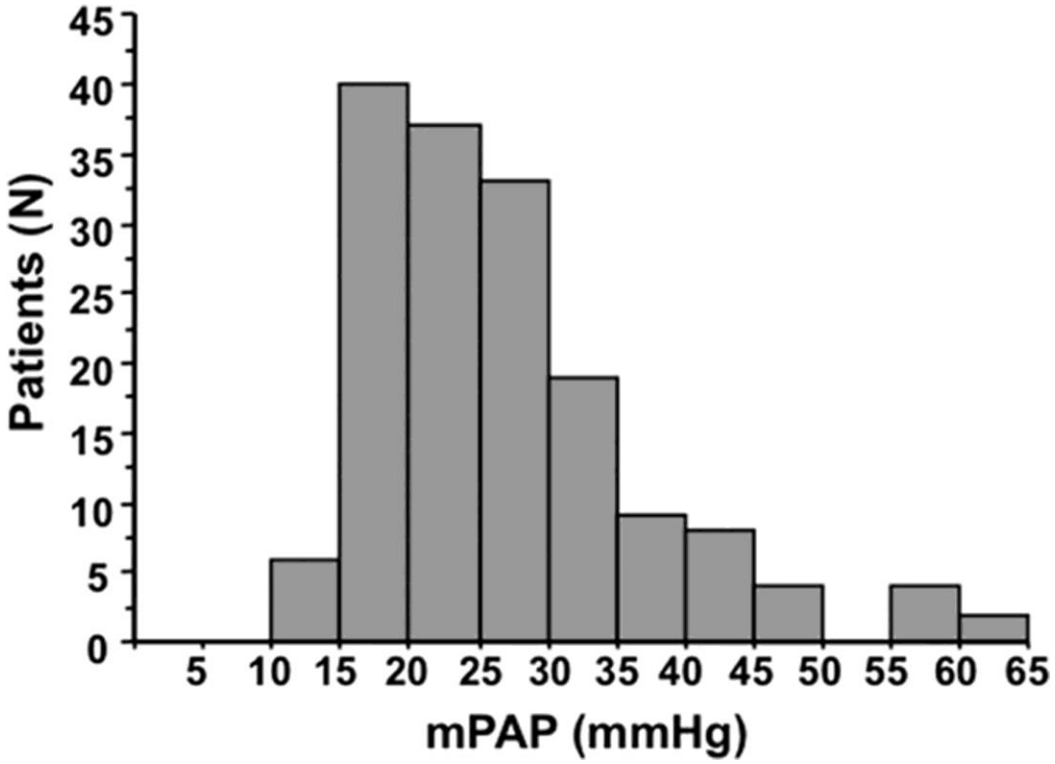


Raphael et al. J Cardiovasc Magn Reson (2021) 23:26

CONSEQUENCES OR CONRIBUTORS?

Pulmonary hypertension in HCM patients

162 consecutive patients with outflow tract gradients (median [interquartile range], 90 mm Hg [70–110 mm Hg]), 59±11 years old, and 49% men, predominately New York Heart Association class III/IV status.

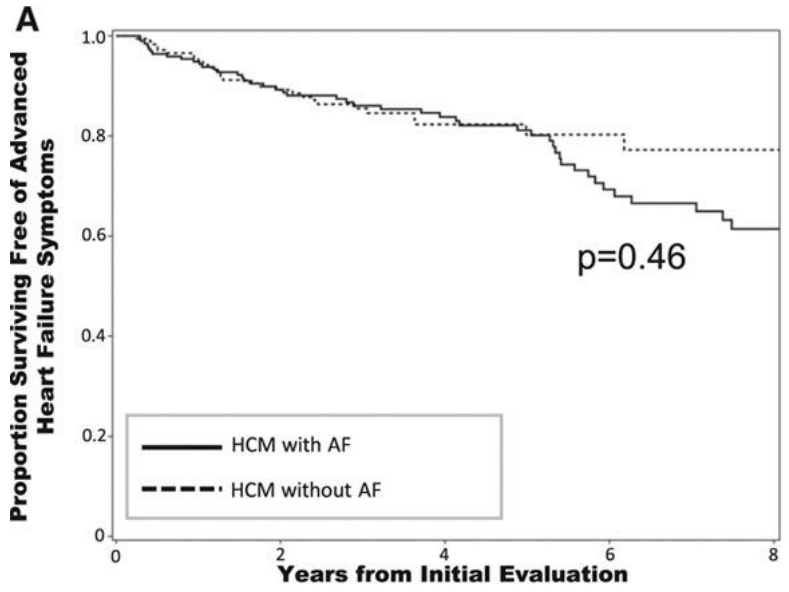


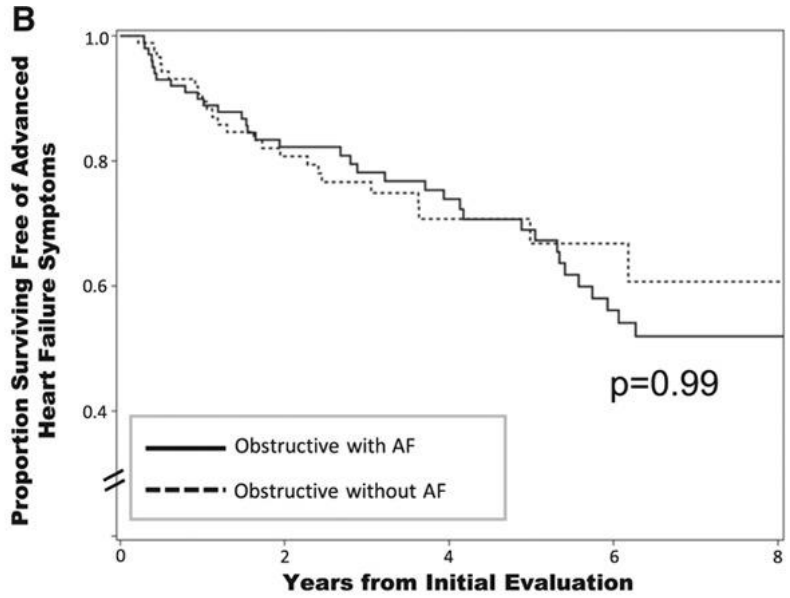
	mPAP <25 mm Hg (n=80)	mPAP≥25 mm Hg (n=82)	P Value
Cardiopulmonary hemodynamics			
PASP, mm Hg	31 [28–34]	46 [41–56]	<0.001
mPAP, mm Hg	20 [18–22]	31 [28–38]	<0.001
Right atrial pressure, mm Hg	6 [3- 8]	9 [7–13]	<0.001
TPG, mm Hg	8 [7–10]	13 [9–16]	<0.001
TPG>12 mm Hg, n (%)	4 (5)	41 (50)	<0.001
PAWP, mm Hg	12 [10–14]	20 [16–24]	<0.001
PAWP>15 mm Hg, n (%)	8 (10.0)	66 (80.5)	<0.001
PVR, WU	1.59 [1.23–2.13]	2.45 [1.66–3.26]	<0.001
CI, L/min per m^2	2.52 [2.21–2.96]	2.51 [2.16–2.85]	0.55
DPG ≥7 mm Hg, %	0 (0)	12 (15)	<0.001

9 patients with hemodynamics of PAH

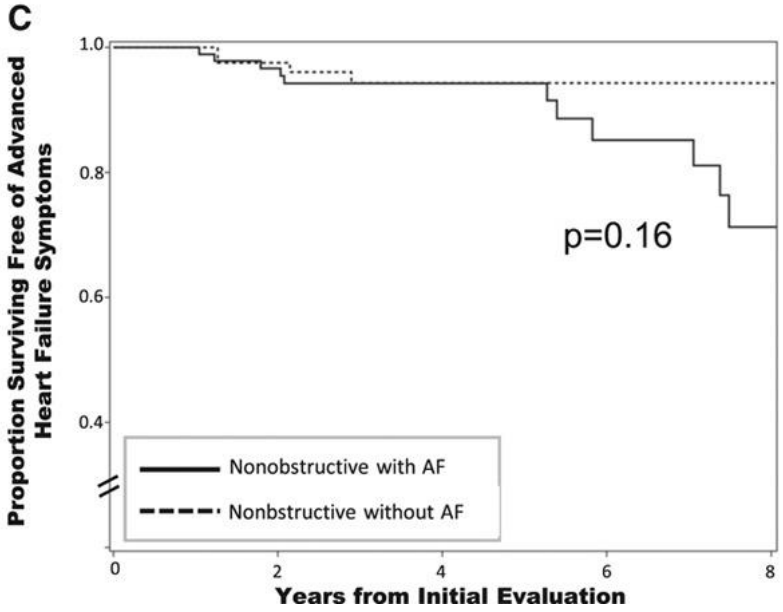
Covella et. Al Circulation: Heart Failure. 2017;10

Prognosis of patients with and without atrial fibrillation





- 1558 patients with HCM,
- 304 (20%) had episodes of AF,
  - 226 (74%) symptomatic paroxysmal AF (average, 5±5; range, 1 to >20),
  - 78 (26%) developed permanent AF

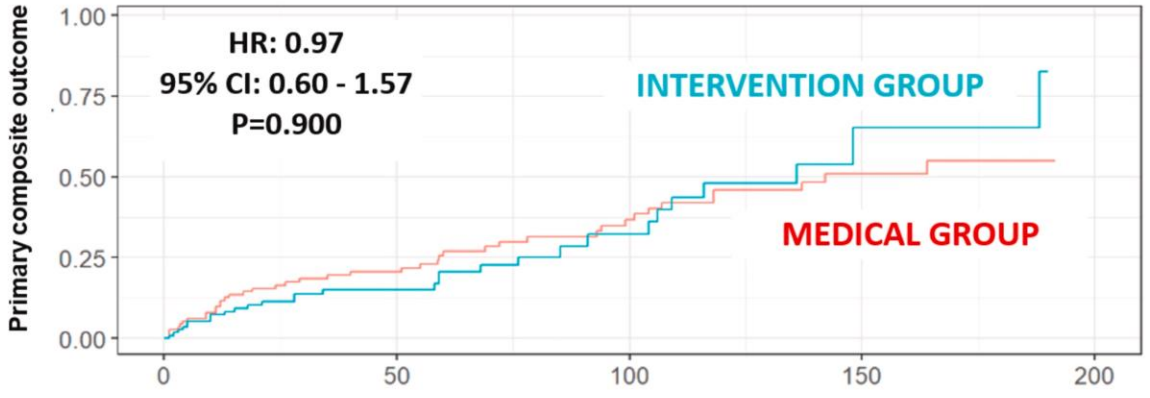


Rowin et al. Circulation. 2017;136:2420–2436

Impact of atrial fibrillation ablation in hypertrophic cardiomyopathy

555 HCM patients with AF were enrolled, 140 undergoing CA and 415 receiving medical therapy. 1:1 propensity score matching led to the inclusion of 226 patients (113 medical group, 113 intervention group)

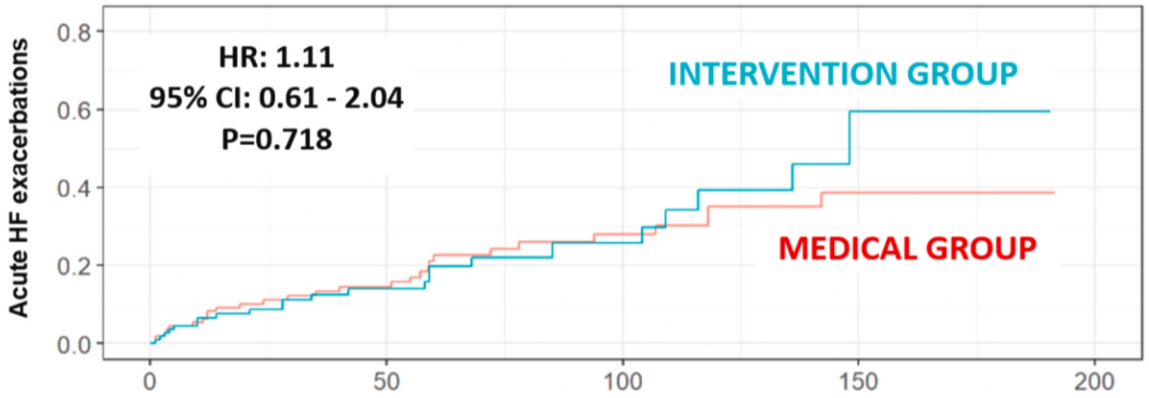
A



MEDICAL GROUP					
At Risk	113	71	36	15	5
Events	0	22	33	40	41

INTERVENTION GROUP					
At Risk	113	51	18	3	0
Events	0	15	22	28	29

C



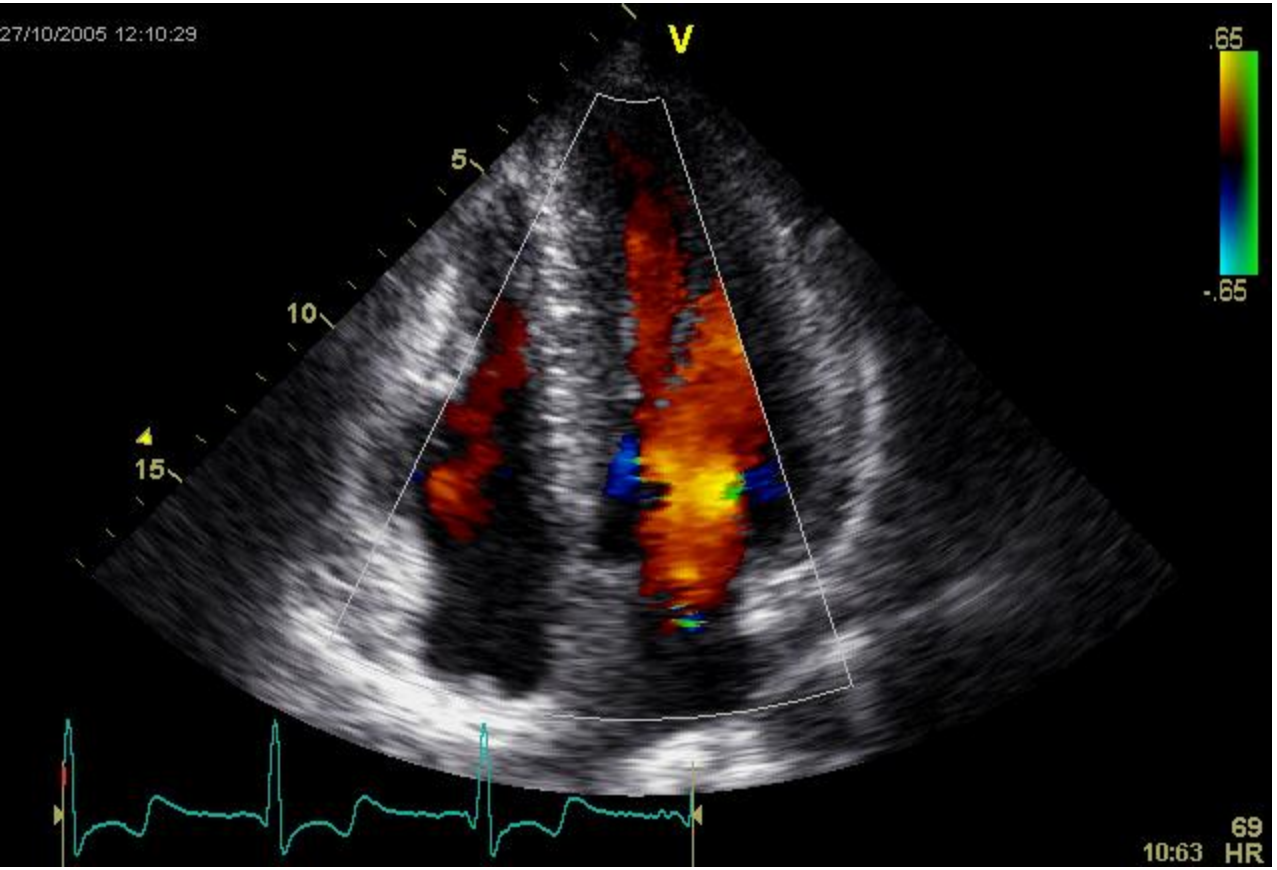
MEDICAL GROUP					
At Risk	113	72	34	14	5
Events	0	15	24	28	28

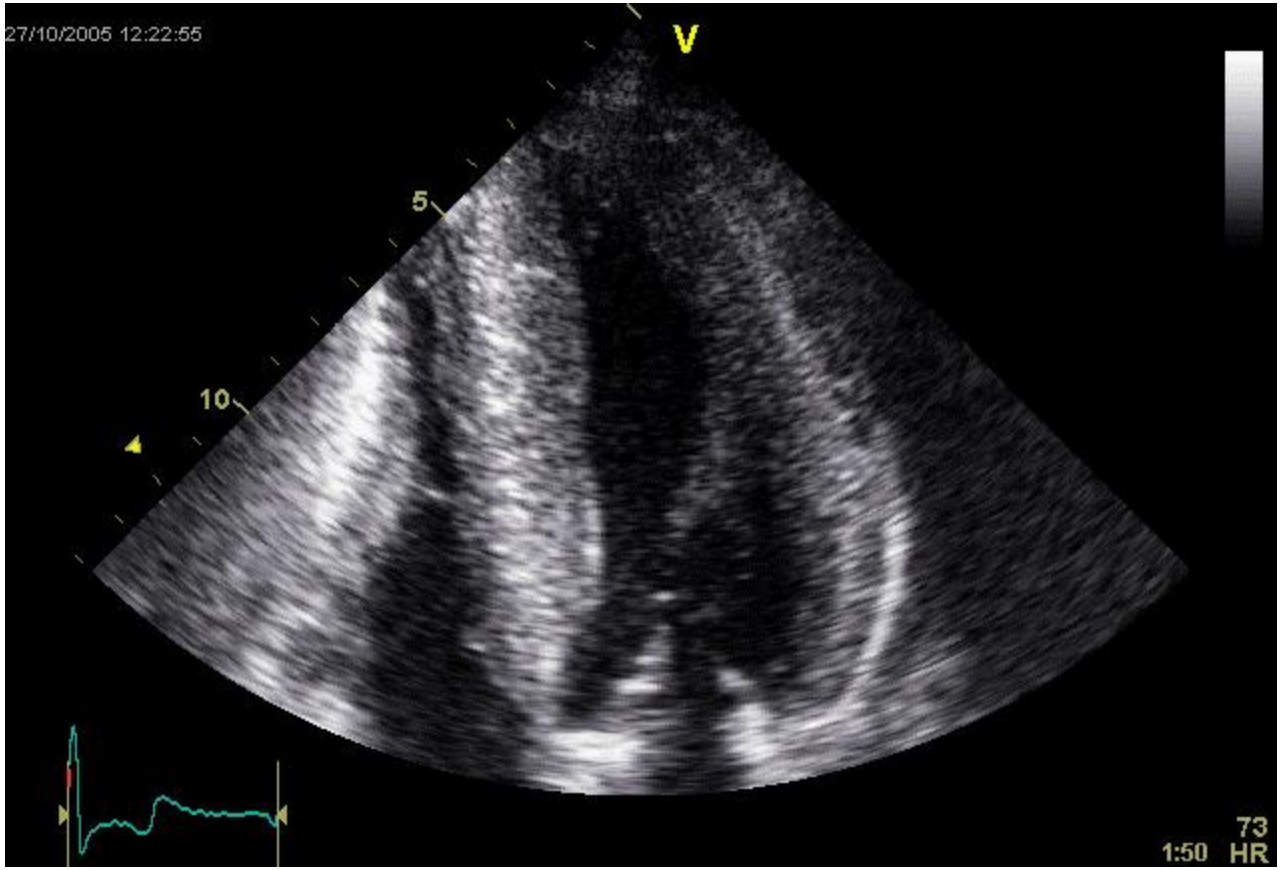
INTERVENTION GROUP					
At Risk	113	49	18	3	0
Events	0	13	18	23	23

Pierri et al. JACC Adv. 2024 May, 3 (5) 100899

END-STAGE HYPERTROPHIC CARDIOMYOPATHY

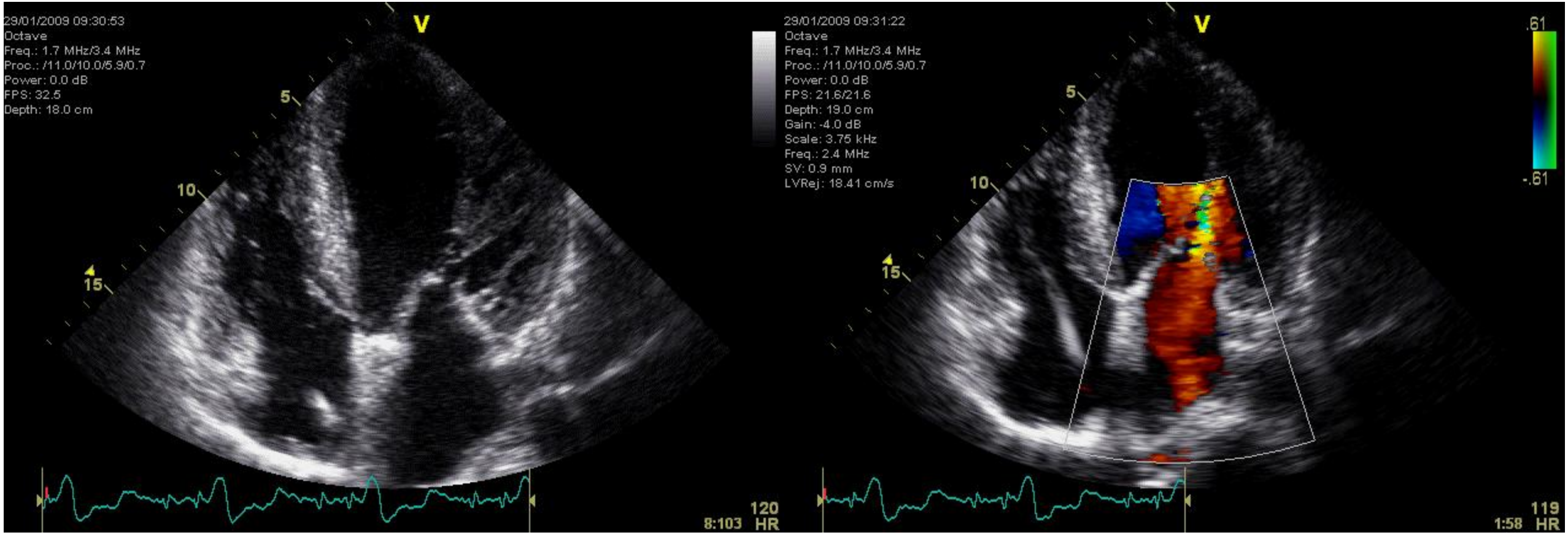
Apical or midventricular obstruction





Imaging: General University Hospital, Prague

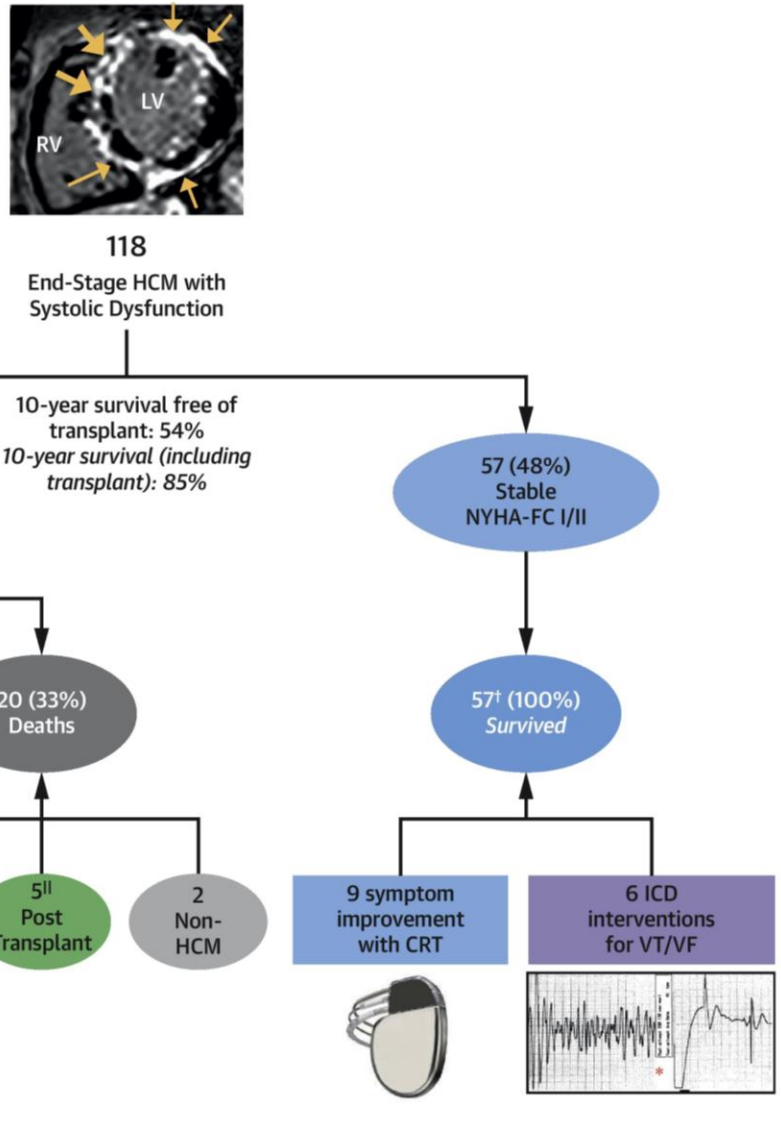
„Burnt-out“ hypertrophic cardiomyopathy



Imaging: General University Hospital, Prague

End-stage HCM with systolic dysfunction

- 2,447 patients in the HCM cohort,
- 118 (4.8%) were identified with ES-HCM,
- 77 had ES at initial evaluation,
- 41 evolved into ES during follow-up

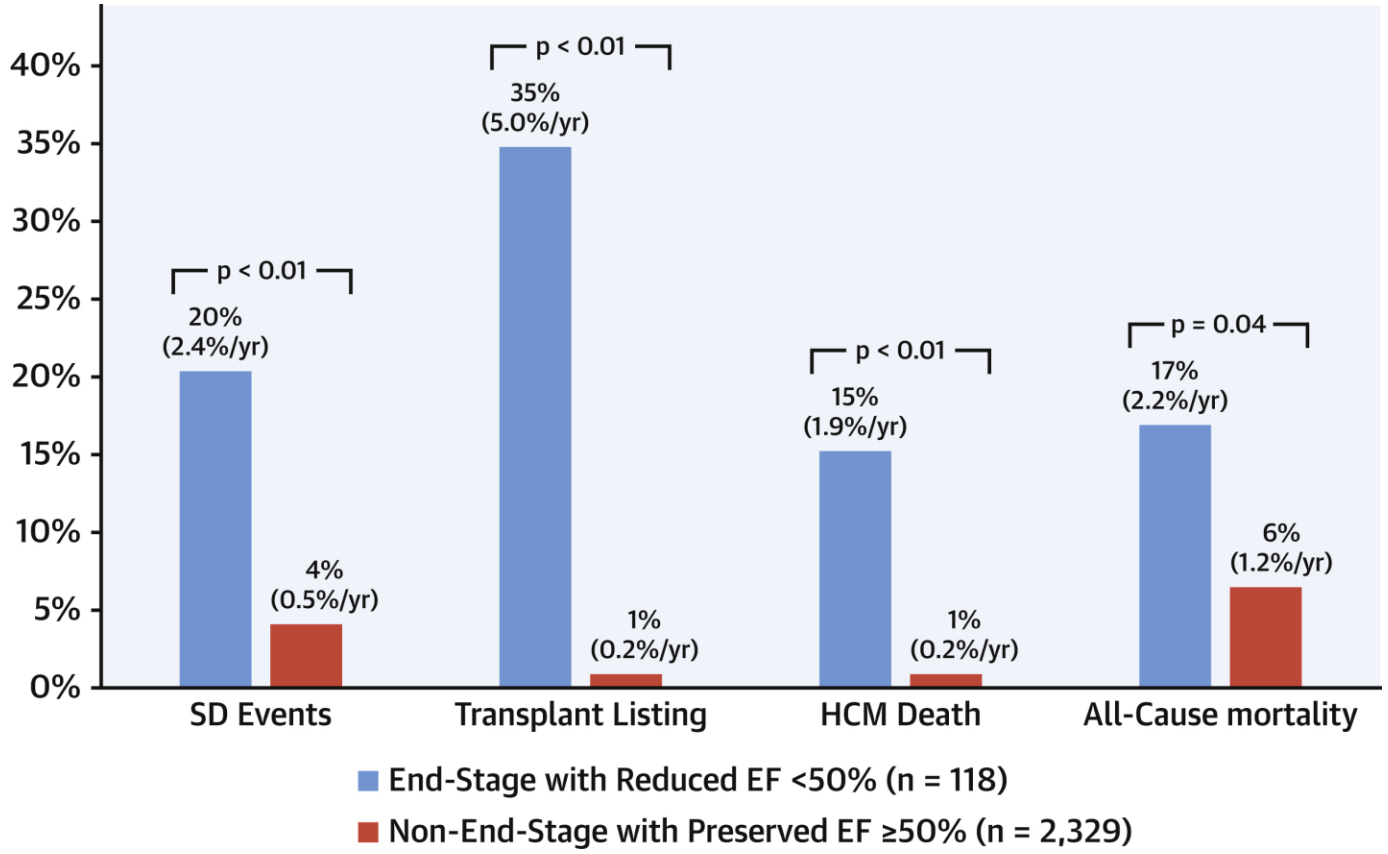


Rowin, E.J. et al. J Am Coll Cardiol. 2020;75(24):3033-43.

End-stage HCM with systolic dysfunction

2,447 patients in the HCM cohort, 118 (4.8%) were identified with ES-HCM

	S-HCM With Systolic Dysfunction (n = 118)	HCM With Preserved Systolic Function (n = 2,329)	p Value
Age at HCM diagnosis, yrs	34 ± 18	47 ± 18	<0.001
Ejection fraction, %	39 ± 9	64 ± 4	<0.001
LVOT gradient at rest ≥30 mm Hg	2 (2)	882 **(38)**	<0.001
No. of CMR studies	21	1,550	—
No. with LGE	20 **(95)**	948 (61)	0.001
% LGE (in patients with LGE)	17 ± 11	5 ± 5	<0.001
No. LGE ≥15% of LV	11 **(52)**	56 (4)	<0.001

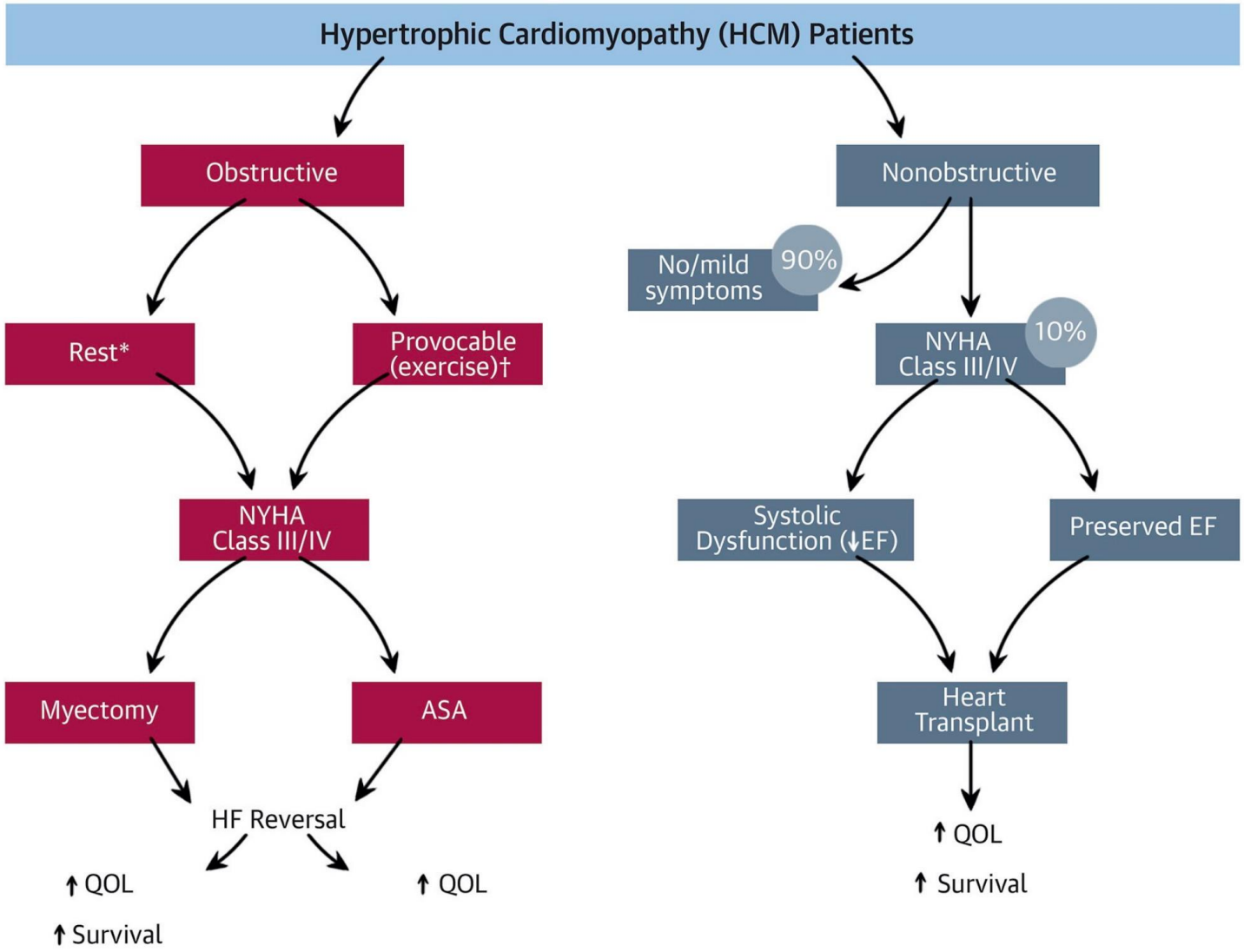


Rowin et al. J Am Coll Cardiol. 2020 Jun, 75 (24) 3033–3043

WHAT DO WE KNOW?

Heart Failure in HCM – Clinical Spectrum

- Systemic congestion less pronounced
- RV dysfunction rare
- Renal function impairment rare
- Reversibility with LVOTO alleviation
- Mimial or no effect of HF EBM-based drugs



Maron BJ et al. J Am Coll Cardiol HF 2018;6:353–63

Heart failure (HF) in hypertrophic cardiomyopathy (HCM)

- HF dominates the spectrum of complications
- Patients with LVOT are more prone to develop HF
- HF is usually caused by elevated filling pressures
- Septal reduction therapy can improve symptoms, but proportion of patients without intervention remains high
- End-stage HCM is often associated with extensive fibrosis
- Mitral regurgitation may contribute to the severity of HF
- Atrial fibrillation may be symptomatic but does not contribute to HF development