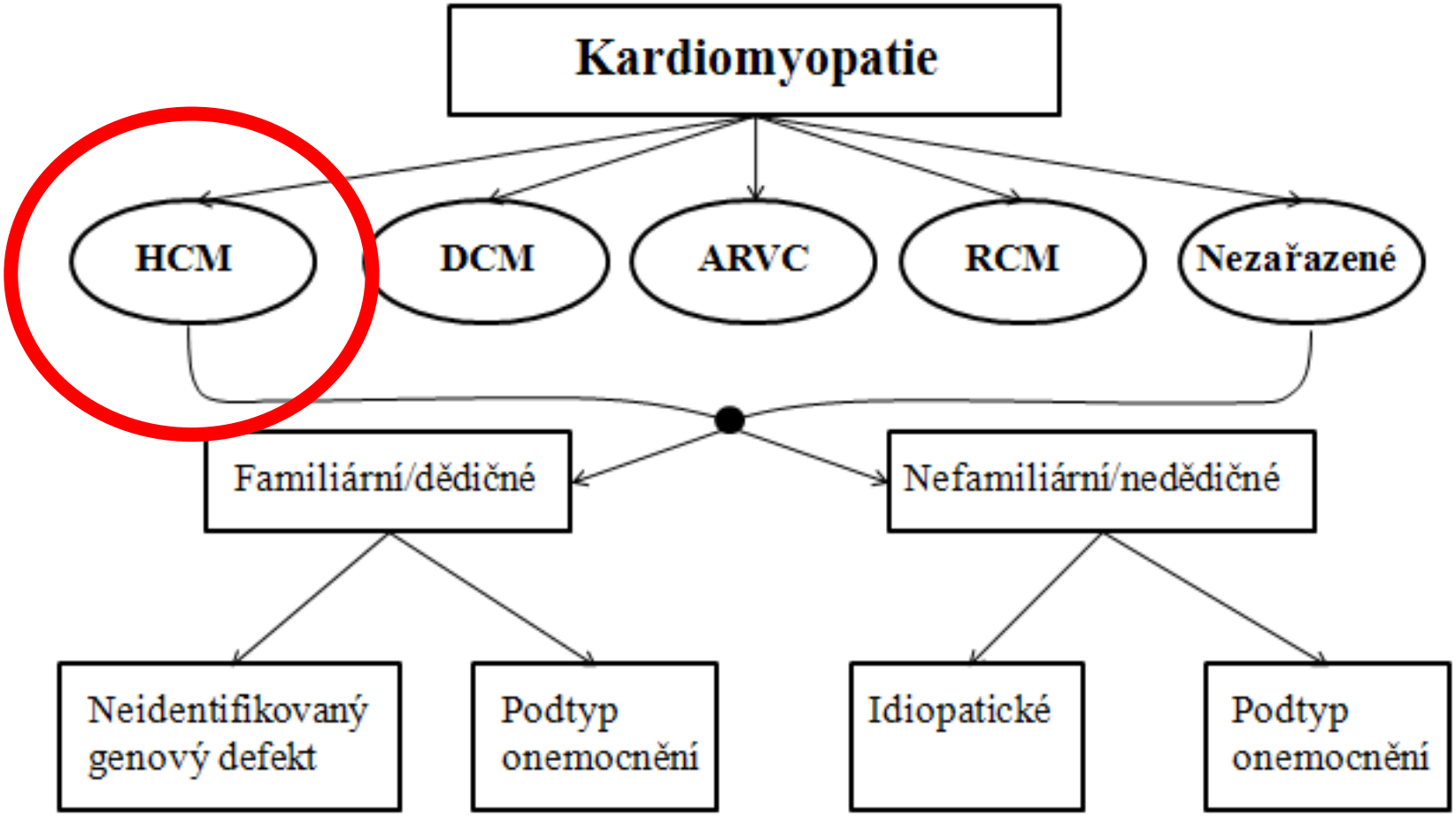
Hypertrofická kardiomyopatie

www.kardiomyopatie.cz

Josef Veselka

Kardiocentrum dospělých
Kardiologická klinika 2. LFUK a FN Motol



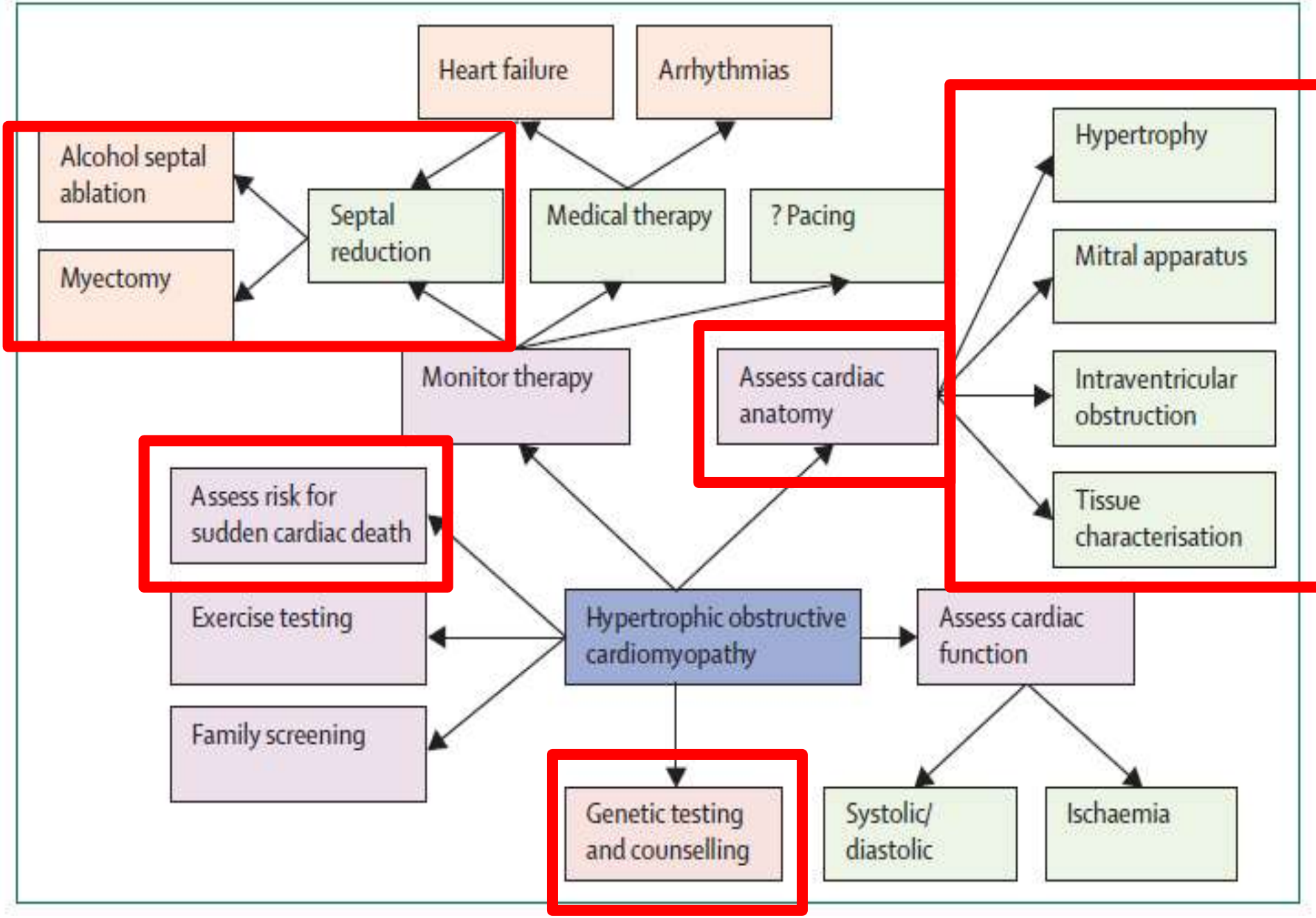
Elliott P et al. Eur Heart J 2014

Definice HCM

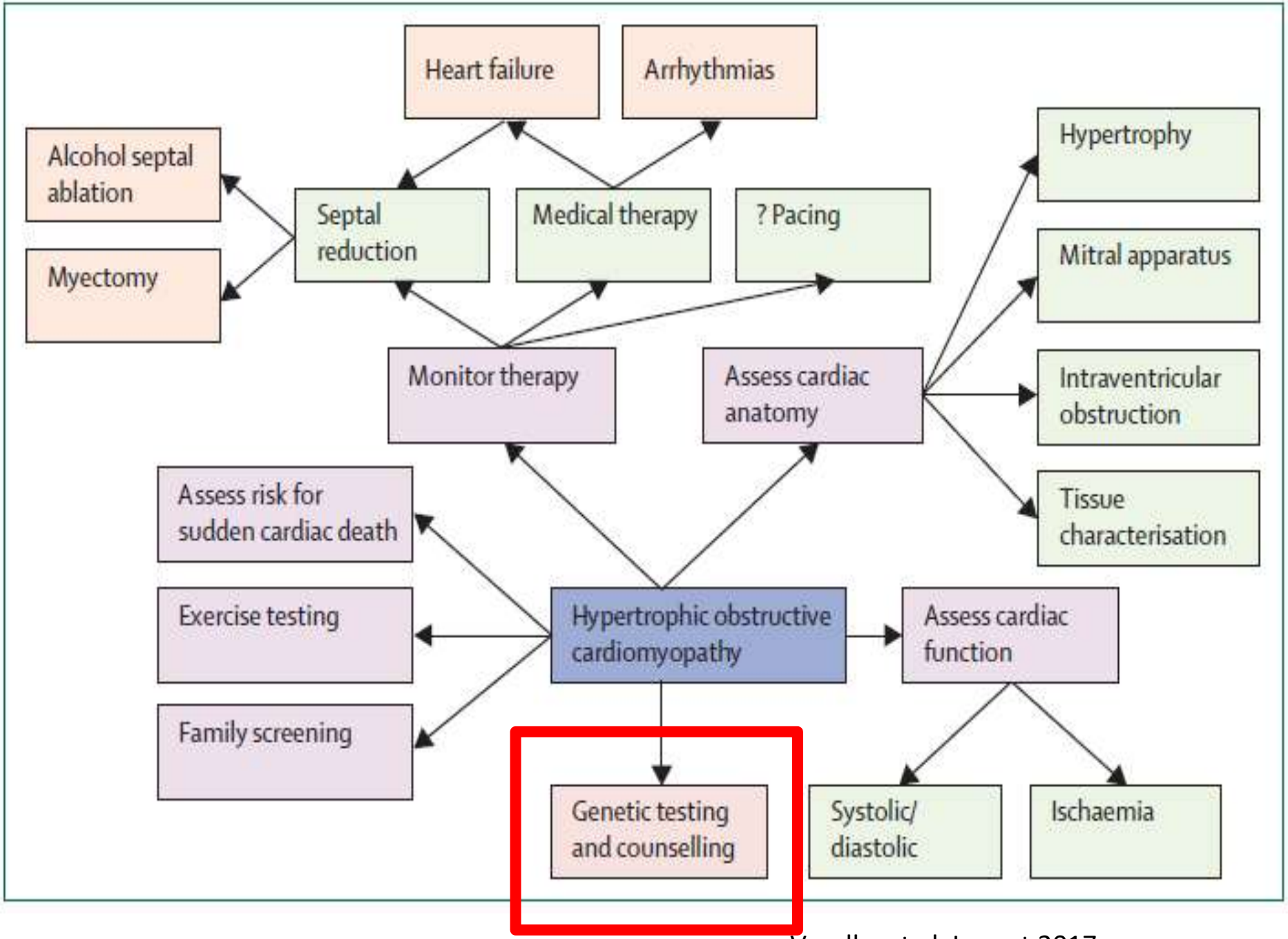
- **Klinická – primární srdeční onemocnění charakterizované jinak nevysvětlitelnou hypertrofií srdce (hypertenze, vada).**

- Patologická – hypertrofie srdce s abnormálním uspořádáním svaloviny doplněné fibrózou a přítomností ložisek abnormální struktury myokardu.
- Genetická – AD dědičné onemocnění způsobené geny kódujícími sarkomerické (i nesarkomerické) proteiny.

Elliott P et al. Eur Heart J 2014

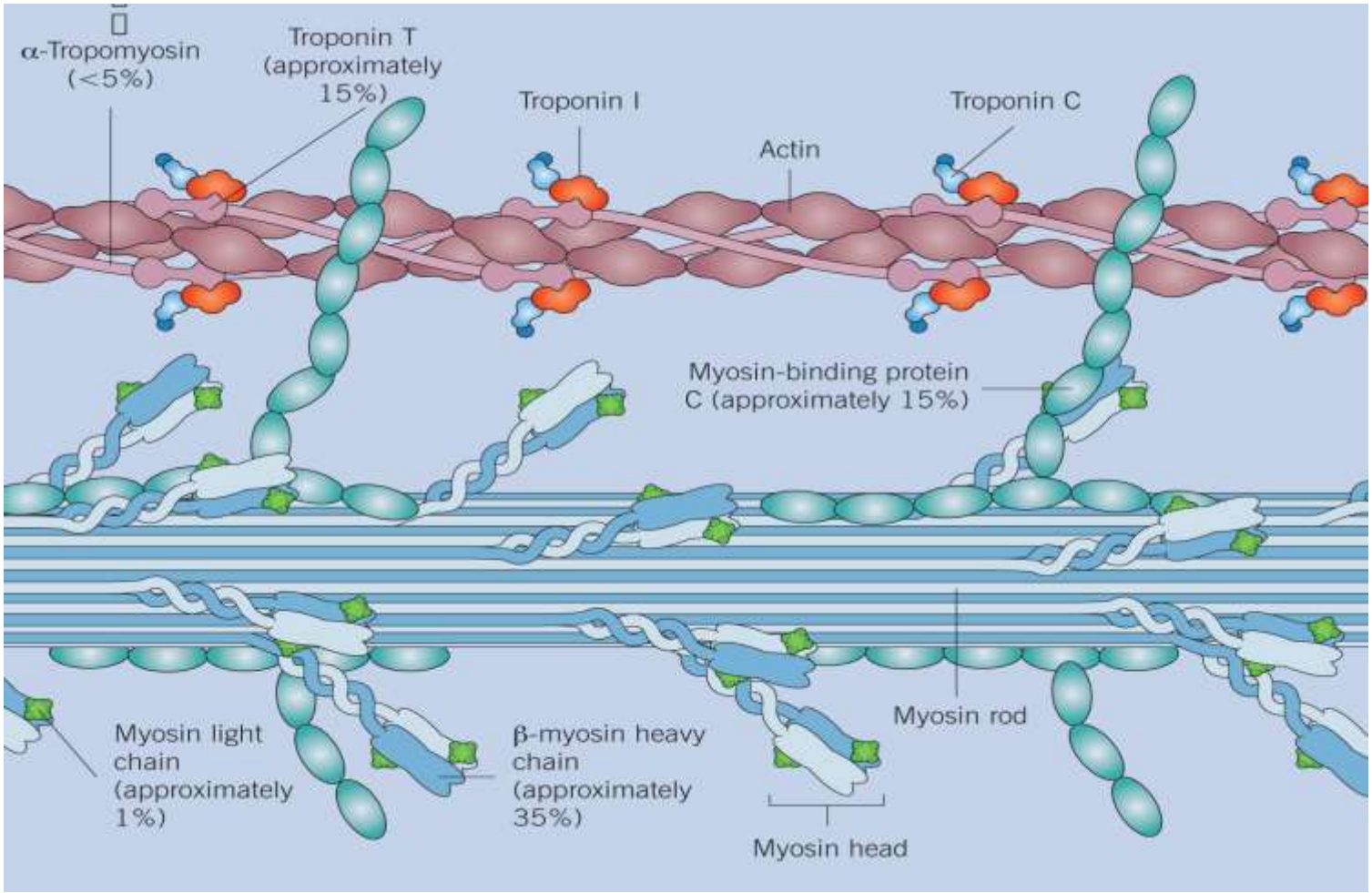


Veselka et al. Lancet 2017

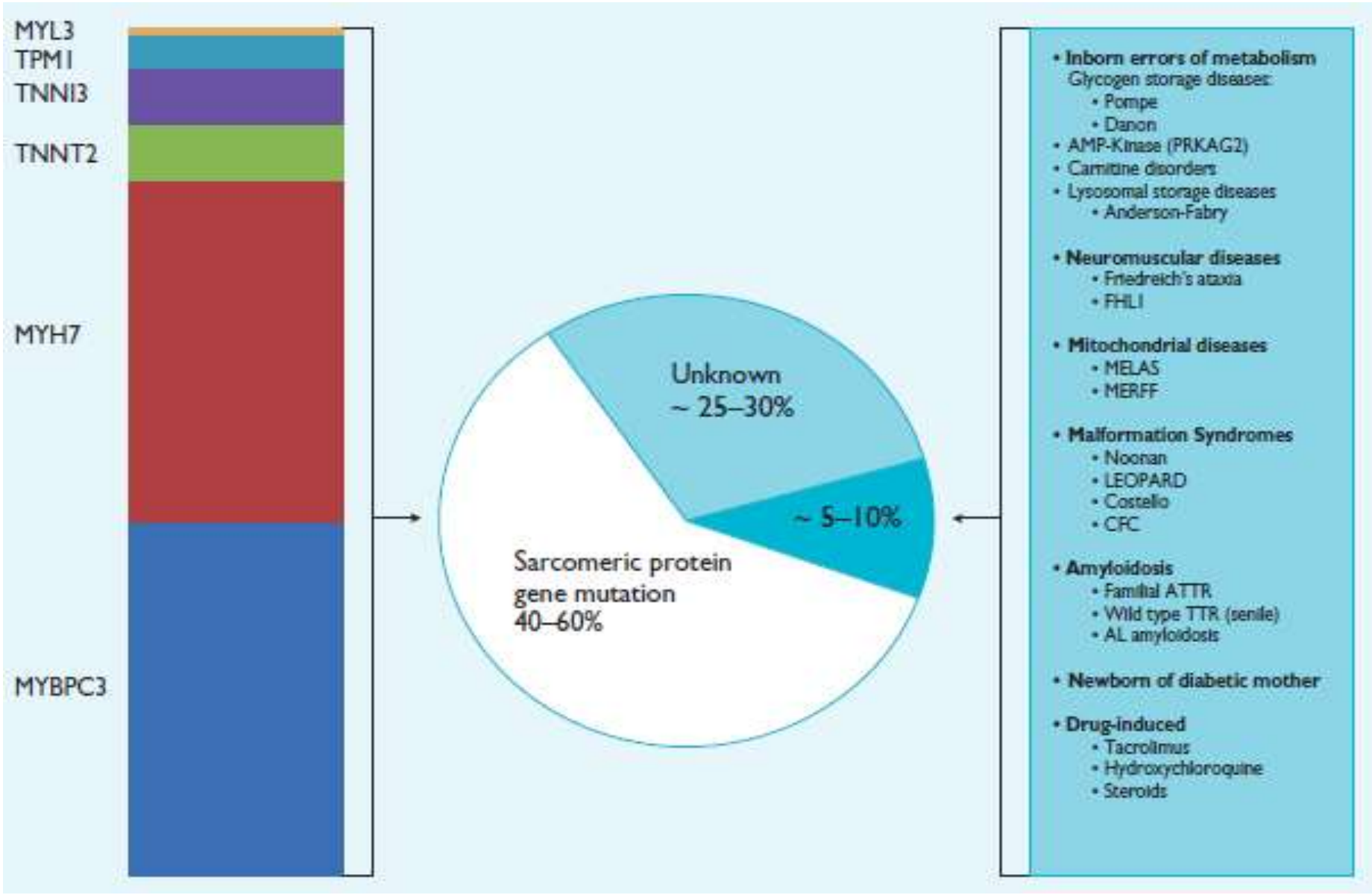


Veselka et al. Lancet 2017

Genetika HCM



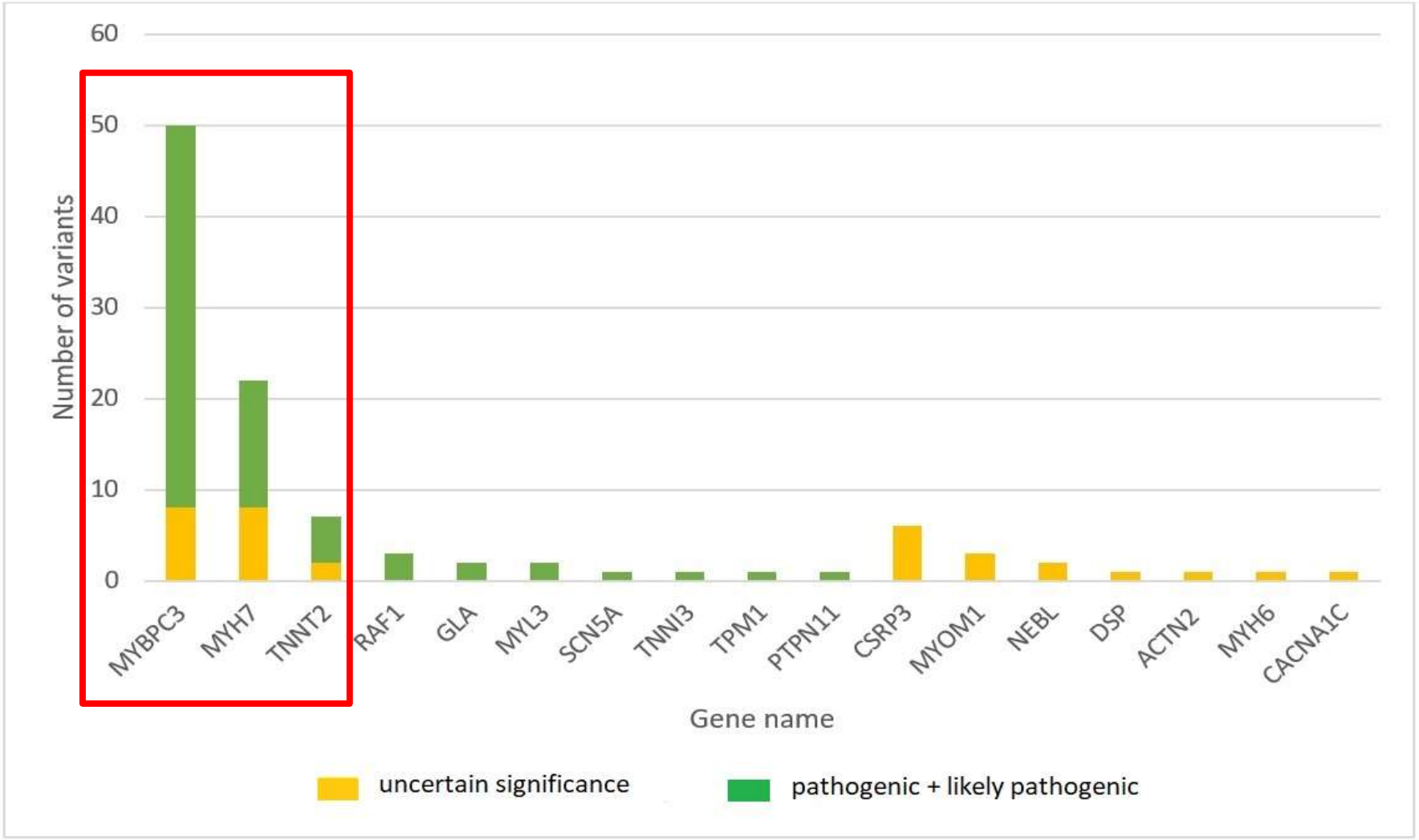
Genotyp HCM



Elliott et al. Eur Heart J 2014

Česká populace

**(336 HCM pac.: 56% mělo genetickou variantu v 71 různých genech;
21% pac. G+ s variantou třídy 4/5 dle ACMG Guidelines)**



Bonaventura J et al. AMS 2019 in press.

G+ versus G-

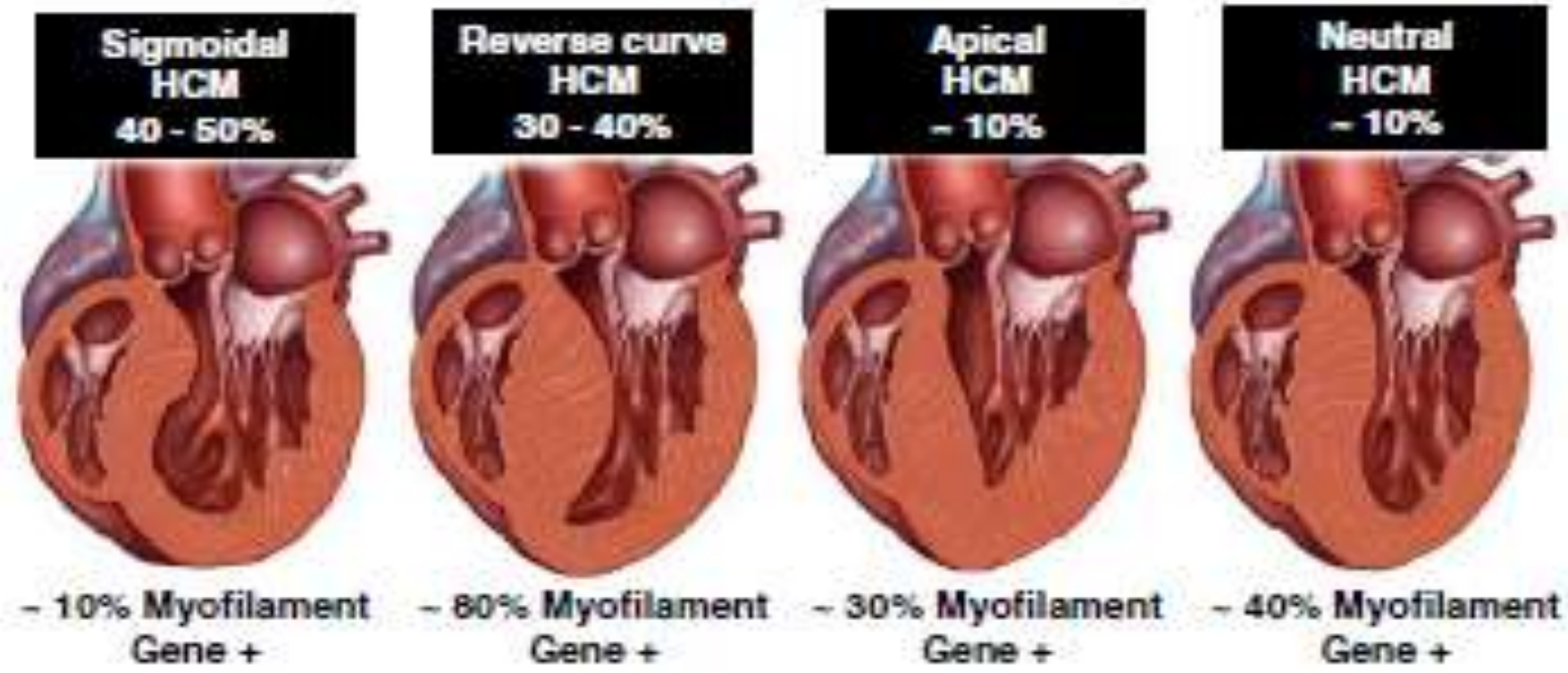
Table VI. Comparison between genotype positive and genotype negative patients

	Genotype positive	Genotype negative	*p* value
N (%)	70 (21)	266 (79)	
Age at diagnosis (years)	44.5 ± 15.6	55.6 ± 13.9	< 0.01
Female sex, n (%)	26 (37)	113 (42)	0.42
FH of HCM, n (%)	15 (21)	22 (8)	0.04
FH of SCD, n (%)	6 (9)	10 (4)	0.75
Arterial hypertension, n (%)	18 (25)	138 (52)	< 0.01
MLVWT (mm)	20.7 ± 4.5	19.6 ± 4.6	0.43
Septal shape, n (%)			
Sigmoid	11 (16)	86 (32)	0.01
Reverse curve	28 (40)	64 (24)	0.01
Neutral	29 (41)	110 (41)	> 0.99
Apical	2 (3)	5 (2)	0.64
Obstruction, n (%)	50 (71)	180 (53)	< 0.01
LVOT gradient (mmHg)	77.8 ± 10.9	76.6 ± 5.3	0.92

*Plus–minus values are means ± SD. FH - family history, HCM - hypertrophic cardiomyopathy, SCD - sudden cardiac death, MLWVT - maximum left ventricular wall thickness, LVOT - left ventricular outflow tract

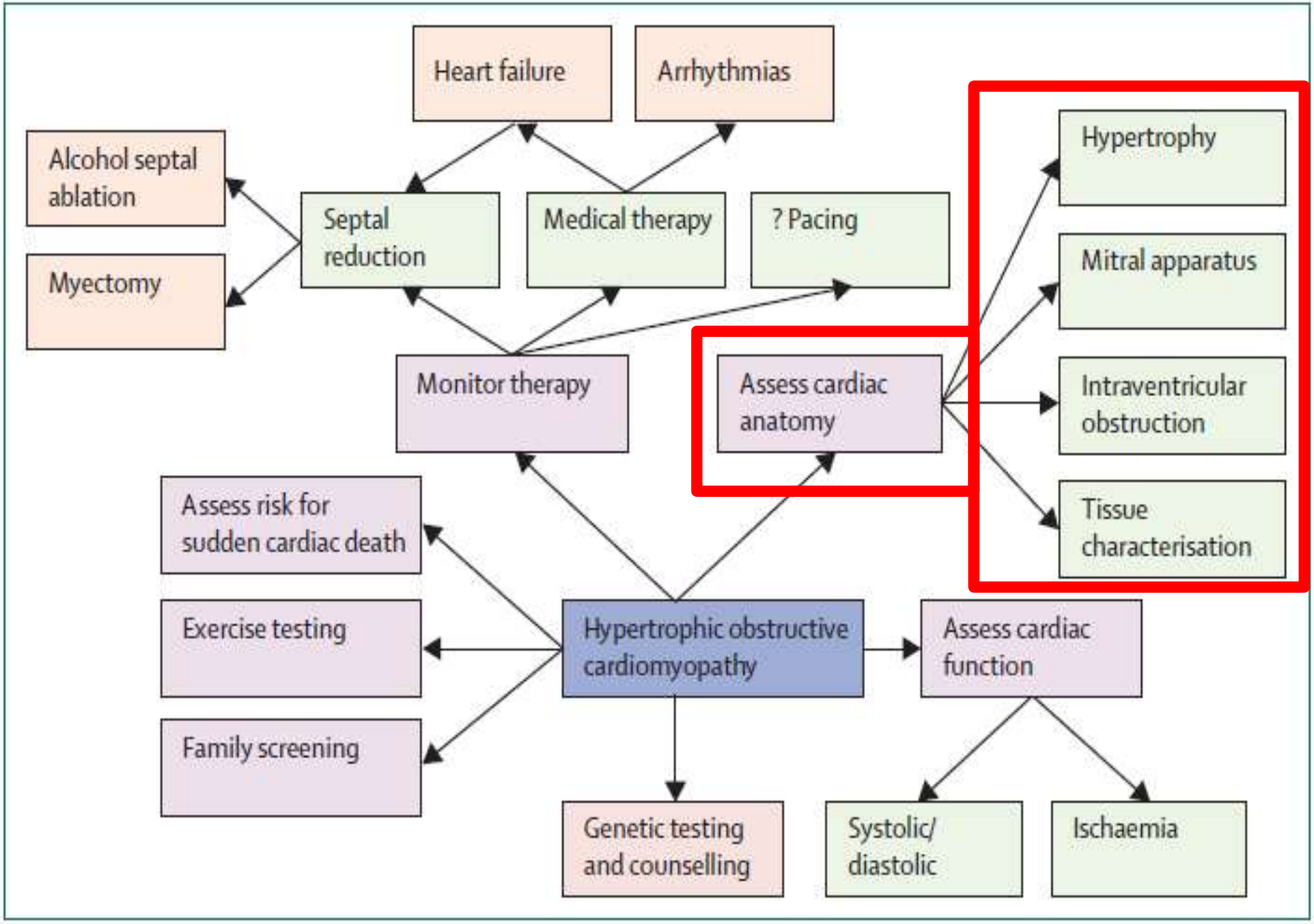
Bonaventura J et al. AMS 2019 in press

Genetika HCM



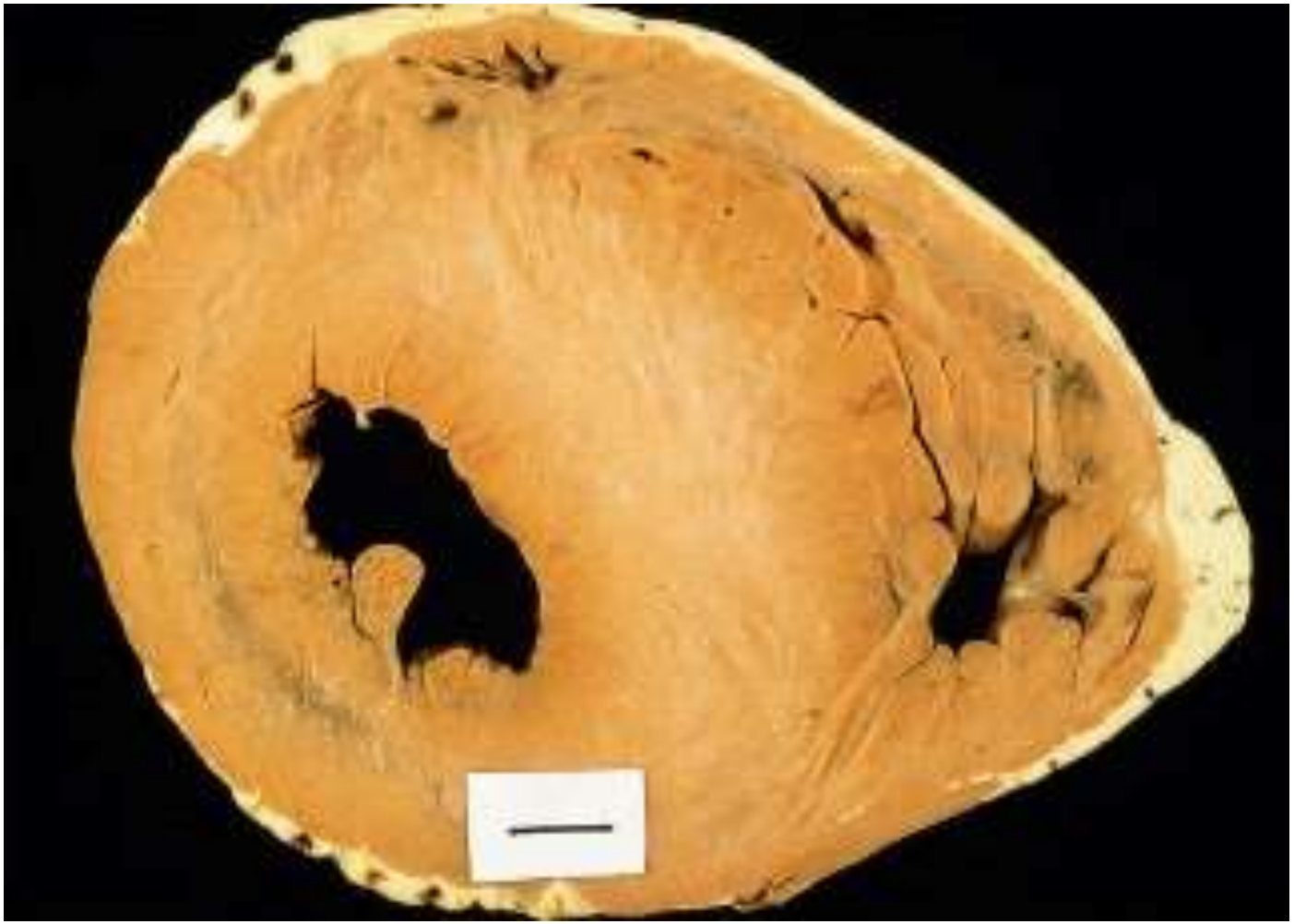
Vyšetřujeme nositele výrazného fenotypu a případně rodinné příslušníky (prvostupňové) a sportovce (druhostupňové)

Bos JM et al. JACC 2009

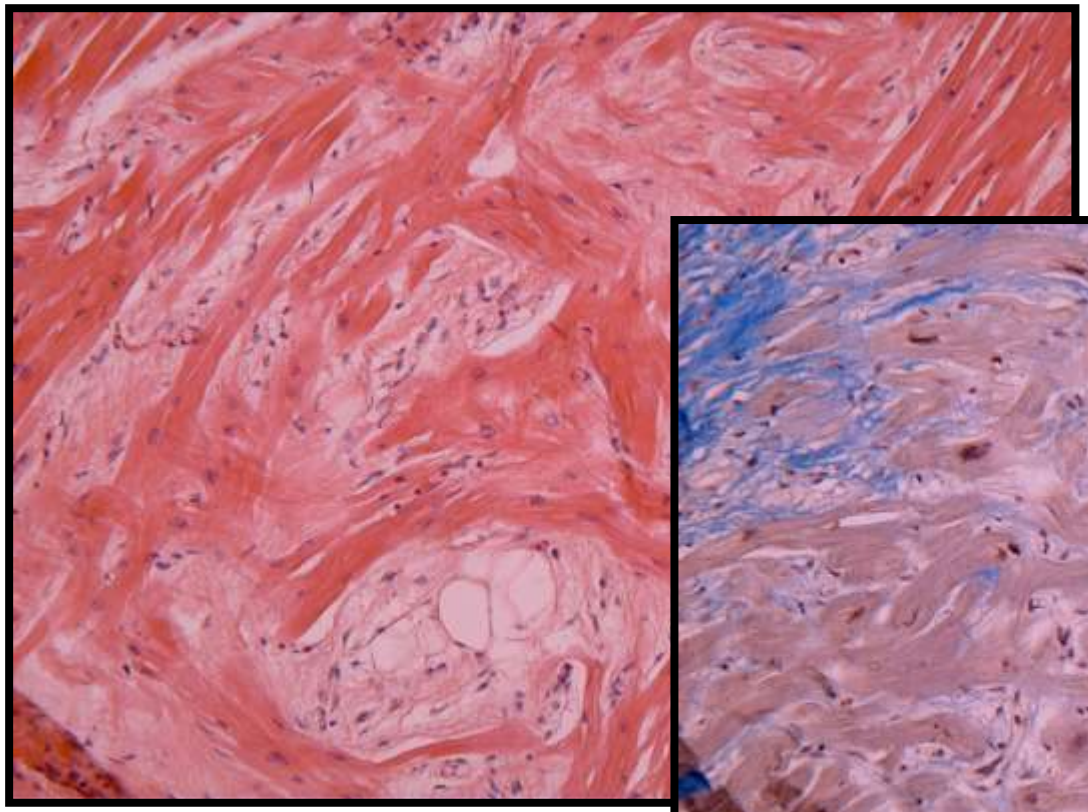


Veselka et al. Lancet 2017

Patologicko – anatomický obraz

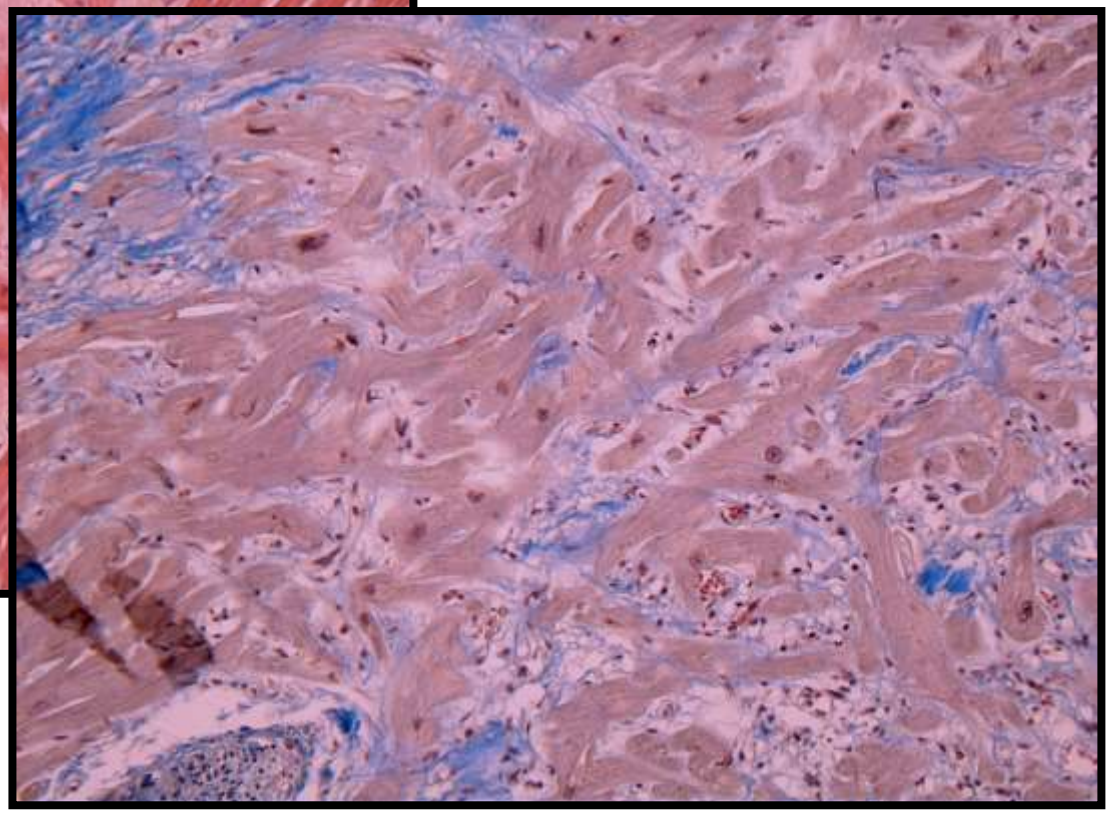


Mikroskopický obraz – „disarray“

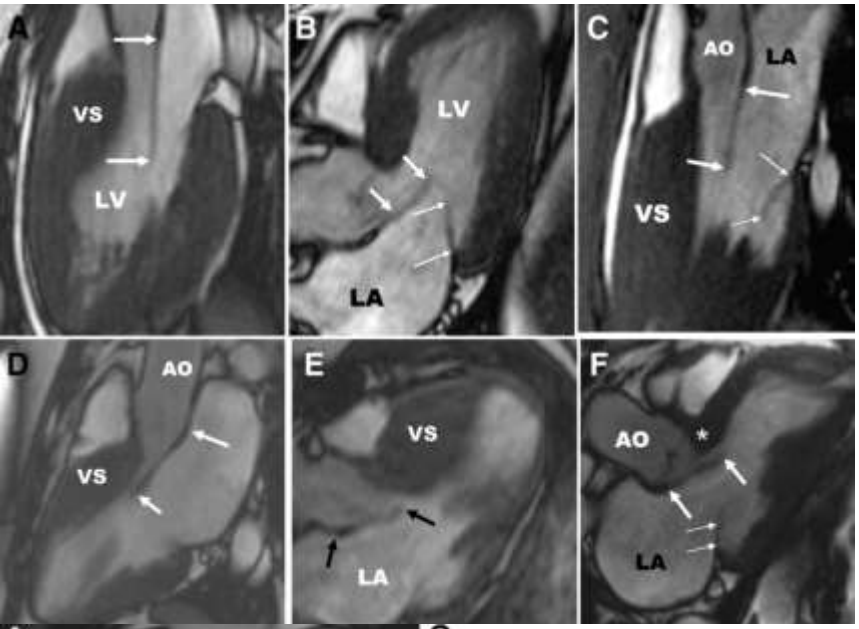


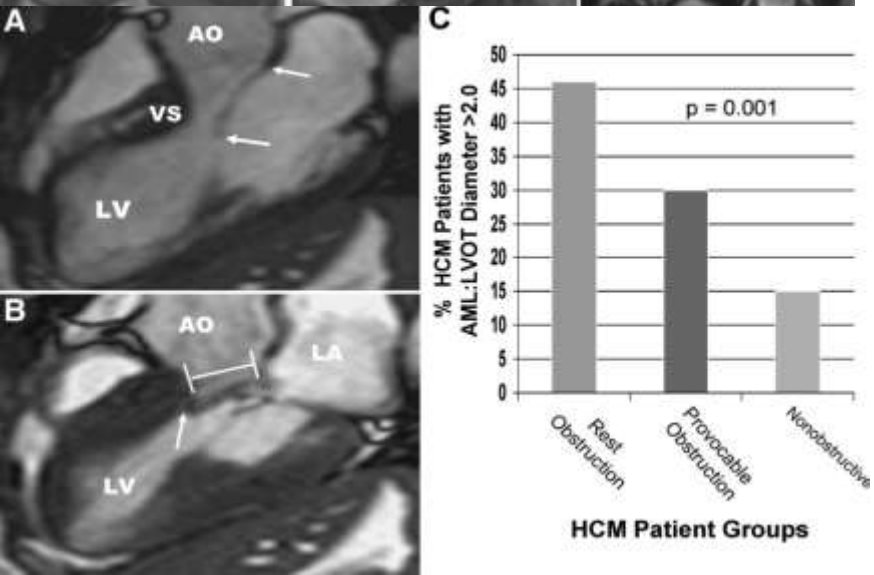
Barvení hematoxilyn-eosin

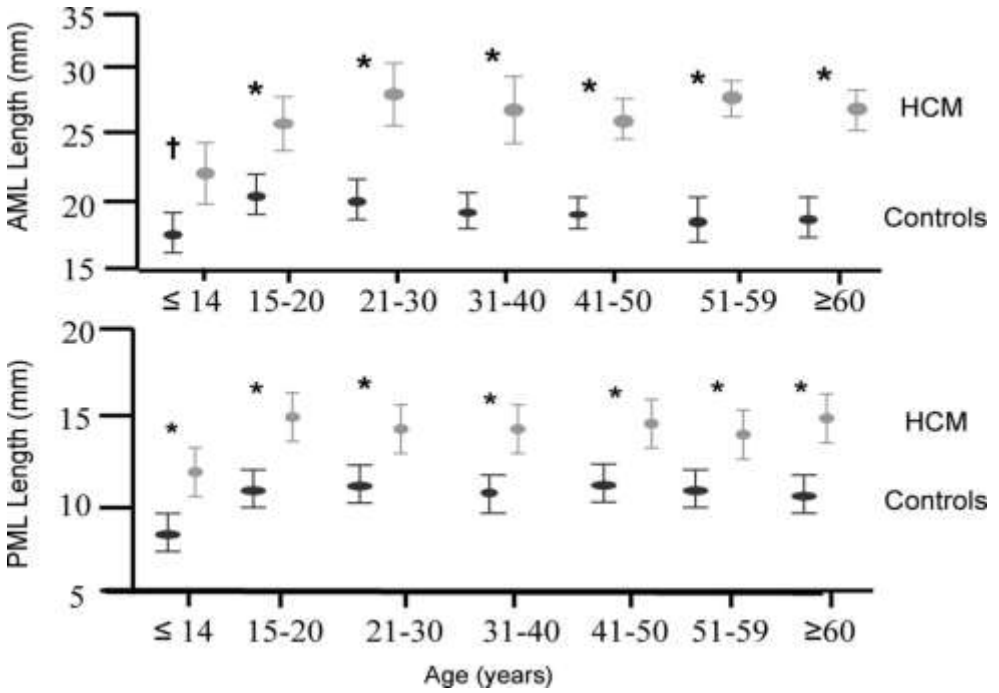
Barvení „modrý“ trichróm



Mitrální chlopeň







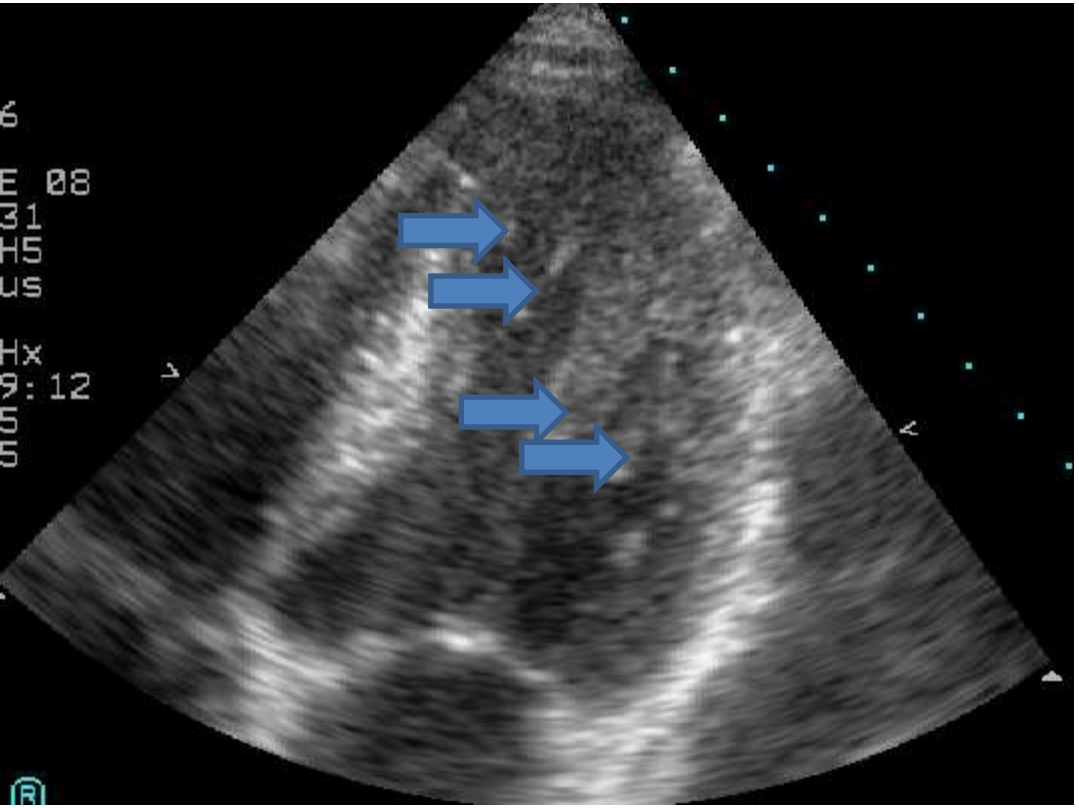
Conclusions—In HCM, mitral valve leaflets are elongated independently of other disease variables, likely constituting a primary phenotypic expression of this heterogeneous disease, and are an important morphological abnormality responsible for LV outflow obstruction in combination with small outflow tract dimension.

Maron MS et al. Circulation 2011

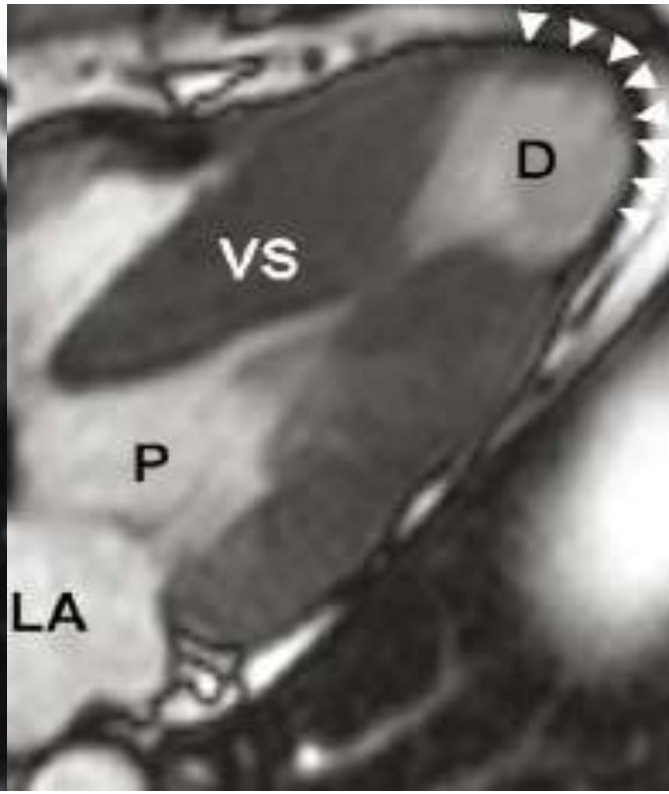
Přímá inzerce PM do Mi chlopně

Anomalies of PMs / apical HCM

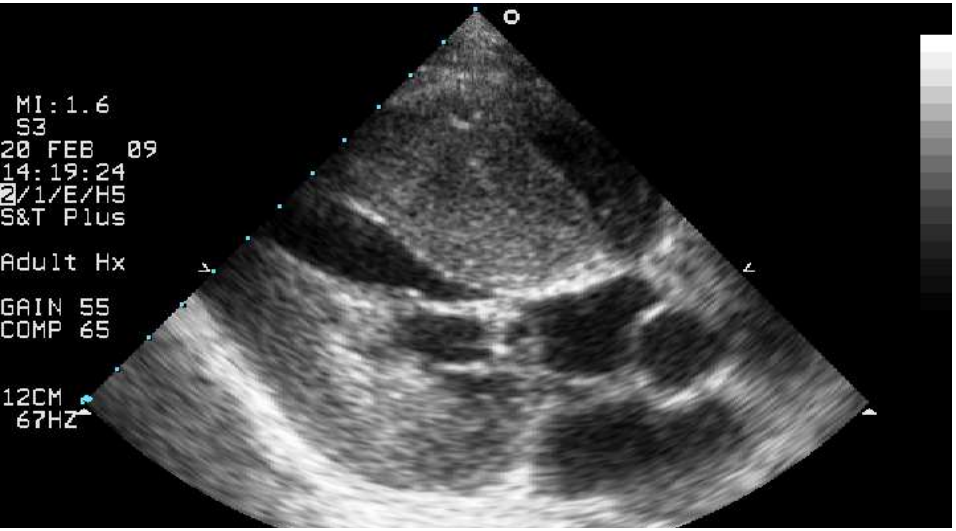
(significant for non-pharmacological therapy)

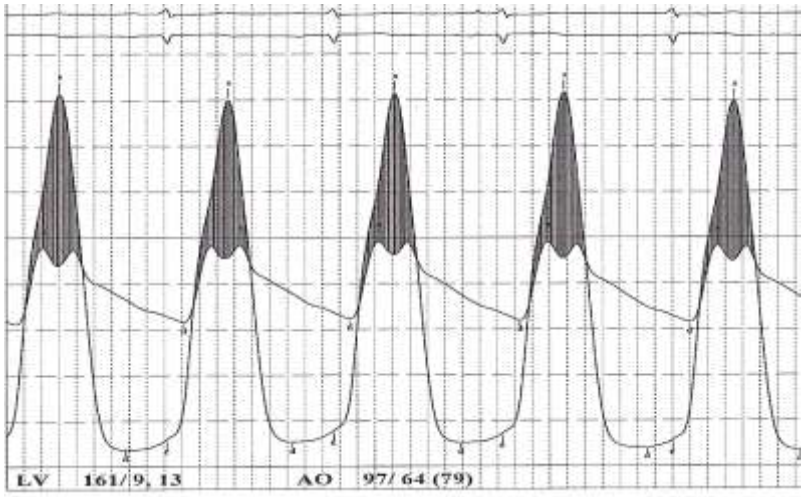


Katenoidní septum a apikální aneurysma

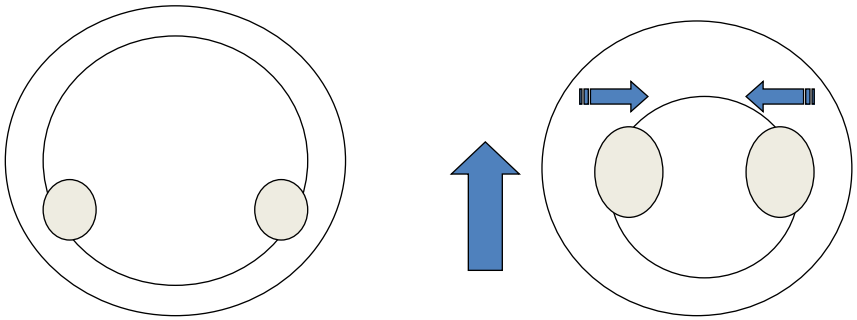


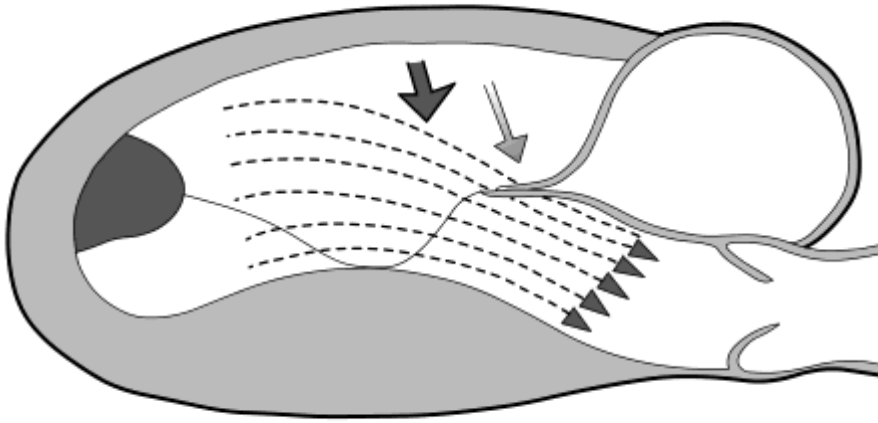
Nitrokomorová obstrukce





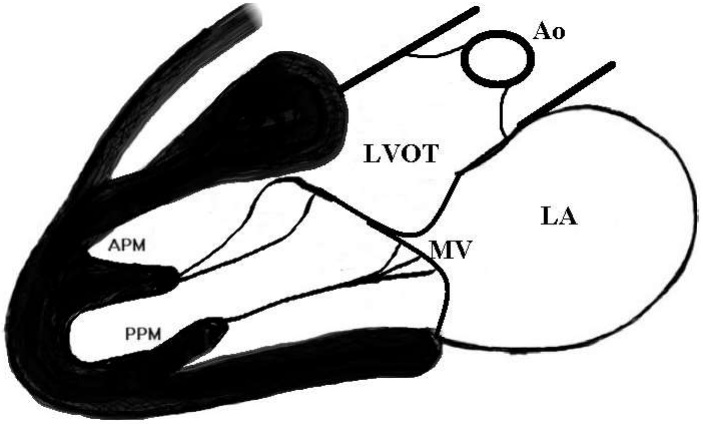
Změna morfologie a lokalizace papilárních svalů



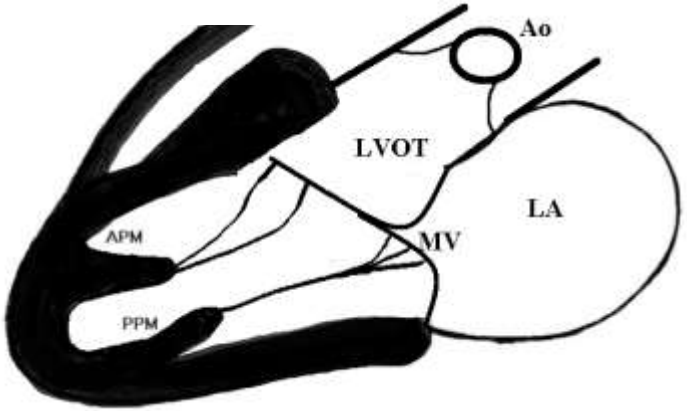


Mechanismus obstrukce

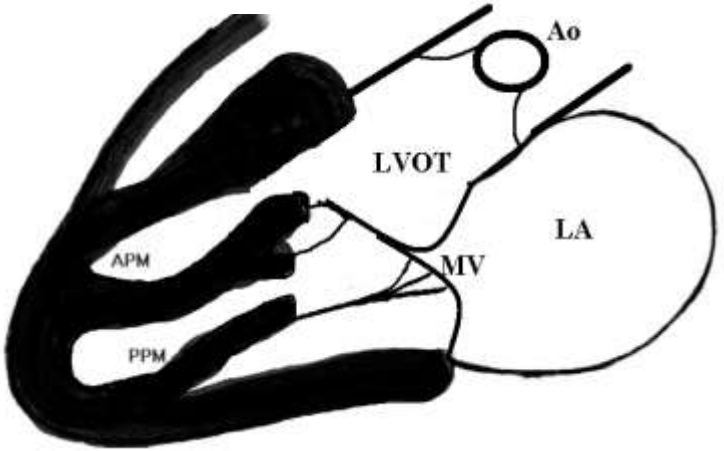
- Septální



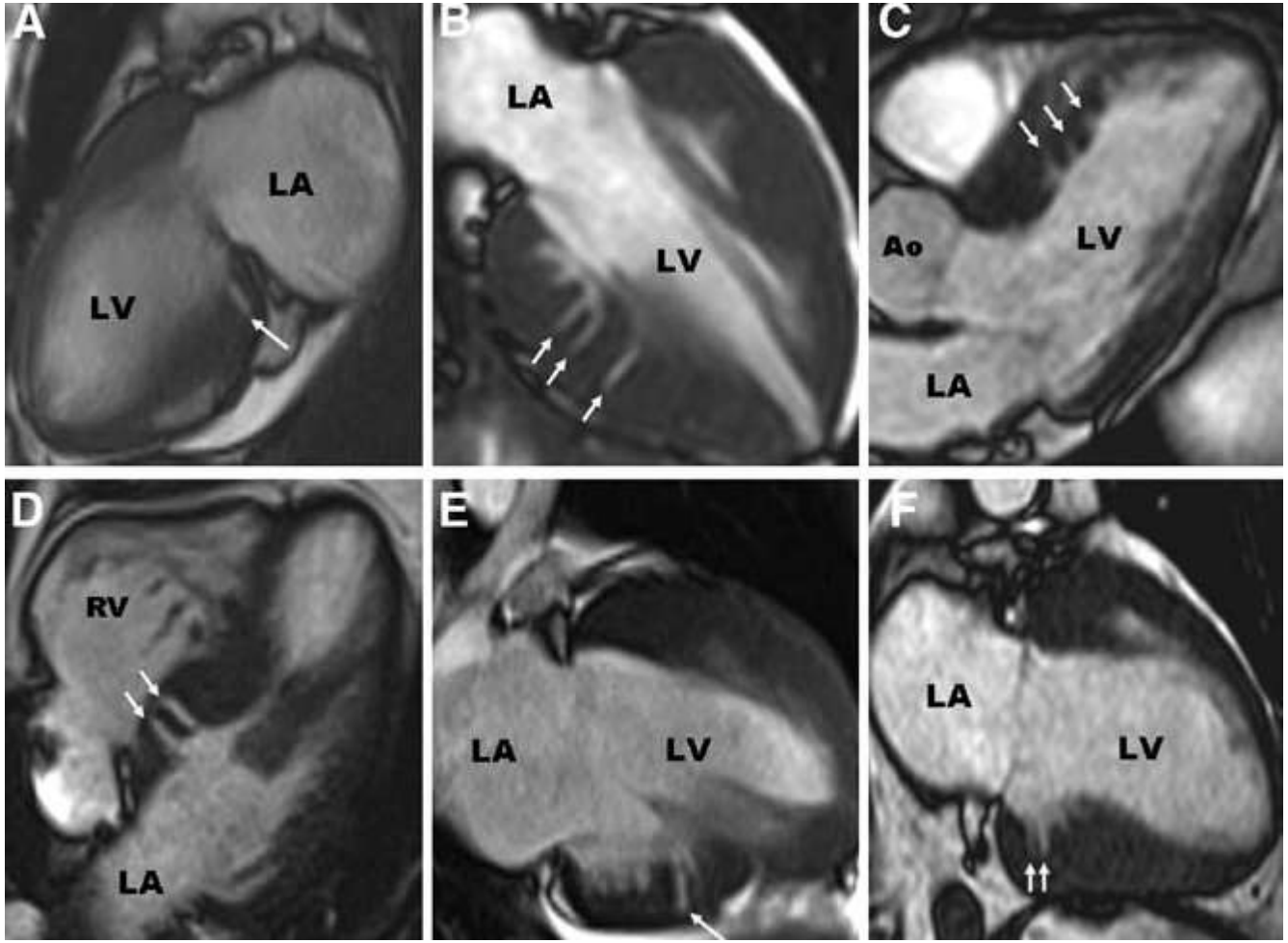
- Mitrální



- Papilární



Krypty



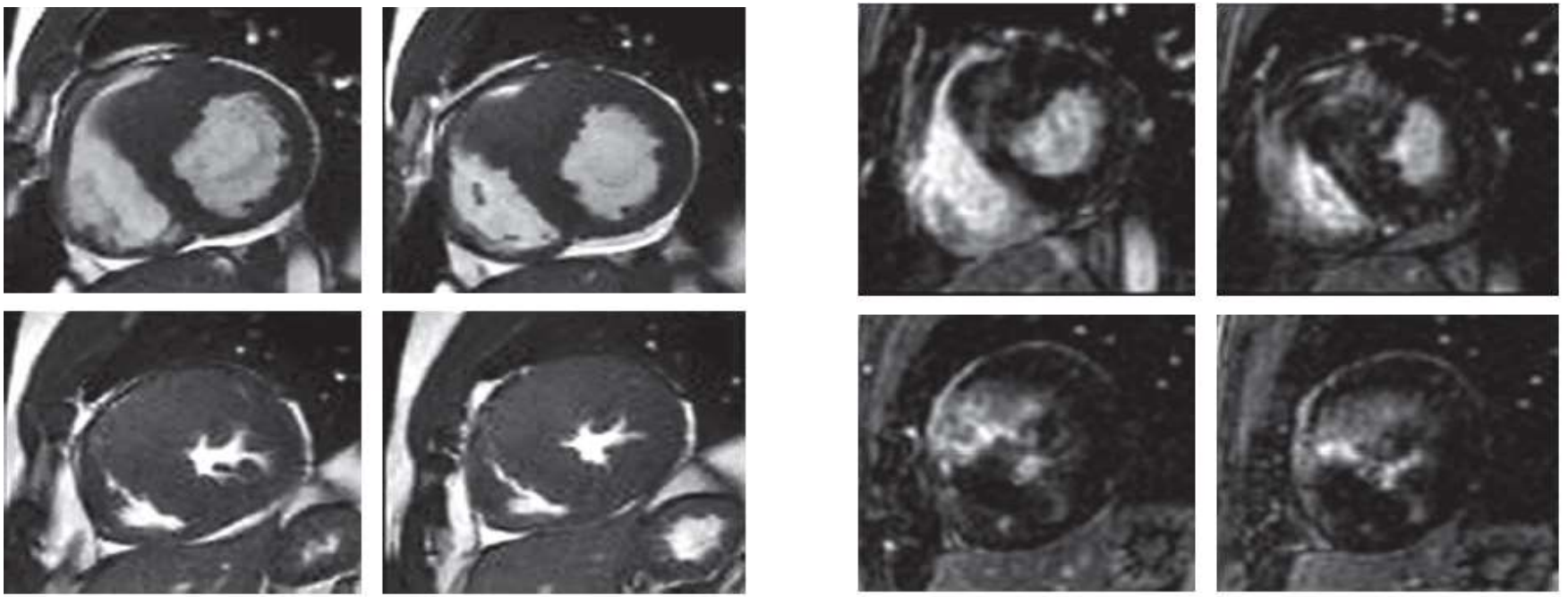
Maron MS et al. Circ Cardiovasc Imag

Each patient needs optimal therapeutic option and experienced physician/center

3D Model

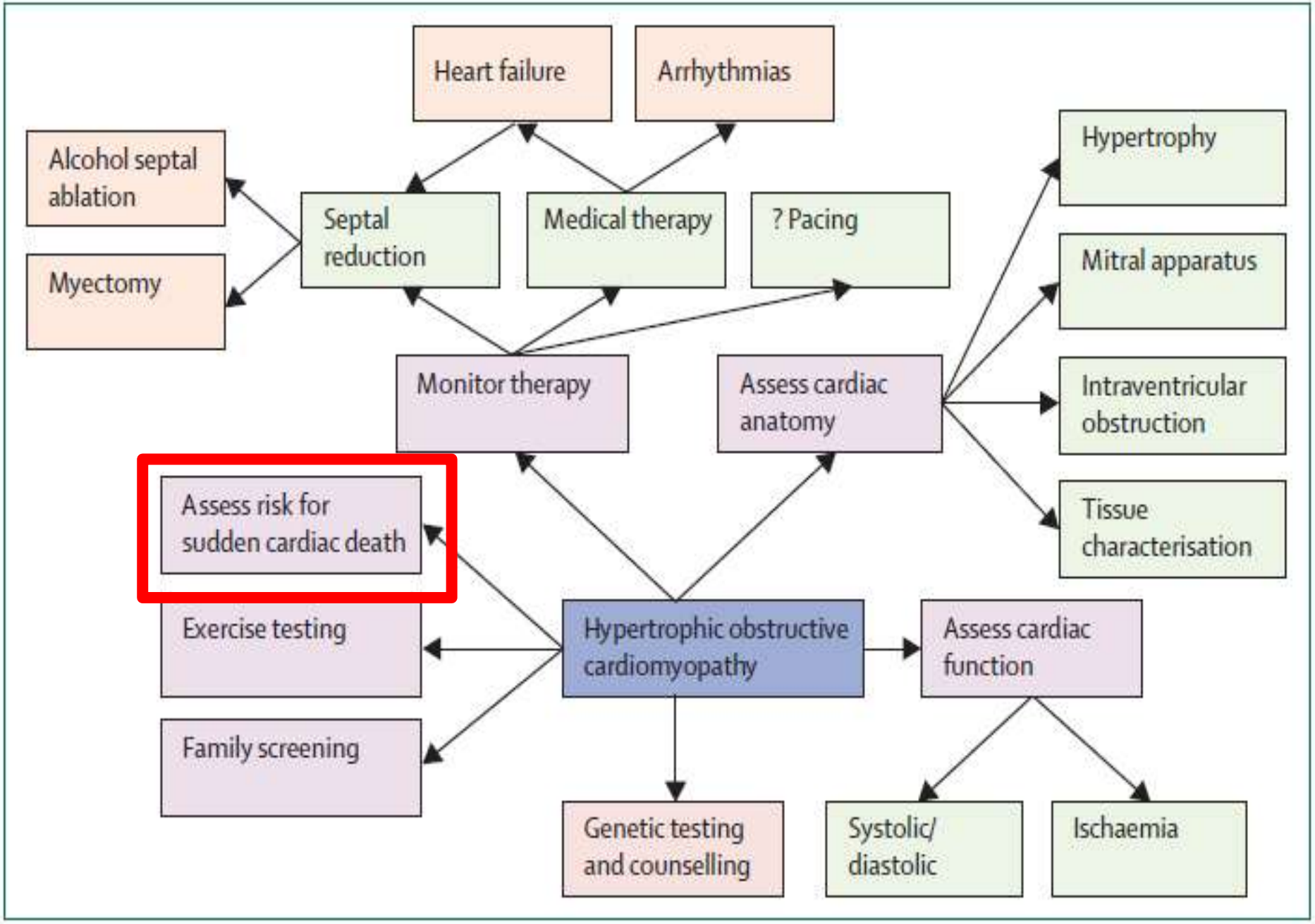
Veselka et al. IJA 2018

CMR



indicated a significant association between myocardial fibrosis, as suggested by LGE on cardiac magnetic resonance, and sudden cardiac death or aborted sudden cardiac death.[64] The extent of LGE appears to correlate with the combined risk of sudden mortality events.[56,65]

Veselka et al. Lancet 2017



Veselka et al. Lancet 2017

Prognóza

- **Náhlá smrt**
- Nejčastější příčina NS u sportovců
- Jedna z nejčastějších příčin NS u mladých lidí.
- Obstrukce je rizikem přežívání

- **Mortalitní příhody**
- 2% u dětí a mladistvých
- 1% u dospělých

I přes léčbu odhadujeme riziko úmrtí v souvislosti s HCM na 1% ročně!

Veselka J et al. Lancet 2017

All-cause mortality

(95% confidence intervals)

A total of 171 (13%) patients died during 7057 patient-years of follow-up, indicating a post-ASA all-cause mortality rate of 2.42 (95% CI, 2.07–2.82) deaths per 100 patient-years.

Veselka et al. Eur Heart J 2016

Riziko náhlé smrti

- **Velká kriteria**

- **Spontánně vznikající komorové tachykardie**
- **Anamnéza kardiopulmonální resuscitace**

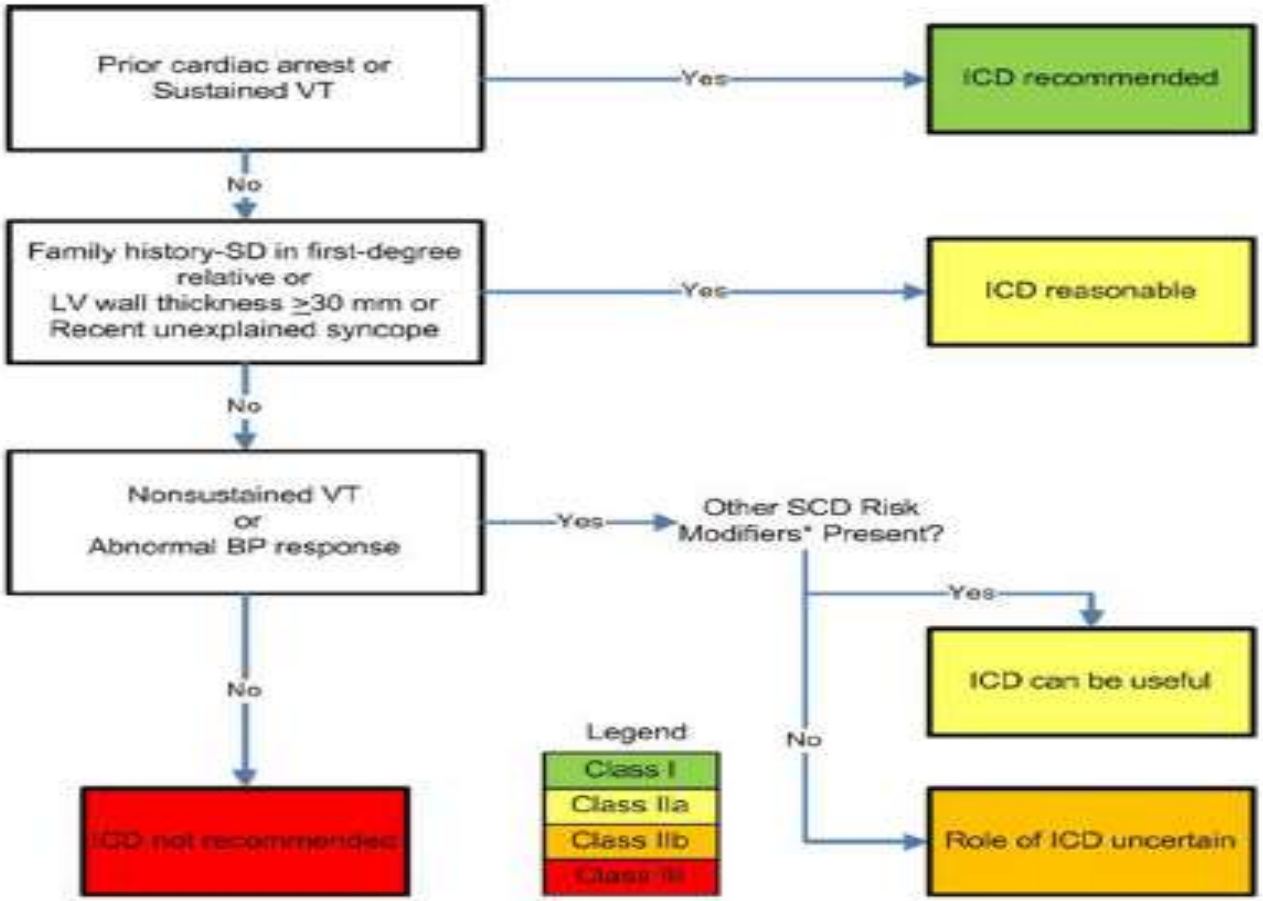
- **Synkopa nejasné etiologie**
- **Rodinná anamnéza náhlé smrti**
- **Tloušťka stěny LK > 30 mm**

- **Hypotenzní reakce na zátěž**
- **NS VT**

- **Malá kriteria**

- **Koronární nemoc**
- **Mikrovaskulární dysfunkce**
- **Nitrokomorová obstrukce > 30 mmHg**
- **„Maligní“ genotyp**
- **Rozsáhlá fibróza myokardu**

Riziko NS dle ACC/AHA Guidelines



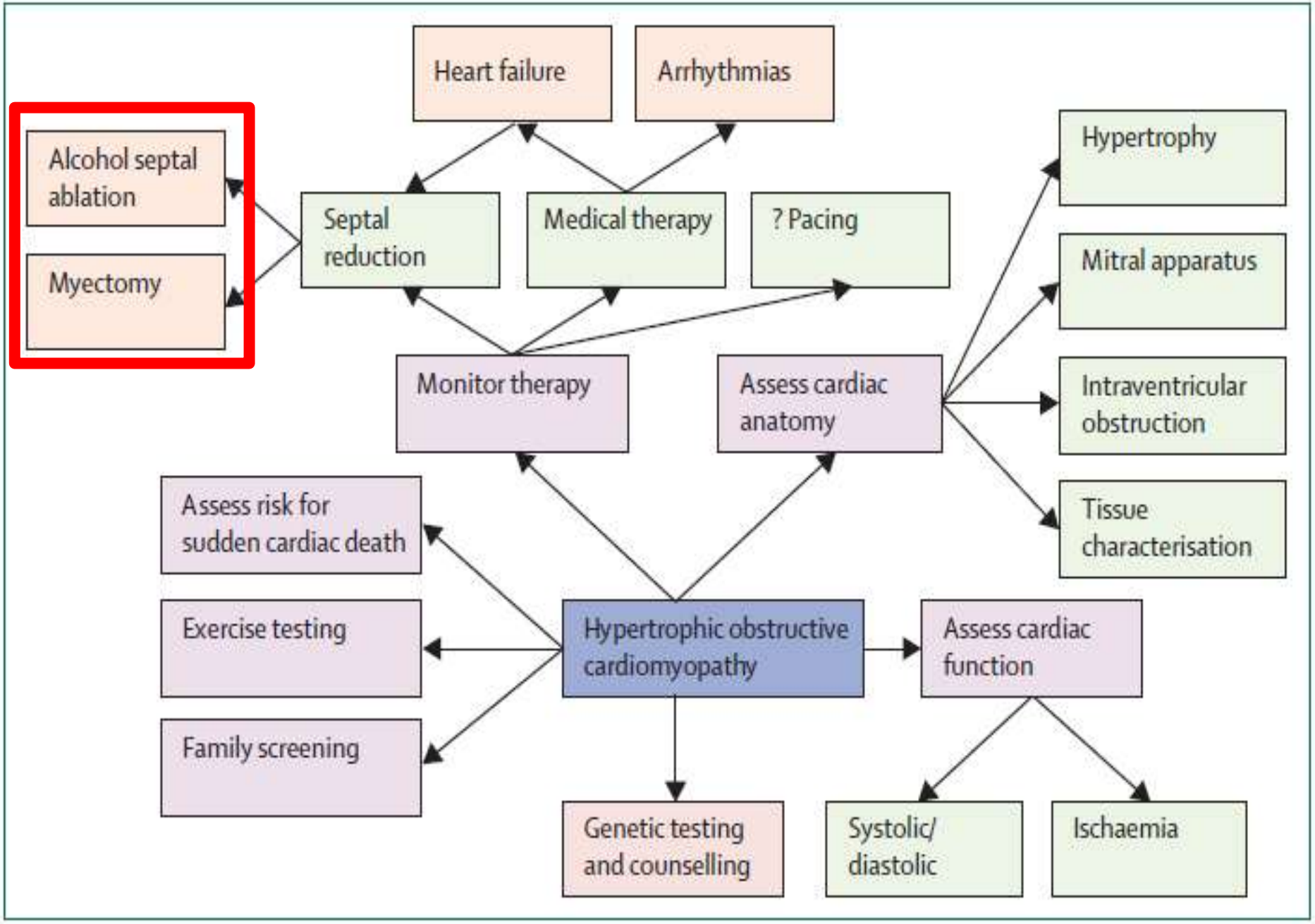
Gersh et al. JACC 2011

HCM Risk-SCD Calculator

Age	30	**Years**	*Age at evaluation*
Maximum LV wall thickness	22	**mm**	*Transthoracic Echocardiographic measurement*
Left atrial size	54	**mm**	*Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane at time of evaluation*
Max LVOT gradient	56	**mmHg**	*The maximum LV outflow gradient determined at rest and with Valsalva provocation (irrespective of concurrent medical treatment) using pulsed and continuous wave Doppler from the apical three and five chamber views. Peak outflow tract gradients should be determined using the modified Bernouilli equation: Gradient= $4V^2$, where V is the peak aortic outflow velocity*
Family History of SCD	(•) No ( ) Yes		*History of sudden cardiac death in 1 or more first degree relatives under 40 years of age or SCD in a first degree relative with confirmed HCM at any age (post or ante-mortem diagnosis).*
Non-sustained VT	(•) No ( ) Yes		*3 consecutive ventricular beats at a rate of 120 beats per minute and <30s in duration on Holter monitoring (minimum duration 24 hours) at or prior to evaluation.*
Unexplained syncope	(•) No ( ) Yes		*History of unexplained syncope at or prior to evaluation.*

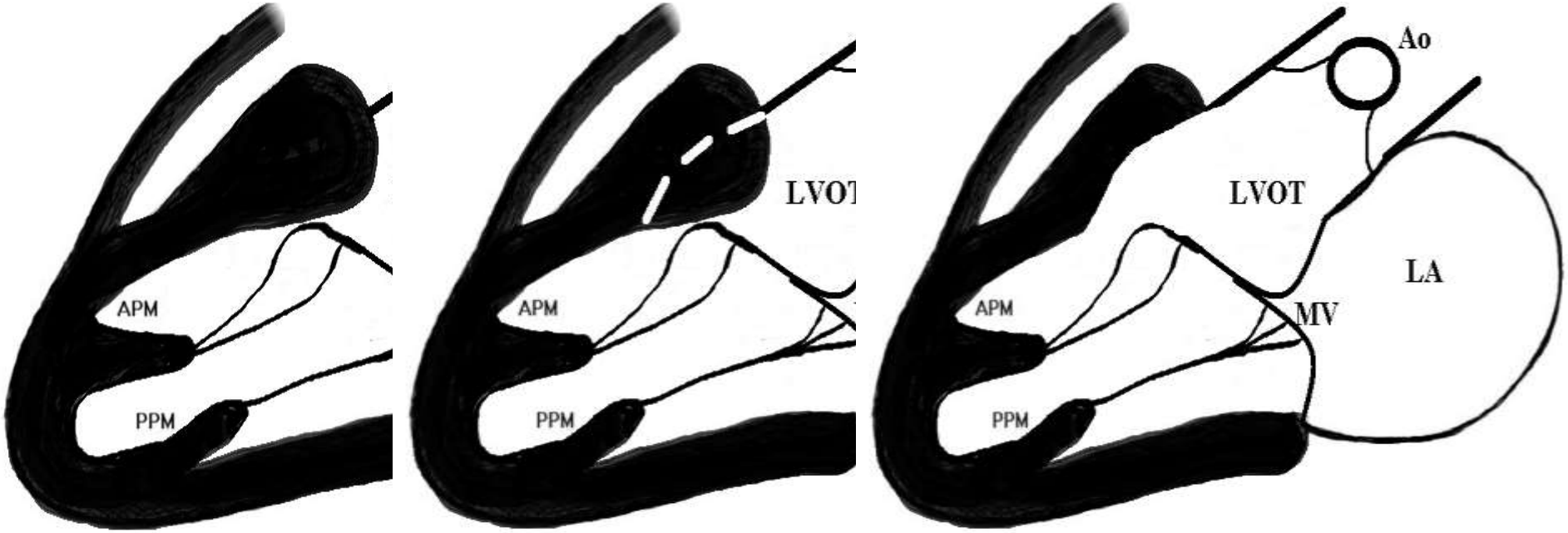
Risk of SCD at 5 years (%):	4.75
ESC recommendation:	ICD may be considered

O´Mahony et al. Eur Heart J 2014



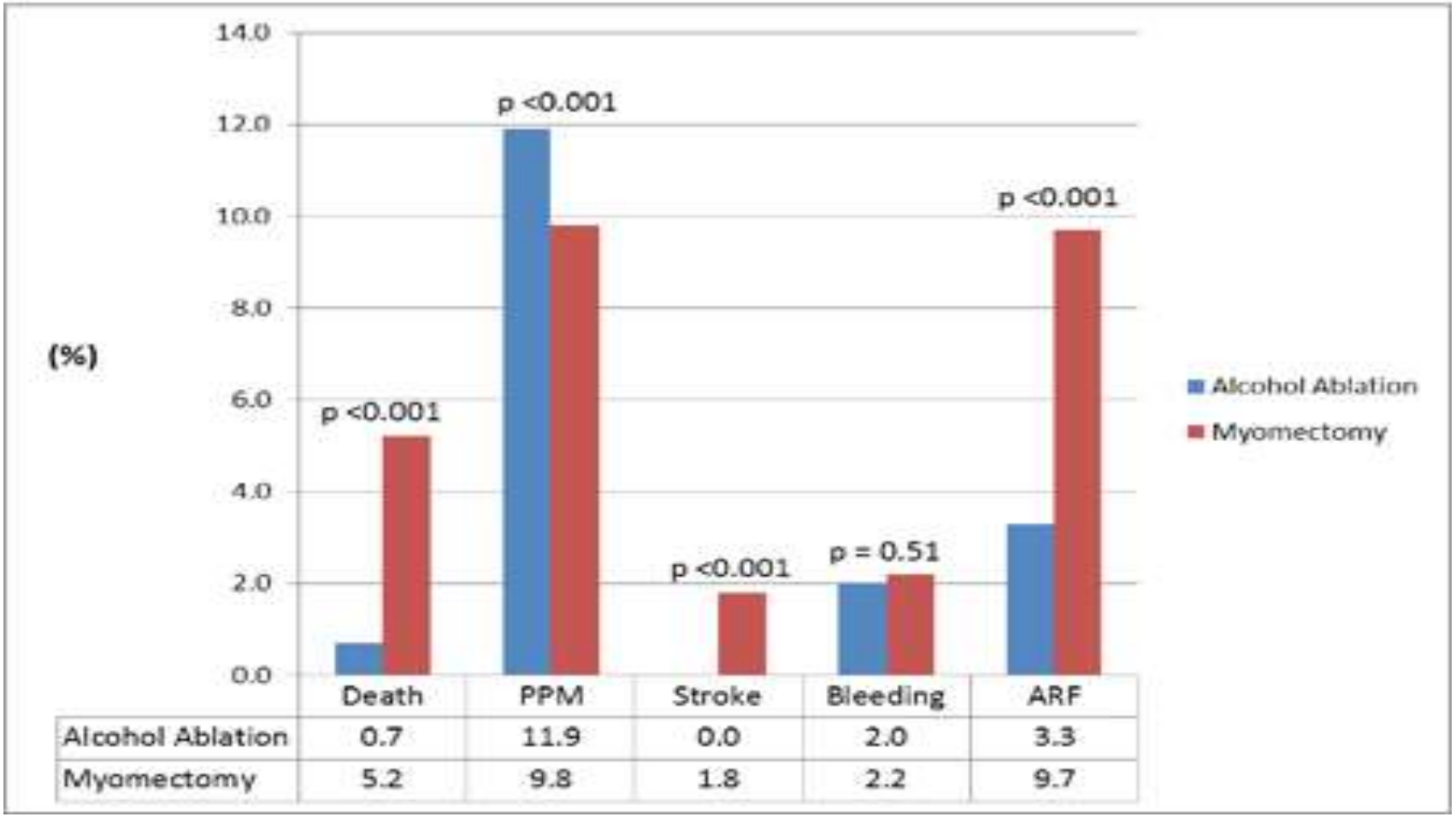
Veselka et al. Lancet 2017

Septal reduction therapy



Septal Myectomy is Associated With Worse In-Hospital Outcomes than Alcohol Septal Ablation: Data From the Nationwide Inpatient Sample in the United States, 2003-2011

Figure 1. Adverse In-Hospital Event Rates after Alcohol Septal Ablation and Septal Myectomy.



	Death	PPM	Stroke	Bleeding	ARF
Alcohol Ablation	0.7	11.9	0.0	2.0	3.3
Myomectomy	5.2	9.8	1.8	2.2	9.7

Kim et al. JAMA Cardiol 2016

Procedure-related mortality in the Central Europe

Comparison of ASA and Myectomy

All-comers study (registry, 5 countries, 9 centers)

Myectomy

35 pts; 49±17 years

Mortality: 14%

ASA

459 pts; 57±13 years

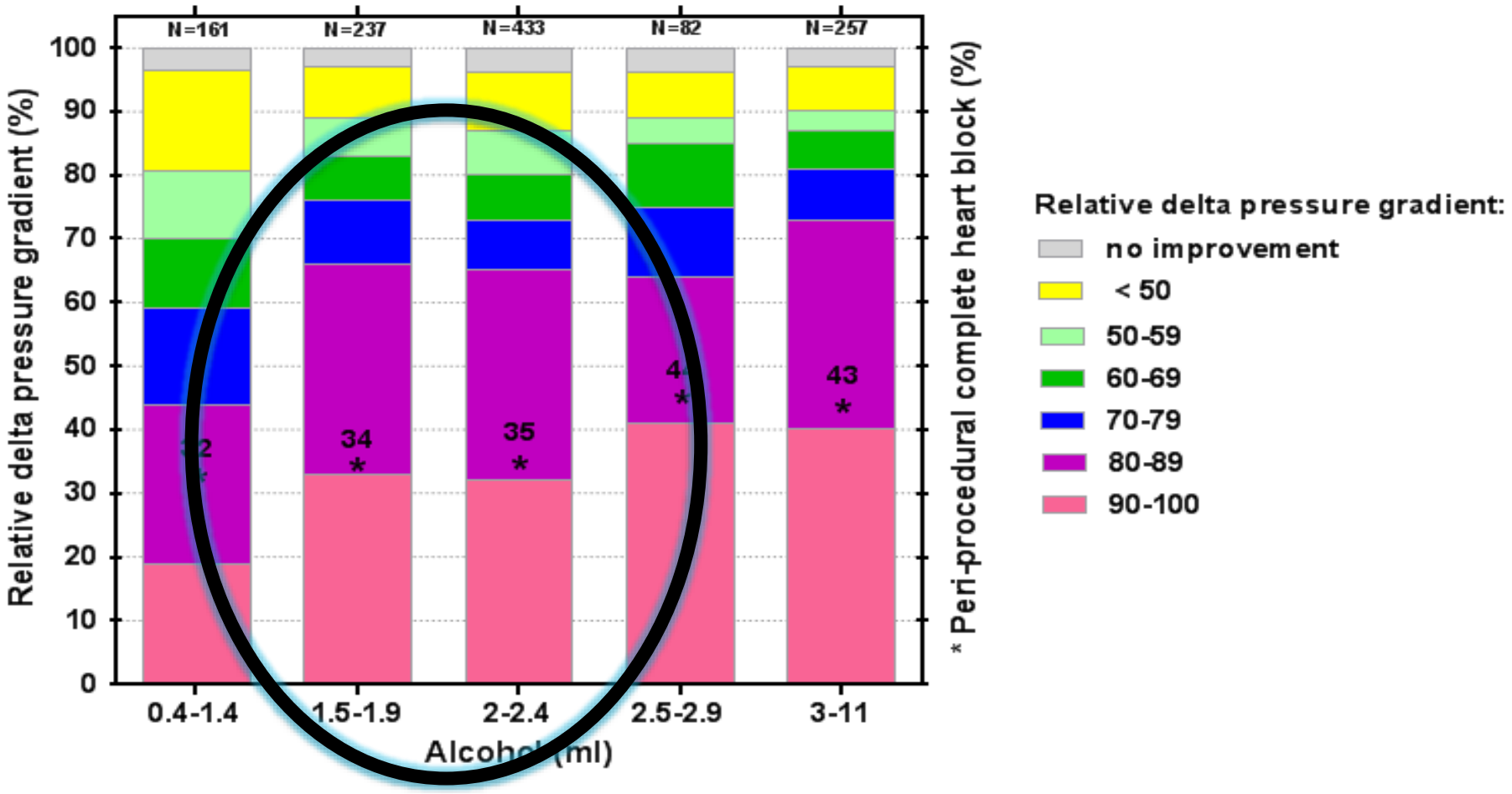
Mortality: 0.7%

Early Outcomes of Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy: A European Multicenter and Multinational Study

Josef Veselka,[1*] MD, PHD, Thorsten Lawrenz,[2,3] md, Christoph Stellbrink,[1] MD, David Zemanek,[1] MD, PHD, Marian Branny,[4] MD, Jaroslav Januska,[4] MD, Jan Sitar,[5] MD, Pawel Dimitrow,[6] MD, PHD, Jan Krejci,[7] MD, PHD, Maciej Dabrowski,[8] MD, PHD, Stanislav Mizera,[9] MD, Thomas Bartel,[10] MD, and Horst Kuhn,[2,3] MD

Catheter Cardiovasc Interv 2014

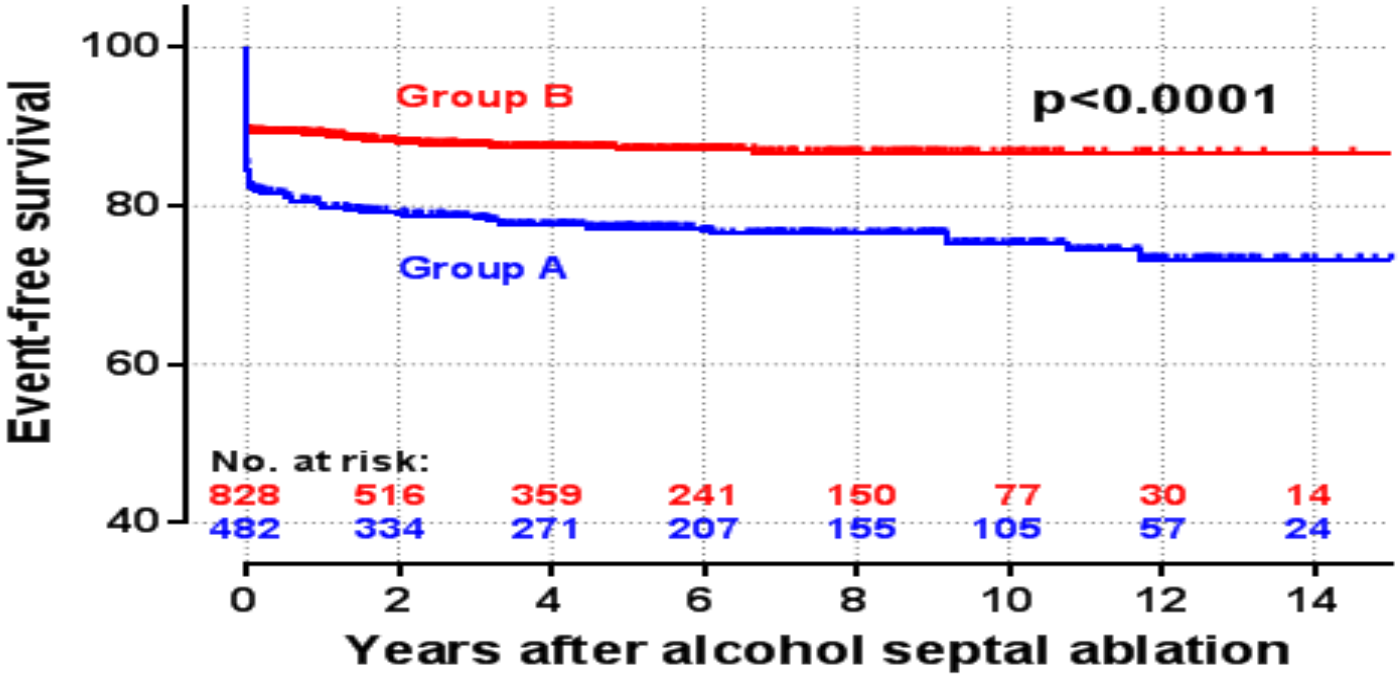
Euro-ASA registry



Veselka J et al. Eur Heart J 2016

Sufficient expertise

Peri-procedural complications and PM



Group A 1-50 ASA interventions

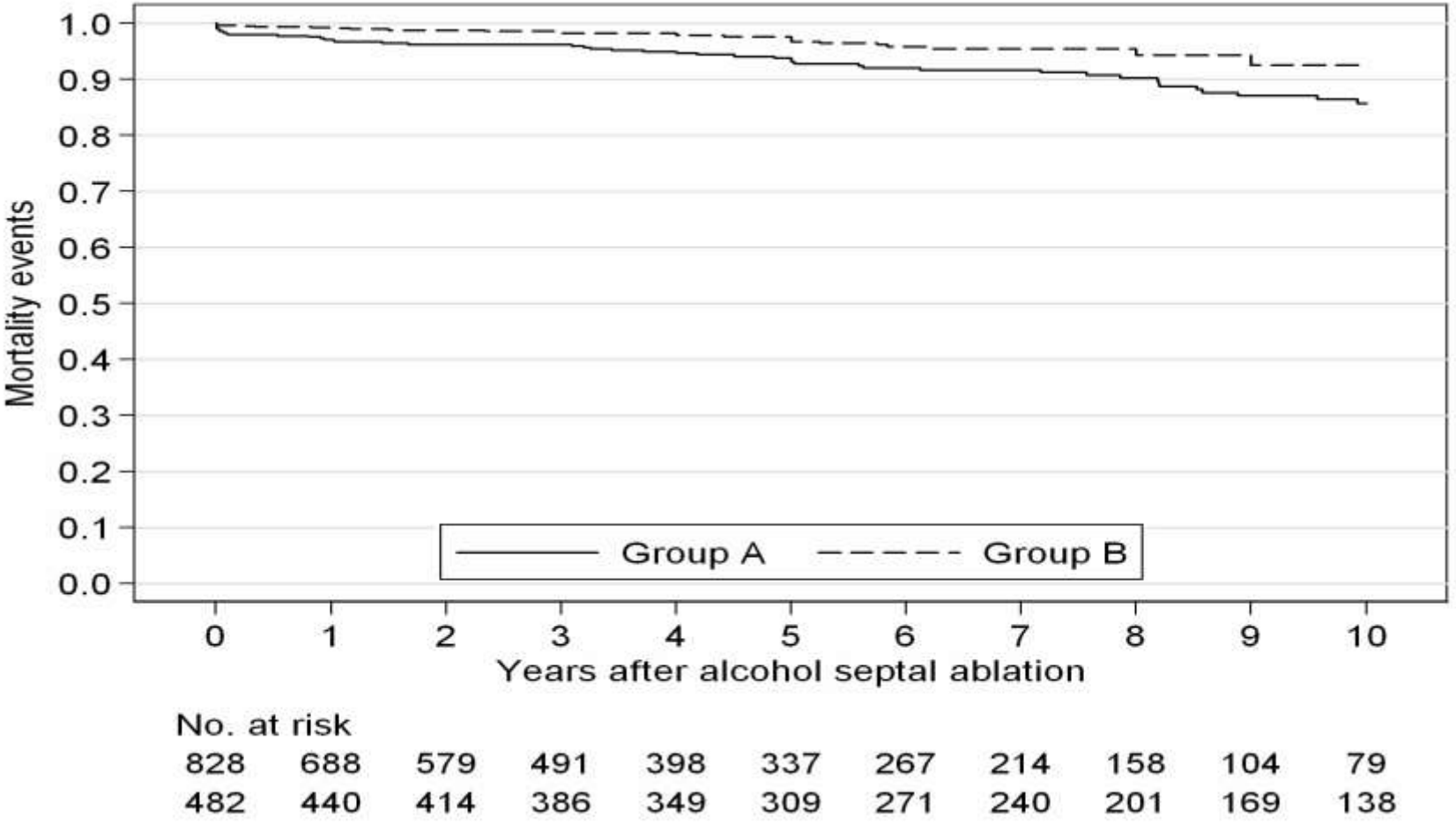
Group B more than 50 ASA interventions

EP = VT/VF up 30 days, death up to 30 days, tamponade up to 30 days, PM implantation

Veselka et al. Can J Cardiol 2018.

Sufficient expertise

CV mortality



Kaplan-Meier curves describing survival free of cardiovascular death in group A versus group B (adjustment for age, baseline pressure gradient, baseline septum thickness, and year of performed procedure) ($p<0.01$).

Veselka et al. Can J Cardiol 2018.

How to treat less symptomatic pts? Pts with a thin septum?

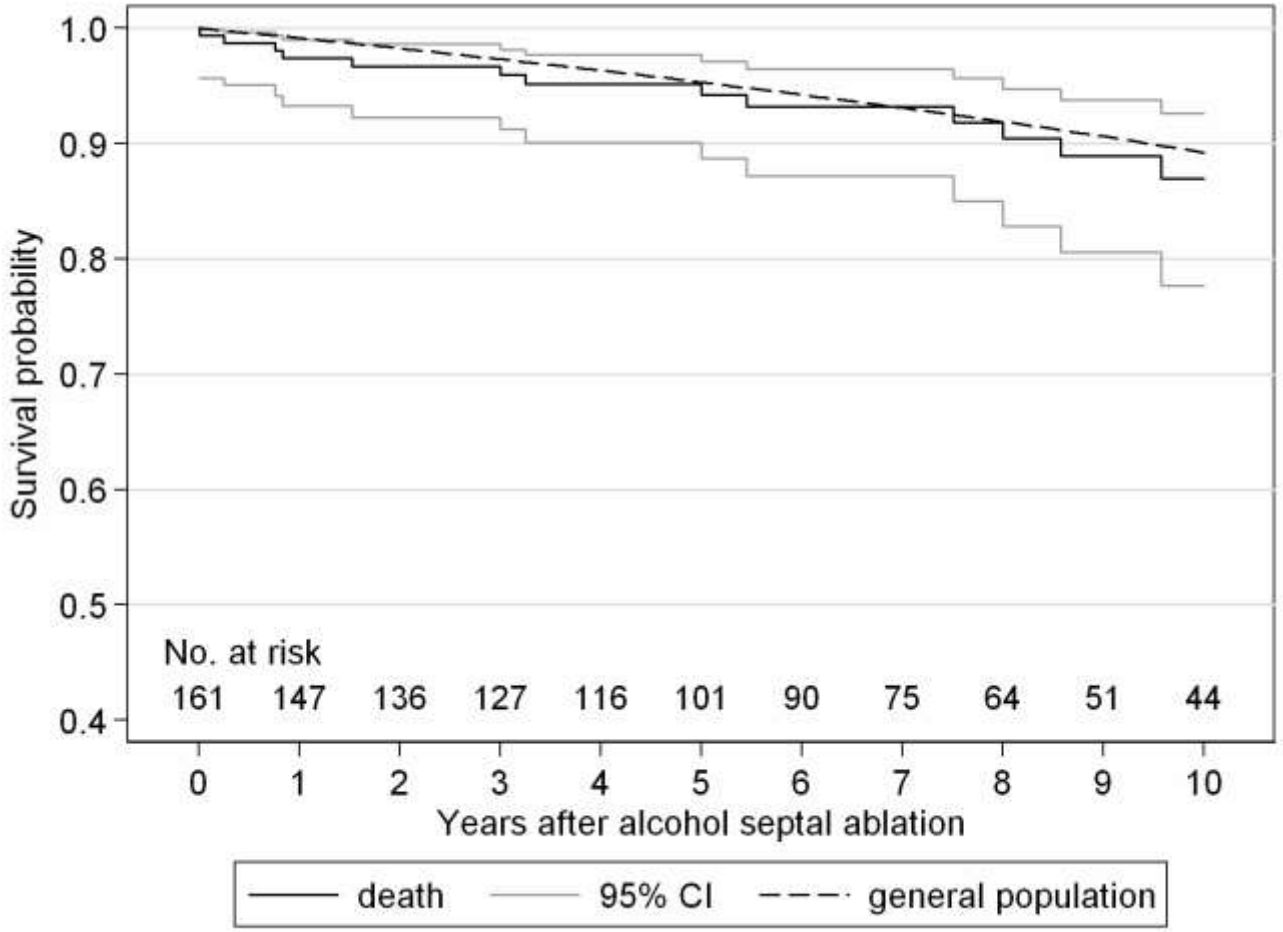
Recommendations	Class[a]	Level[b]
It is recommended that septal reduction therapies be performed by experienced operators, working as part of a multidisciplinary team expert in the management of HCM.	I	C
Septal reduction therapy to improve symptoms is recommended in patients with a resting or maximum provoked LVOT gradient of ≥50 mm Hg, who are in NYHA functional Class III–IV, despite maximum tolerated medical therapy.	I	B

European guidelines caution of a risk of ventriculoseptal defect following ASA in patients with only mild hypertrophy (≤16 mm) at the point of the mitral leaflet-septal contact. The recommendation is to treat them with dual chamber pacing or mitral valve repair/replacement

Elliott et al. 2014

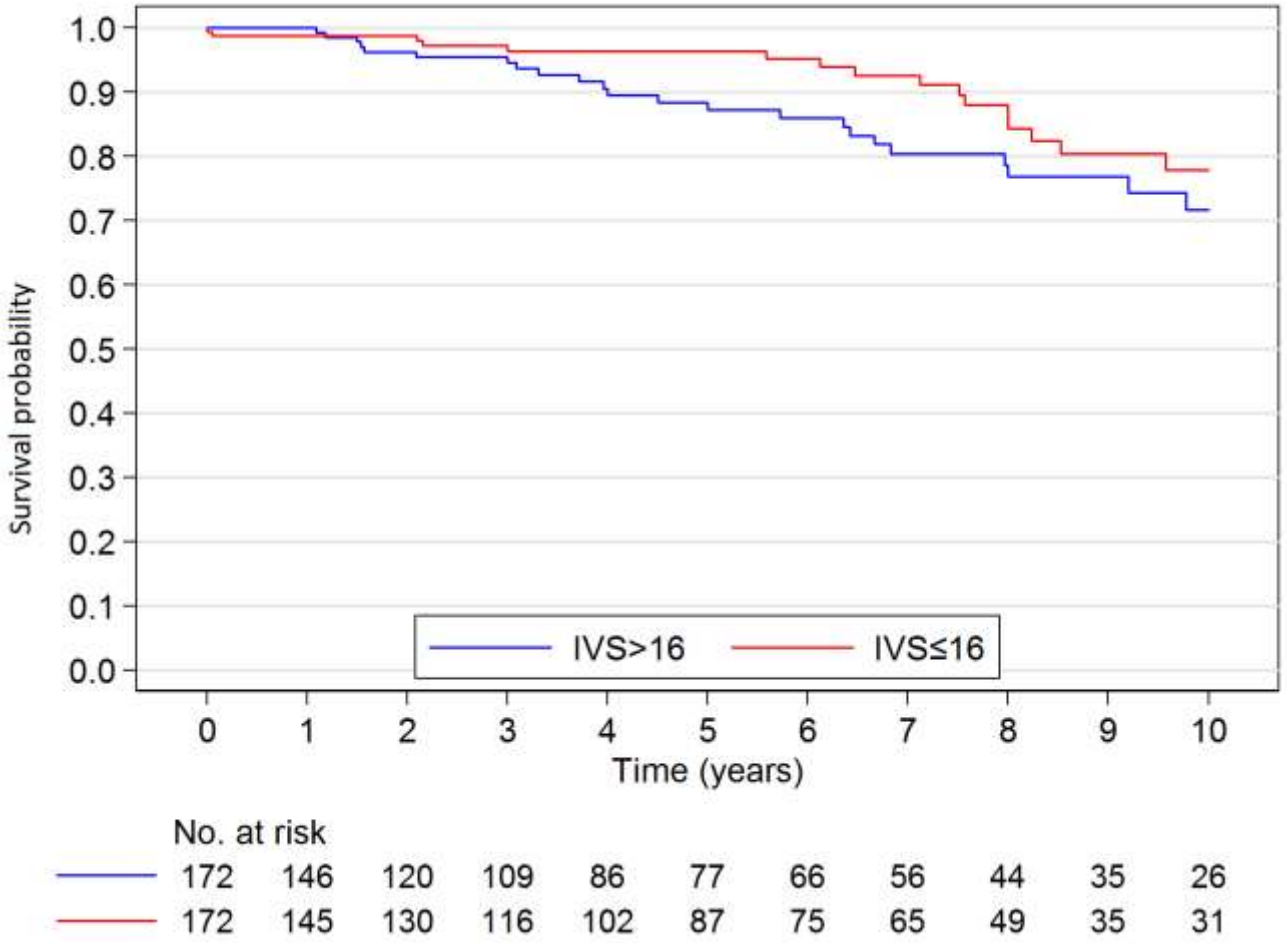
Outcome of Alcohol Septal Ablation in Mildly Symptomatic Patients with Hypertrophic Obstructive Cardiomyopathy

A Long-Term Follow-Up Study Based on the Euro-ASA Registry



Veselka et al. JAHA 2017

Selected patients treated with alcohol septal ablation for hypertrophic obstructive cardiomyopathy with mild left ventricular hypertrophy (septum thickness ≤16 mm) **had higher rate of early post-procedural complications, but their long-term survival was better than for those with septum thickness >16 mm**.



Veselka et al. Eur Heart J 2019; in press.

Cardiovascular mortality events and post-ASA obstruction

Freedom from cardiovascular mortality events occurring after the first post-ASA check-up in patients with residual **LVOTO ≥ 30 mmHg and < 30 mmHg**

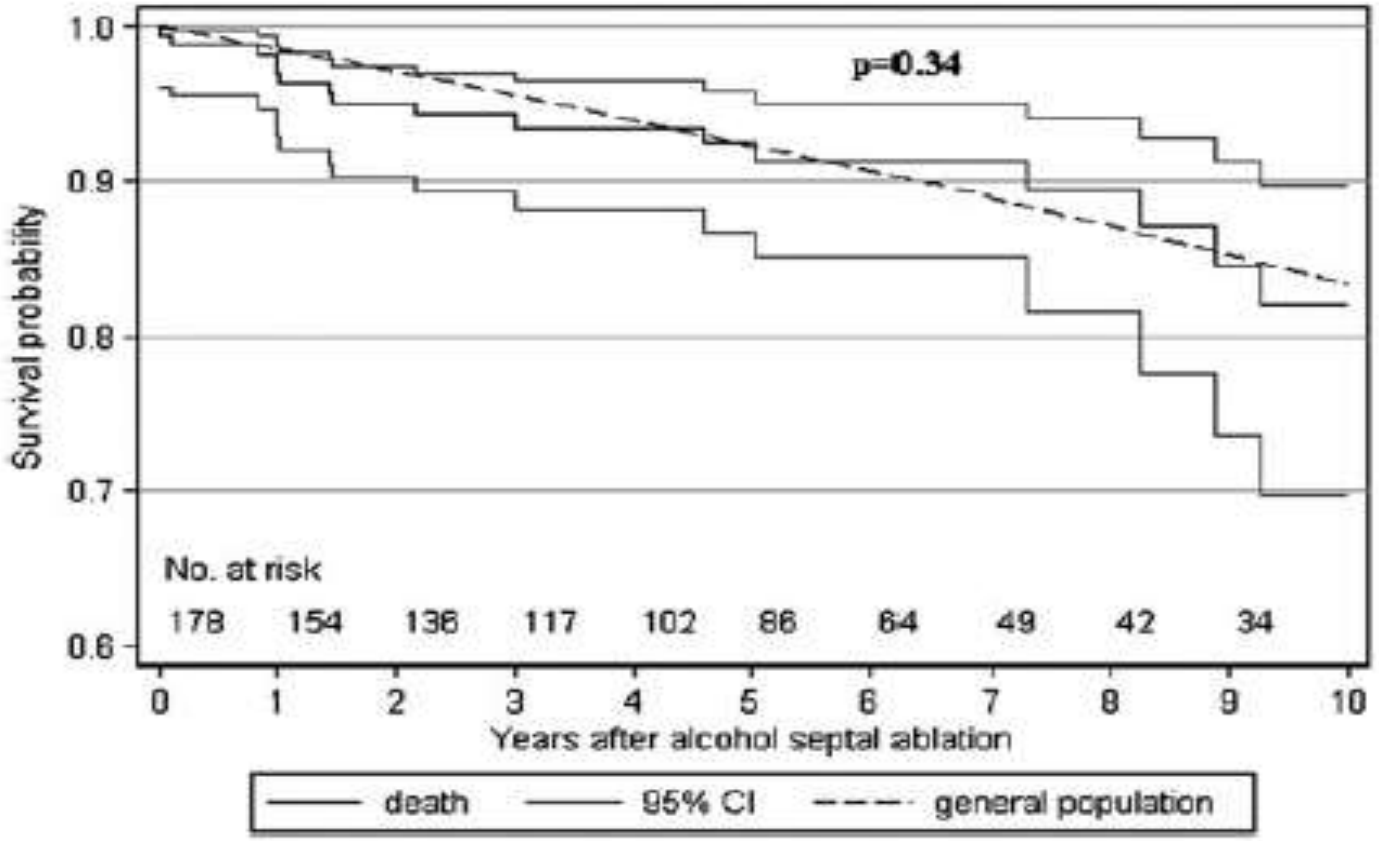
(adjustment for age, sex, baseline LVOTO, and baseline septum thickness).

HR 2.95, 95% CI 1.26-6.91

Veselka et al. Heart 2016

Survival

Comparison with sex- and age-matched general population



Veselka J. Eur Heart J 2014

Take-home messages

- Genetika má omezený dopad pro kliniku.
- Popis morfologie má terapeutické konsekvence.
- HCM – SCD kalkulátor je „the best of the worst“.
- Septální redukční terapie připomíná léčbu aortální stenózy.
- HCM léčit pouze v centru.