# Riziková stratifikace náhlé smrti u hypertrofické kardiomyopatie

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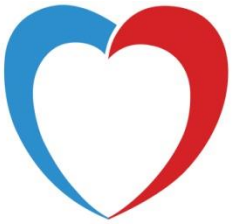


DEPARTMENT OF CARDIOLOGY
MOTOL UNIVERSITY HOSPITAL, 2nd MEDICAL SCHOOL,
CHARLES UNIVERSITY, PRAGUE, CZECH REPUBLIC

# Úvod

- 1957 D. Teare popsal 8 případů zemřelých (14-44 let) s „asymetrickou hypertrofií srdce“
- 70. léta zvýraznění zájmu vzhledem k rozvoji jednorozměrné a později dvourozměrné echokardiografie
- 1970 (Goodwin) a 1979 (Maron) byl přijat název „hypertrofická kardiomyopatie“
- prevalence 0,2%-0,4% (v ČR tedy lze očekávat 20-40 tis. nemocných s HCM)

# Definice HCM

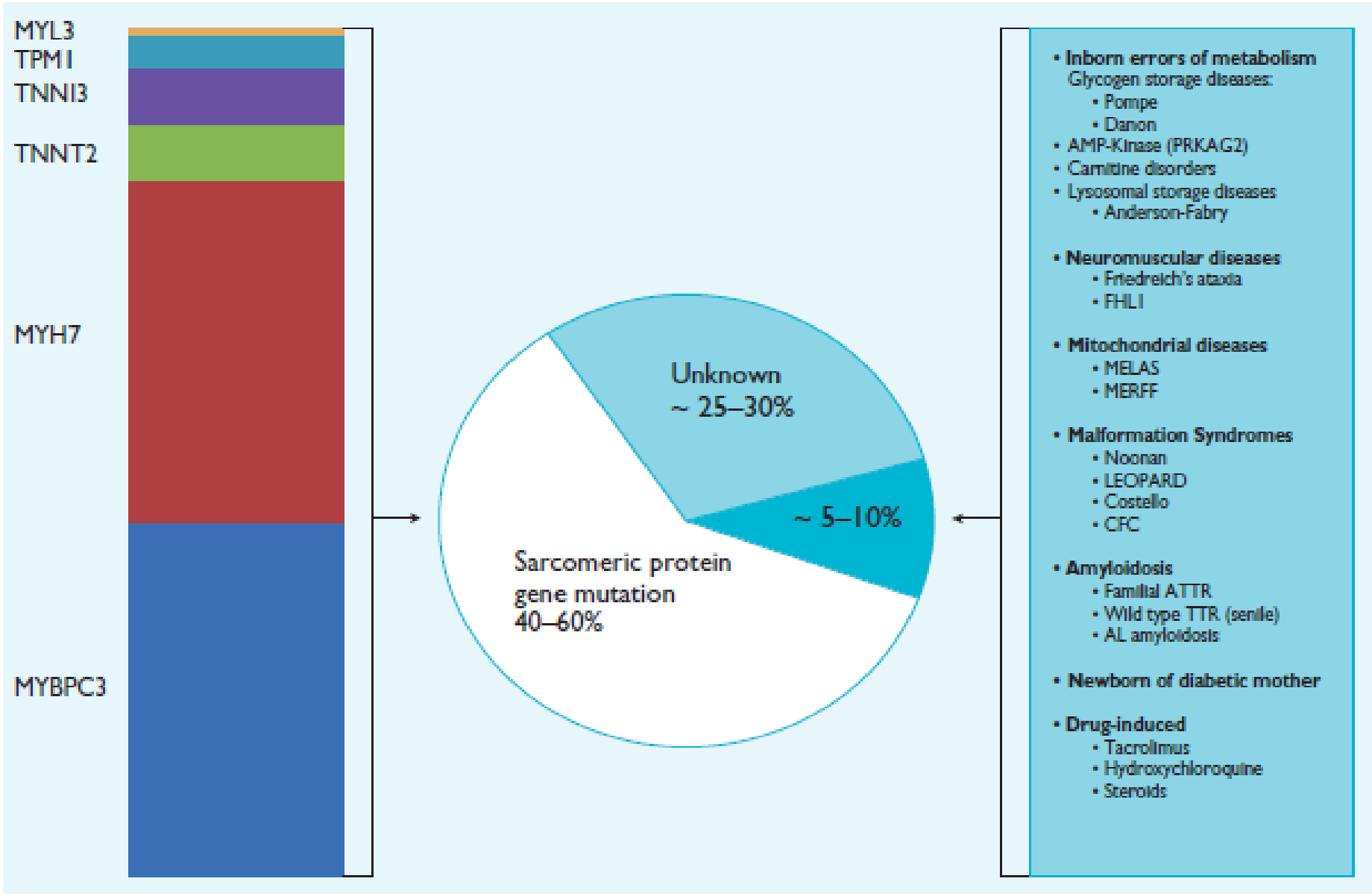
- **Klinická – primární srdeční onemocnění charakterizované jinak nevysvětlitelnou hypertrofií srdce (hypertenze, vada).**
- Patologická – hypertrofie srdce s abnormálním uspořádáním svaloviny doplněné fibrózou a přítomností ložisek abnormální struktury myokardu
- Genetická – AD dědičné onemocnění způsobené geny kódujícími sarkomerické (avšak i nesarkomerické) proteiny

Elliott P et al. Eur Heart J 2008

# Genetika HCM

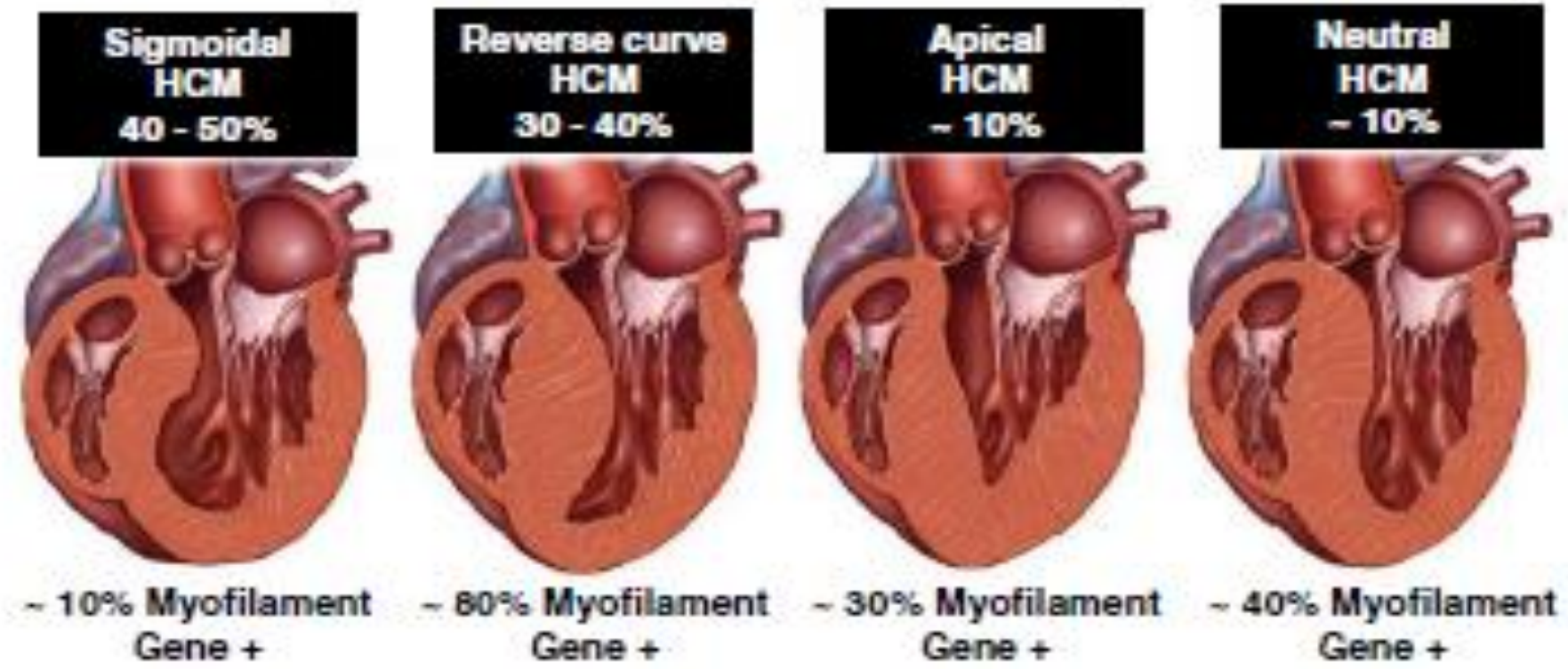
- mutace sarkomerických proteinů většinou na základě dědičnosti, ale i nové mutace
  - **těžký řetězec β-myozinu (20-25%)**
  - **vazebný protein C (15-20%)**
  - troponin T (3-5%) a I (1-2%)
  - α-tropomyosin (1-2%)
  - reg. podjednotka lehkého řetězce myozinu
  - ostatní méně než 1%
- celkem identifikujeme příčinné mutace u 50% (?) pacientů

# Genotyp HCM




Elliott et al. EHJ 2014

# Genetika HCM




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

Bos JM et al. JACC 2009

# Patologicko – anatomický obraz

- Makroskopické změny

  - ztluštění komorového septa s/nebo bez ztluštění ostatních stěn

- Mikroskopická charakteristika

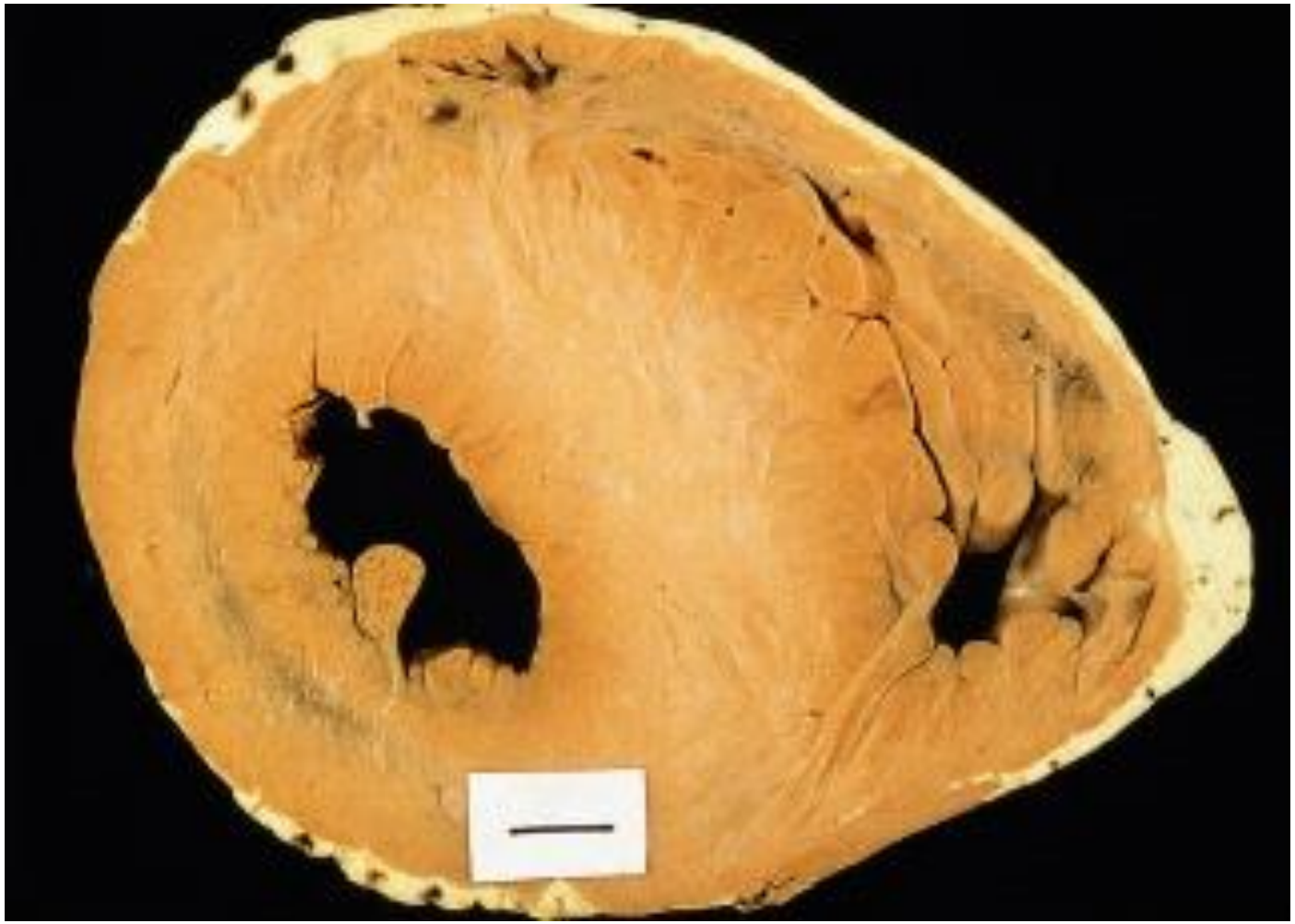
  - nepravidelné zvětšení kardiomyocytů

  - ložiska neuspořádanosti „disarray“

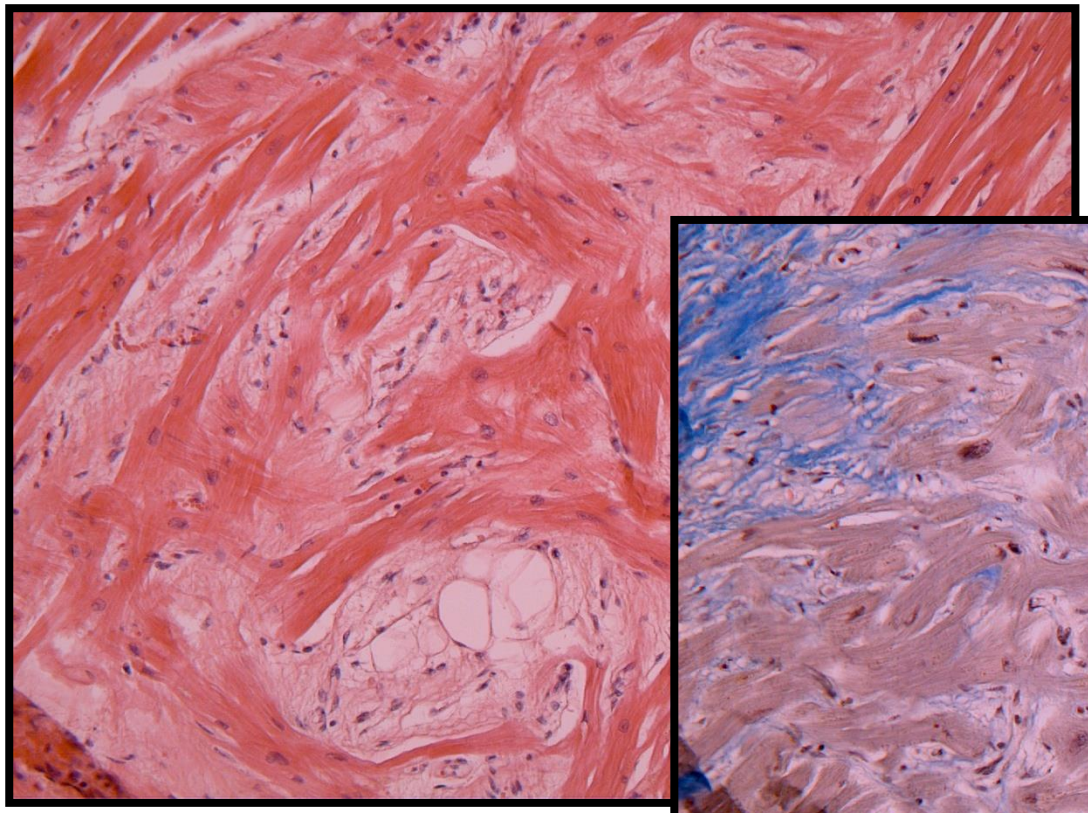
- Ultrastrukturální změny

  - zmnožení sarkomer, mitochondrií

# Patologicko – anatomický obraz

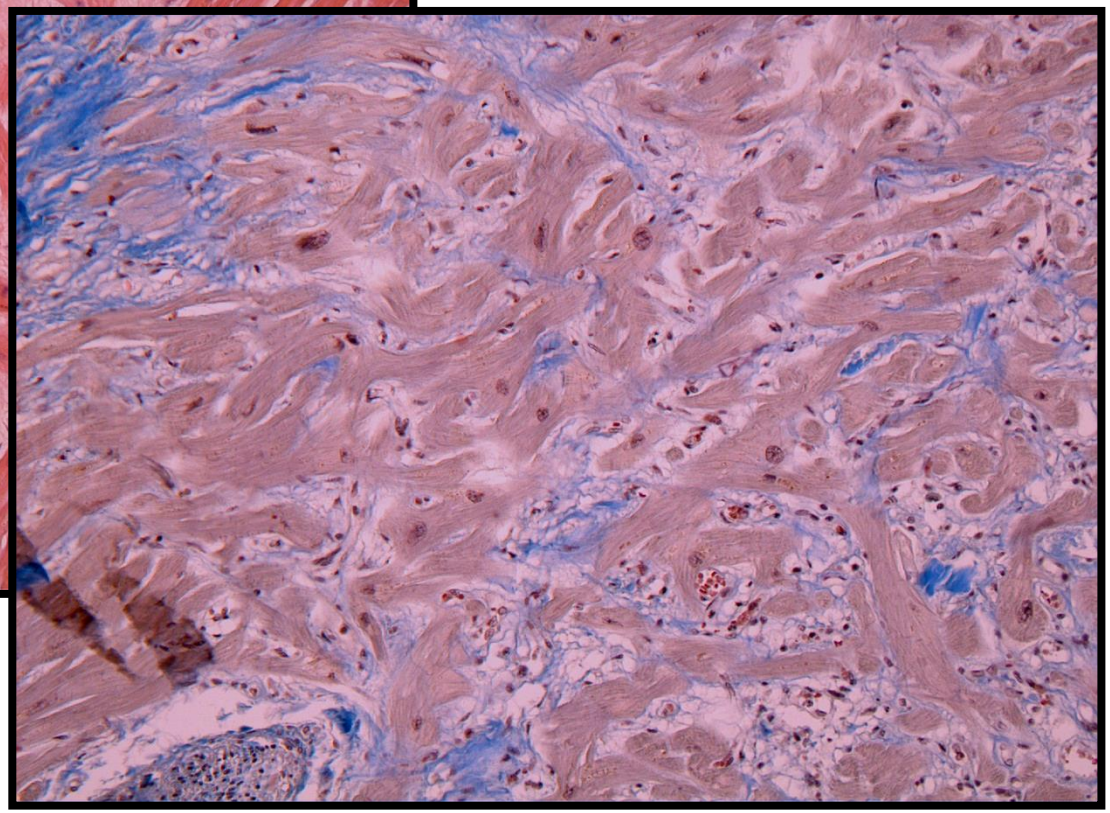


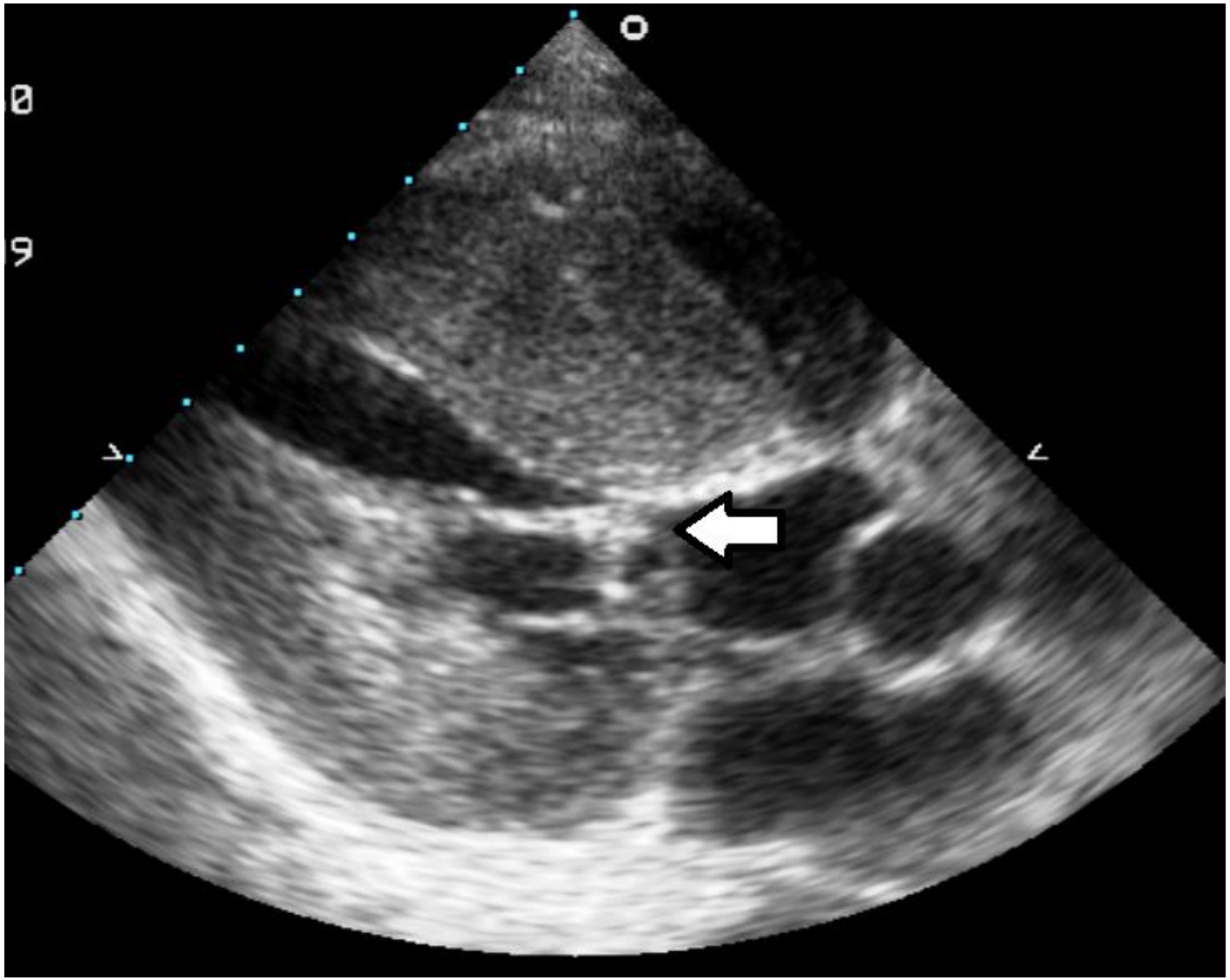
# Mikroskopický obraz – „disarray“



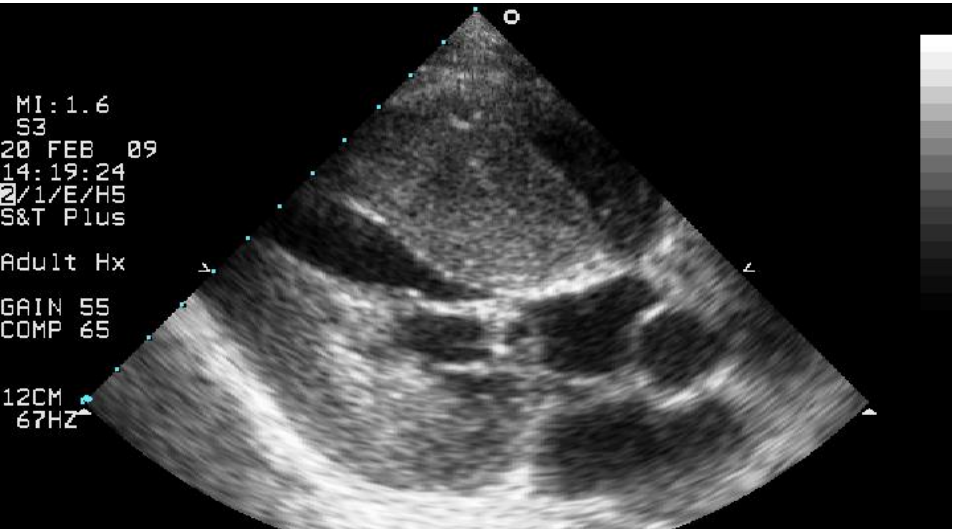
Barvení hematoxilyn-eosin

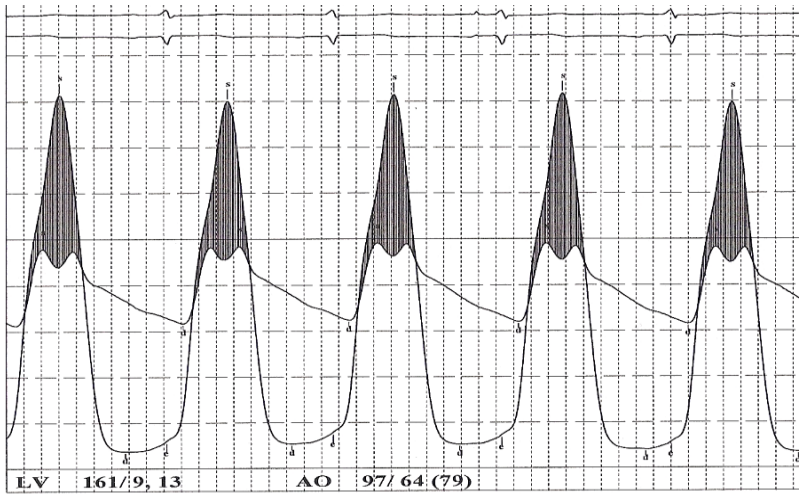
Barvení „modrý“ trichróm



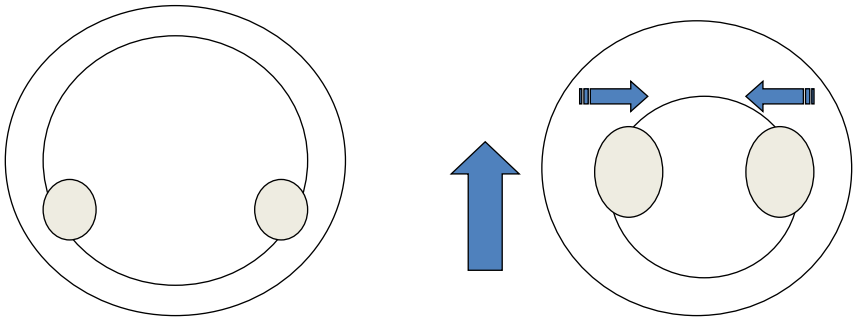


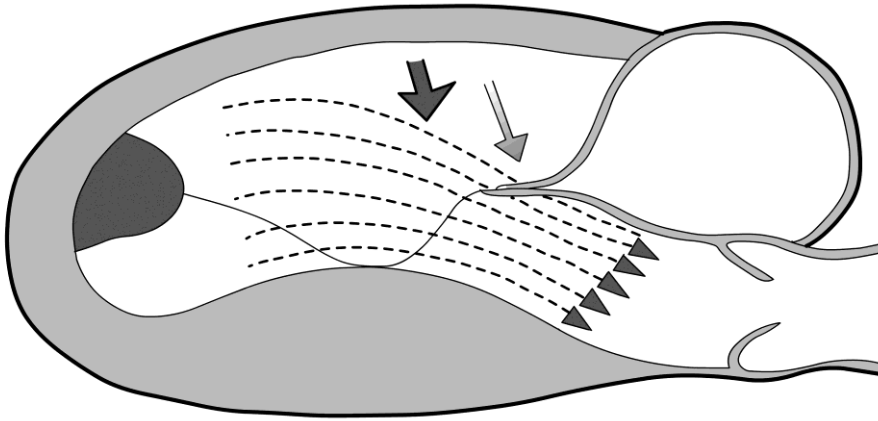
# Nitrokomorová obstrukce

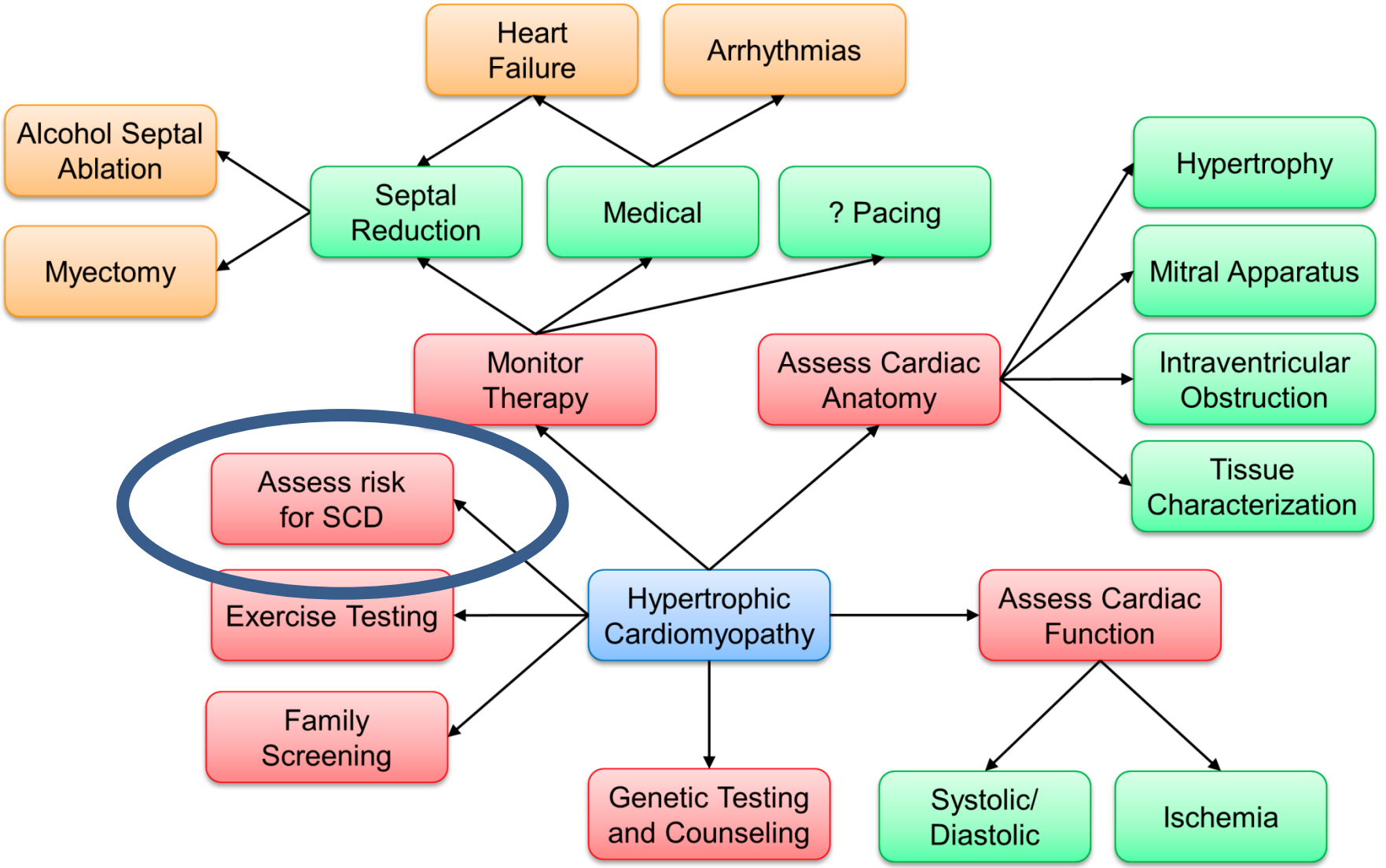



Změna morfologie a lokalizace papilárních svalů








Veselka J et al. Lancet; in press.

# Prognóza

- Dobrá ve vyšším věku (NS 0,5-1%/r).
- Jedna z nejčastějších příčin NS u mladých lidí (2%/r).
- Nejčastější příčina NS u mladých sportovců.

Bharucha T et al. JACC 2015
Maron BJ et al. AM J Med 2016

# Stratifikace rizika NS

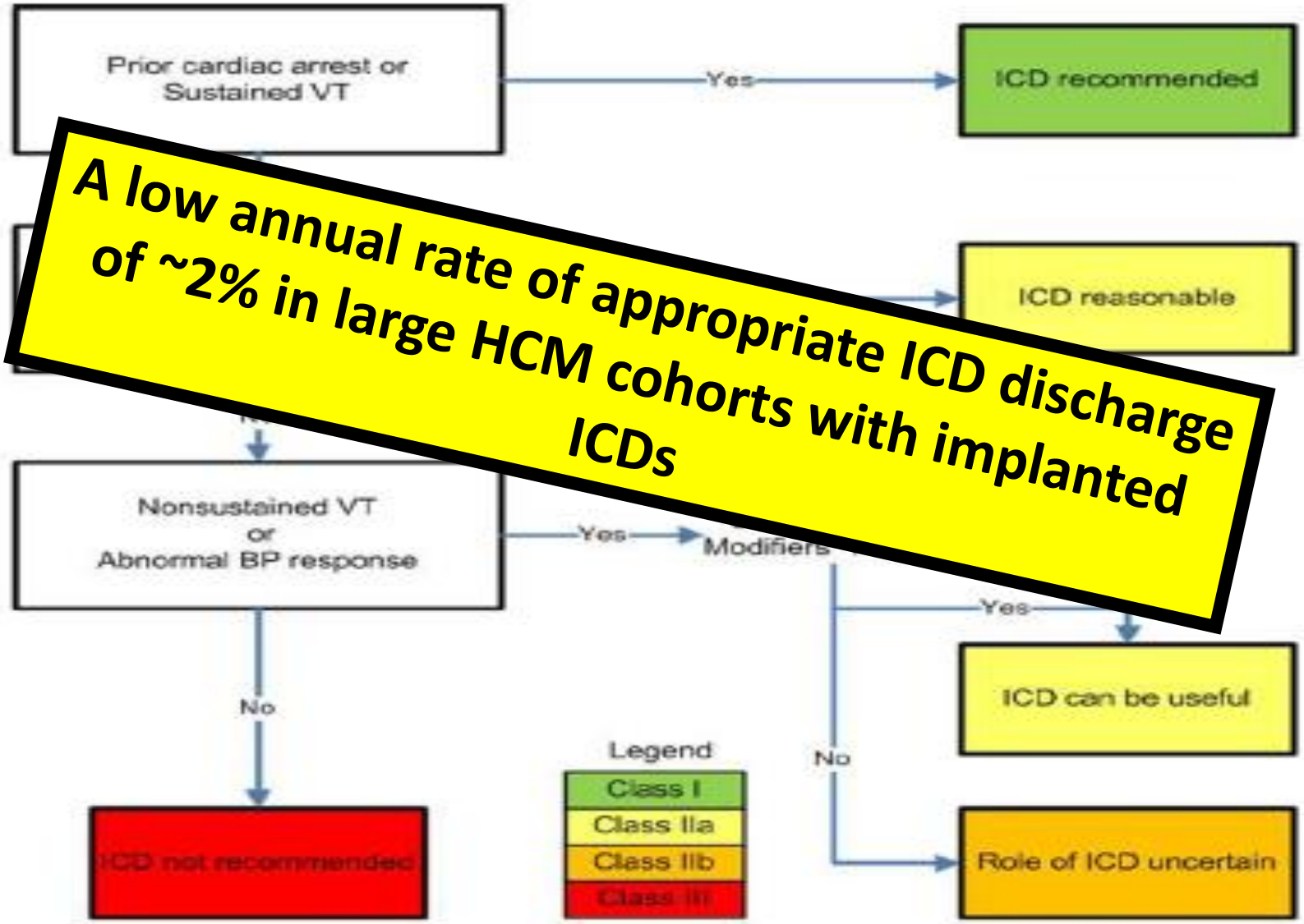
- The challenge remains to identify the optimal path to identify the relatively small group of patients with the highest risk of SCD.

- These patients should be treated with ICD implantation since it is the only therapy with sound evidence demonstrating its life-saving potential.

| European model | North American model |
| --- | --- |
| **Secondary prevention:**<br><br>Sustained ventricular tachycardia<br><br>Resuscitation for ventricular fibrillation<br><br>*ICD is recommended in all patients* | **Secondary prevention:**<br><br>Sustained ventricular tachycardia<br><br>Resuscitation for ventricular fibrillation<br><br>*ICD is recommended in all patients* |

| | |
|---|---|
| **Primary prevention:**<br><br>**Family history of sudden death**<br><br>**Unexplained syncope**<br><br>**Maximum left ventricular wall thickness**<br><br>**Non-sustained ventricular tachycardia**<br><br>**Age**<br><br>**Left atrial diameter**<br><br>**Left ventricular outflow gradient (rest or Valsalva)**<br><br>*5-year risk <4%, ICD is not indicated*<br><br>*5-year risk ≥4%–6%, ICD is considered*<br><br>*5-year risk >6%, ICD is recommended* | **Primary prevention:**<br><br>**Family history of sudden death in a 1st degree relative**<br><br>**Unexplained syncope**<br><br>**Maximum left ventricular thickness ≥30 mm**<br><br>**Non-sustained ventricular tachycardia**<br><br>**Abnormal blood pressure response during exercise (fall or failure to increase systolic blood pressure by at least 20 mmHg during exercise test)**<br><br>*When ≥1 risk factor is present ICD may be reasonable (Class IIa)*<br><br>*The role of modifiers of risk including young age, LVOT obstruction with no plan for intervention, LGE, remote family history and a wall thickness is uncertain (Class IIb)* |

# Riziko NS dle US Guidelines




**A low annual rate of appropriate ICD discharge of ~2% in large HCM cohorts with implanted ICDs**

Gersh B et al. Circulation 2011

# HCM Risk-SCD Calculator

| | | | |
|---|---|---|---|
| **Age** | 30 | **Years** | *Age at evaluation* |
| **Maximum LV wall thickness** | 22 | **mm** | *Transthoracic Echocardiographic measurement* |
| **Left at** | | **mm** | *Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane at time of evaluation* |
| **M** | | | *imum LV outflow gradient determined at rest and with Valsalva ative of concurrent medical treatment) using pulsed from the apical three and five chamber be determined using the is the peak aortic* |
| **Family His… of SCD** | | | *es under HCM at* |
| **Non-sustained VT** | ◉ No ○ Yes | | *3 conse… ute and <30s in duration o… hours) at or prior to evaluation.* |
| **Unexplained syncope** | ◉ No ○ Yes | | *History of unexplained syncope at or prior to e…* |

**This model was shown to be sufficiently specific and associated with a lower rate of ICD implantations (20–26%), but some patients with a predicted low risk of sudden mortality events were found to be high risk in clinical practice in one study.**

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

# Transatlantic differences in assessment of risk of sudden cardiac death in patients with hypertrophic cardiomyopathy

Denisa Ja… …l Tomašov, David Zemánek, Josef Veselka *

*Department … …nd Faculty of Medicine and Motol University Hospital, Prague, Czech Republic*

… 186 (2015) 3–4

**At the current stage, fully informed care, taking into account the potential advantages and disadvantages of either strategy of risk stratification is recommended. An equally important adjunct to the conversation for ICD implantation is the discussion about ICD-related complications including inappropriate discharges, infections, and lead or device dysfunctions as the incidence of these complications is higher than the incidence of appropriate discharges.**

IVS > 30…

NsVT

Inadequate BP increase

FH — family history of sudden death, IVS — inter…

NsVT — non-sustained ventricular tachycardia, inadequ…

increase — an increase of the systolic blood pressure by ≤ 20 mm Hg during exercise stress testing.

# Dva systémy

## EU

- Kvantifikace rizika
- Vyšší specificita
- Nižší senzitivita
- 20% HCM pac dostane ICD
- Menší ochrana
- Méně komplikací

## USA

- Binární systém
- Nižší specificita
- Vyšší  senzitivita
- 50% HCM pac dostane ICD
- Vyšší ochrana
- Více komplikací

# Obstrukce a mortalita

- Elliott et al. demonstrated that LVOTO ≥30 mm Hg was an independent predictor of sudden cardiac death among an unselected population of obstructive patients with HCM. They also found that the relative risk of sudden cardiac death or ICD discharge increased by 1% for each 1 mm Hg of LVOTO.
- Similarly, data from the Euro-ASA registry showed that each mm Hg increase in post-ASA LVOTO was associated with a 1% increase in the long-term risk of all-cause death.

Elliott et al. Eur Heart J 2006
Veselka et al. Eur Heart J 2016

# 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.

# Take-home message

- Riziko NS je relativně nízké, nikoliv však zanedbatelné.
- Existují dva nedokonalé systémy odhadu rizika, které lze používat, pokud víme „jak na to“.
- Vzhledem k heterogenitě HCM nebudeme mít nikdy dostatečně senzitivní i specifický systém odhadu rizika NS.

# Praktický návod

- Odhad rizika dle HCM Risk Score Calculator
- Vyšší riziko – ICD
- Nižší riziko – US systém a diskuse s pacientem.

**Většina úmrtí nastane u nízkorizikových pacientů, ALE proporce pacientů zemřelých v této skupině bude malá.**