2023 ESC Guidelines pro diagnostiku a léčbu kardiomyopatií: *multimodalitní zobrazení*

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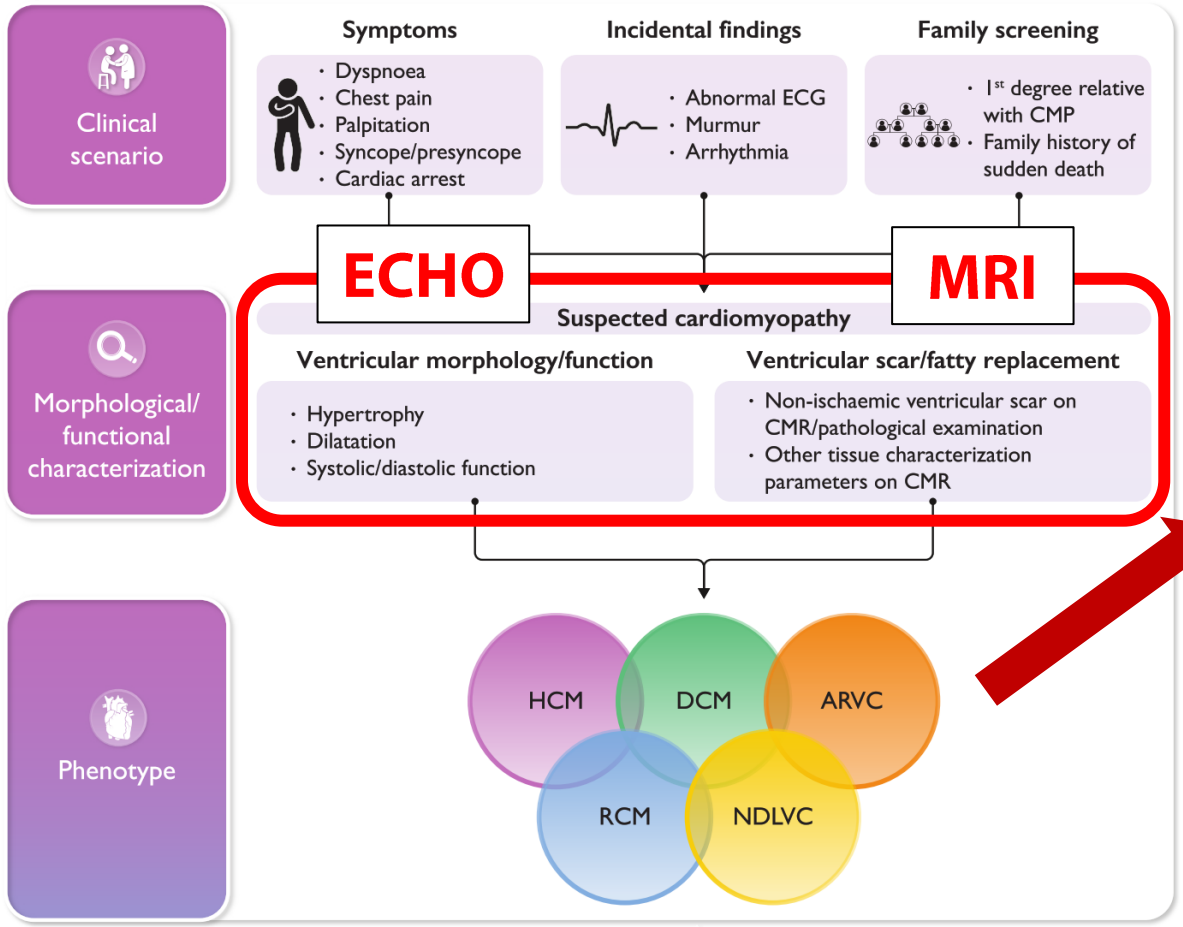
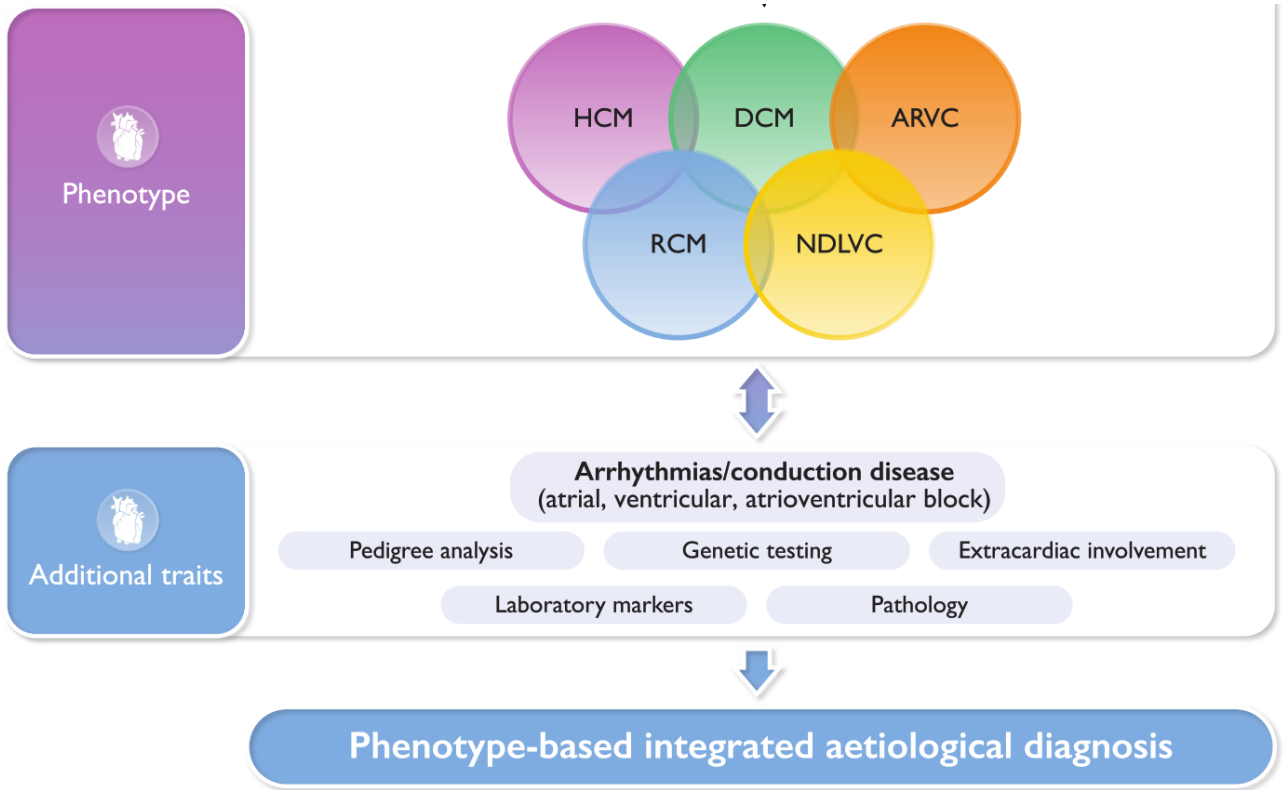
KOMPLEXNÍ KARDIO VASKULÁRNÍ CENTRUM VFN Praha

2023 ESC Guidelines: Fenotypický přístup

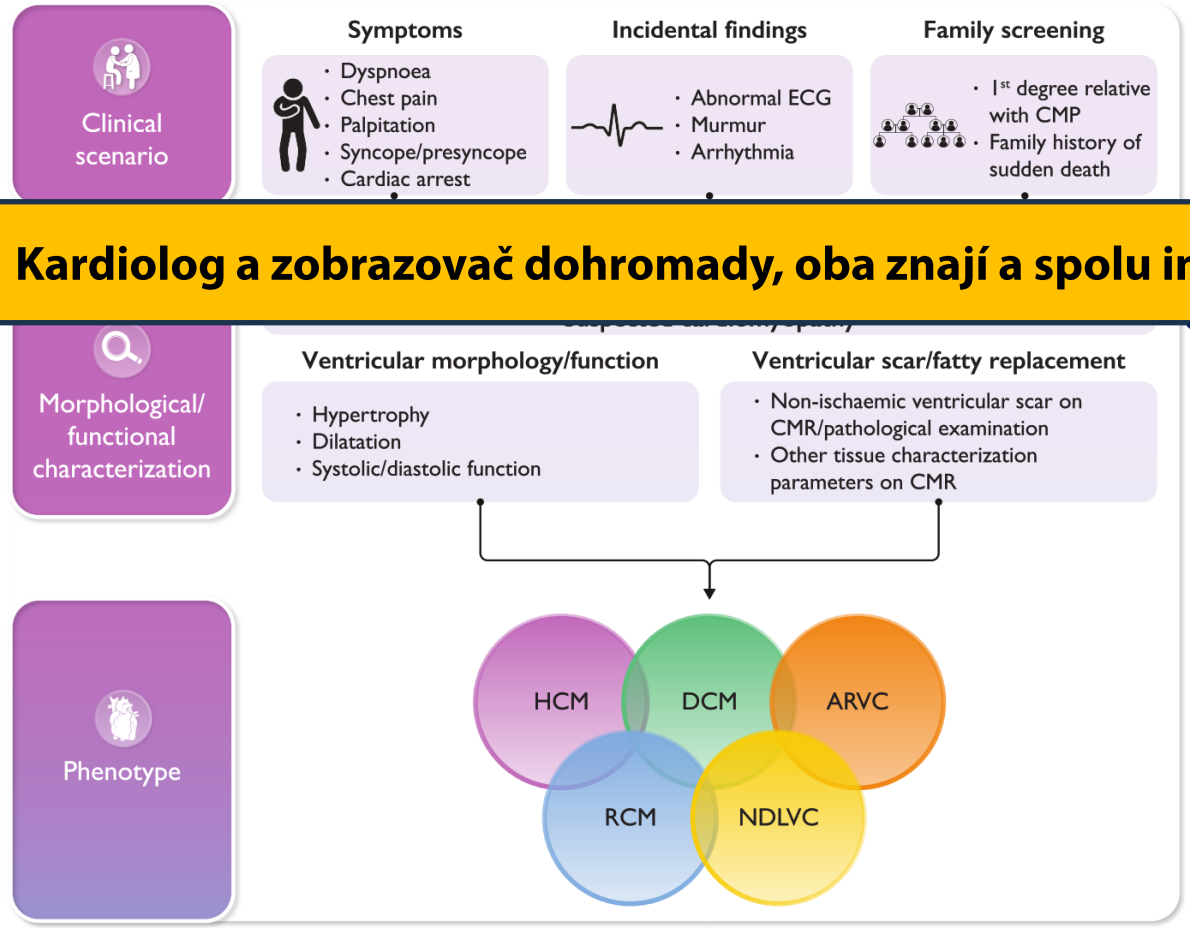


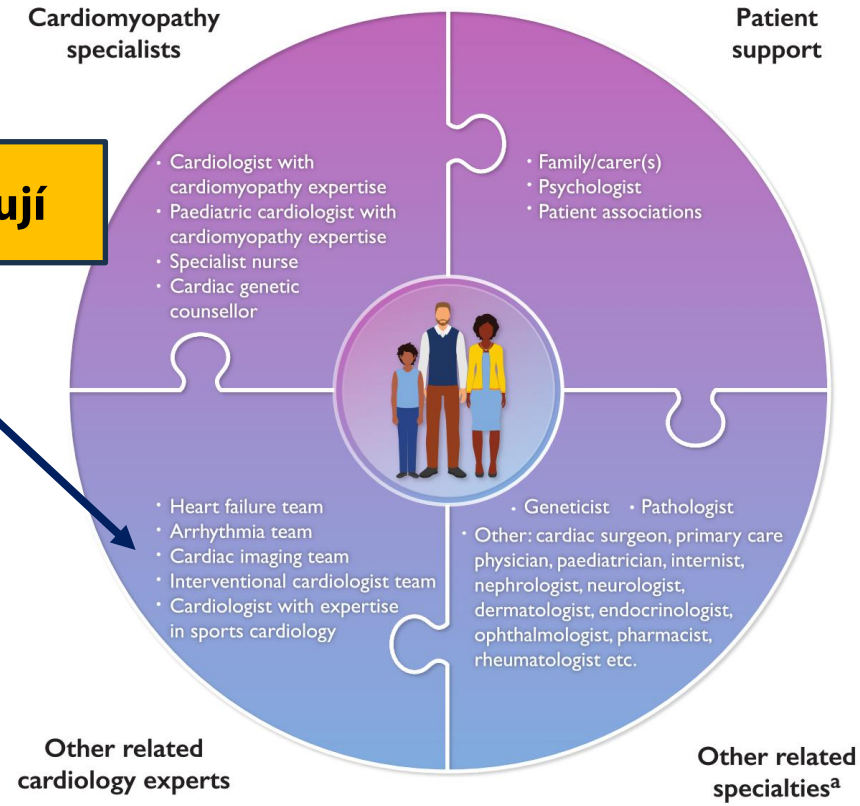
„Cardiomyopathy Mind-Set“



2023 ESC Guidelines:
„Cardiomyopathy Mind-Set“ a spolupráce odborností

Kardiolog a zobrazovač dohromady, oba znají a spolu interpretují



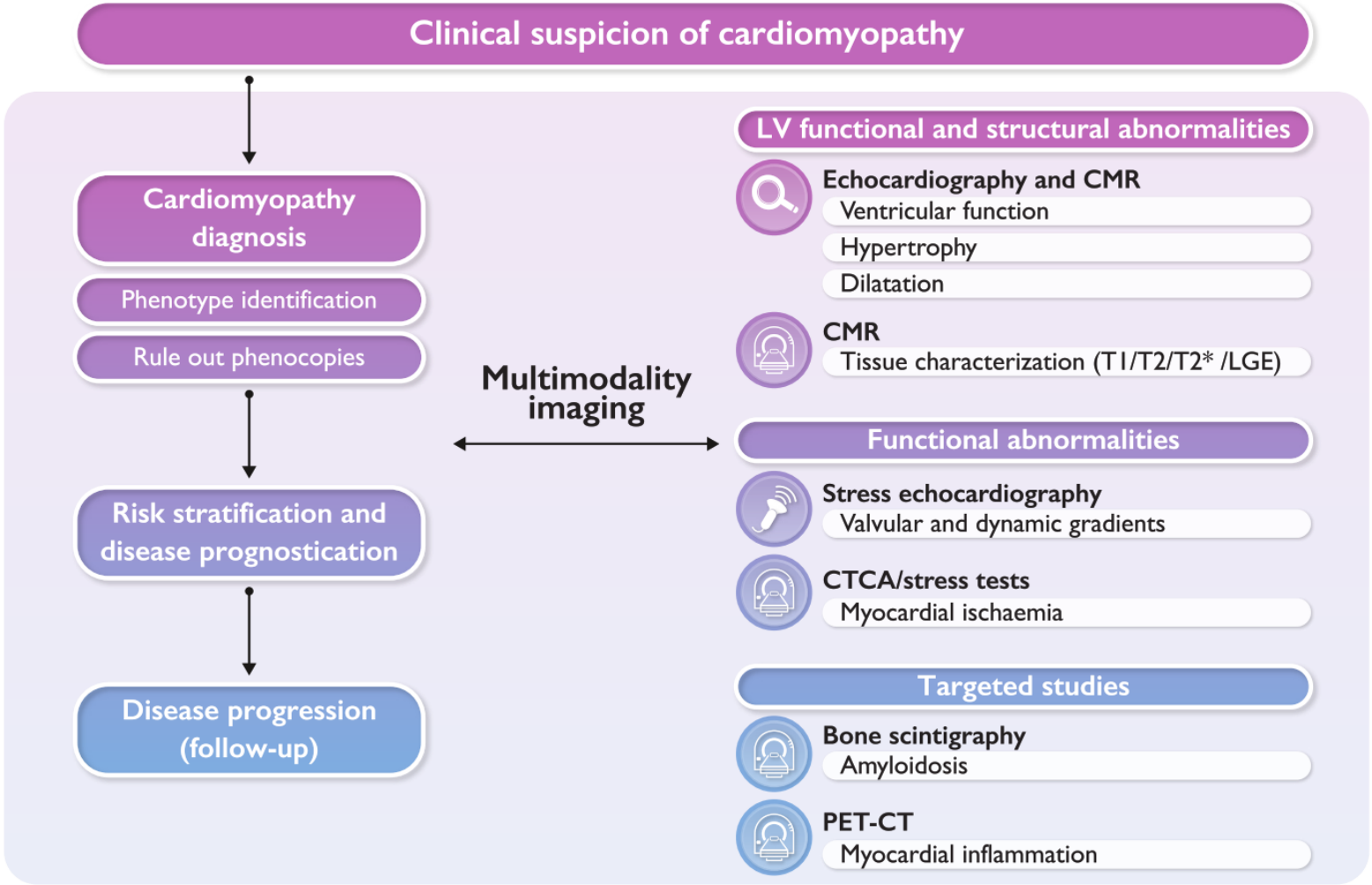


2023 ESC Guidelines: spolupráce odborností

Diagnostika

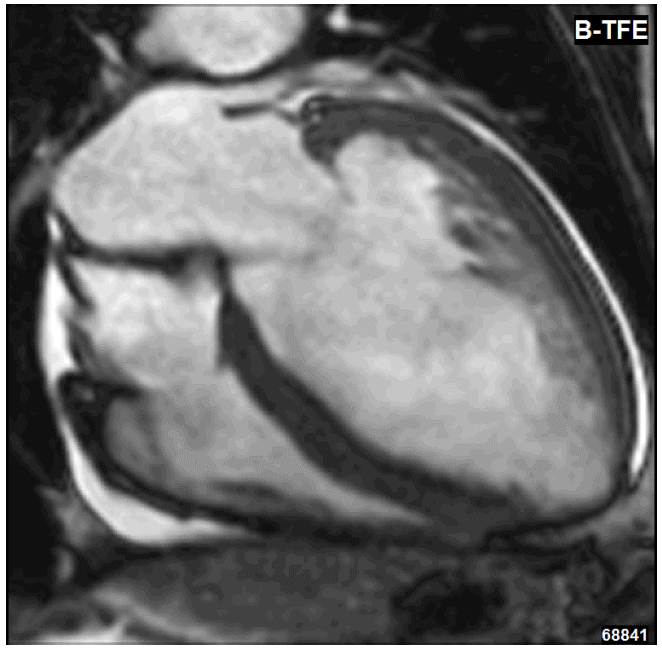
Riziková stratifikace, prognóza

Follow-up



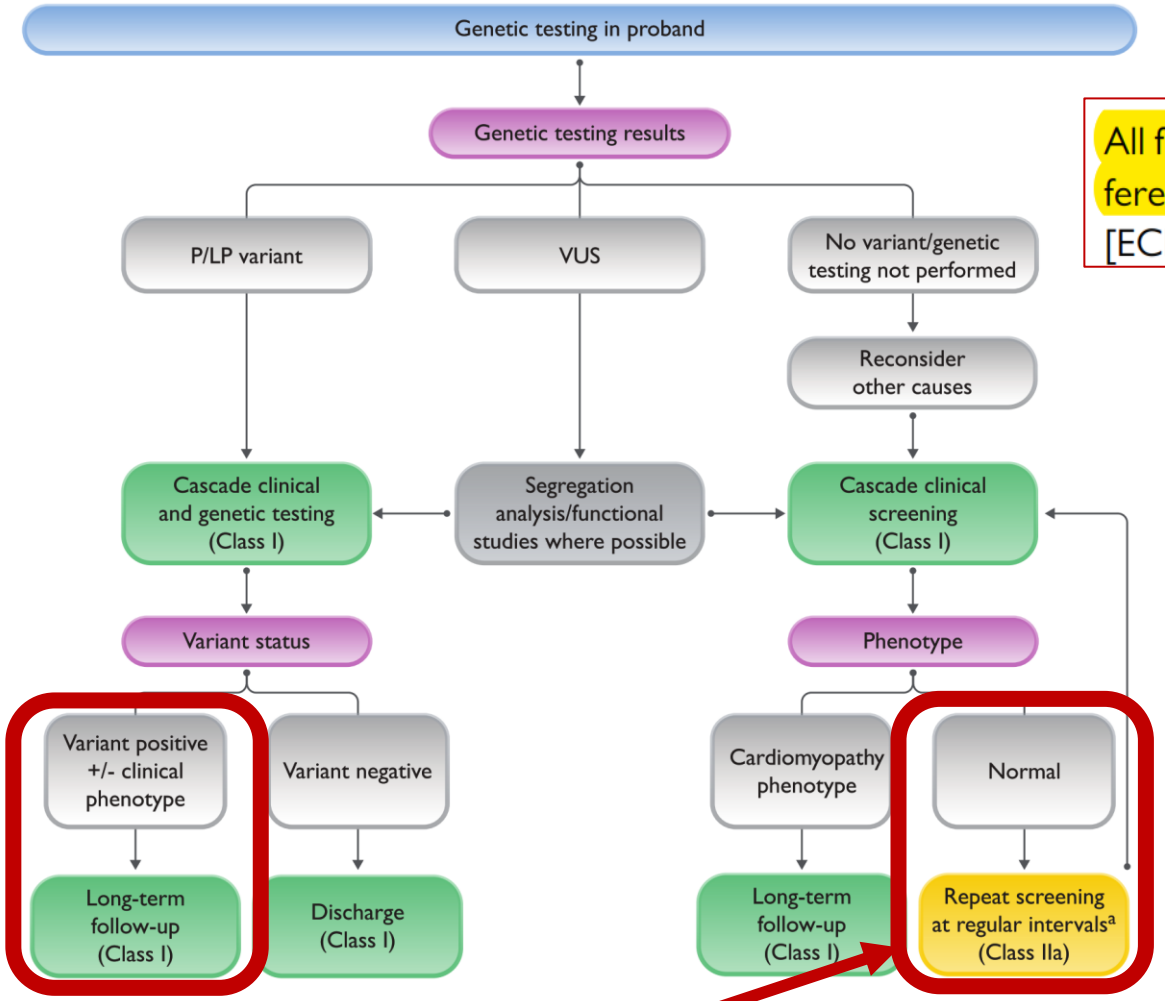
O echokardiografii až v 11.10 hodin …

2023 ESC Guidelines: MRI doporučení



Recommendations	Class[a]	Level[b]
Contrast-enhanced CMR is recommended in patients with cardiomyopathy at initial evaluation.[10,90,116,119–143]	I	B
Contrast-enhanced CMR should be considered in patients with cardiomyopathy during follow-up to monitor disease progression and aid risk stratification and management.[89,90,120–122,127,129,136–147]	IIa	C
Contrast-enhanced CMR should be considered for the serial follow-up and assessment of therapeutic response in patients with cardiac amyloidosis, Anderson–Fabry disease, sarcoidosis, inflammatory cardiomyopathies, and haemochromatosis with cardiac involvement.[148–152]	IIa	C
In families with cardiomyopathy in which a disease-causing variant has been identified, contrast-enhanced CMR should be considered in genotype-positive/phenotype-negative family members to aid diagnosis and detect early disease.[10,122,126,128,129,135–143,145,153–159]	IIa	B

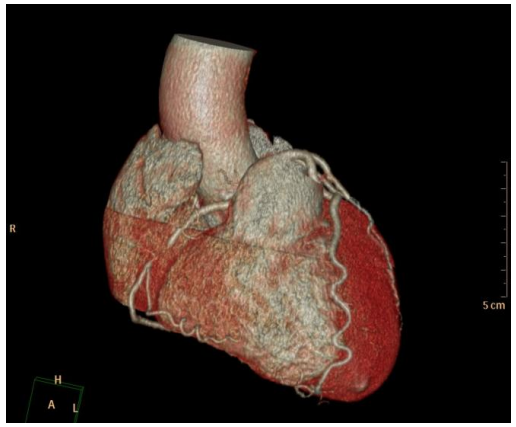
2023 ESC Guidelines: rodinný screening a follow-up

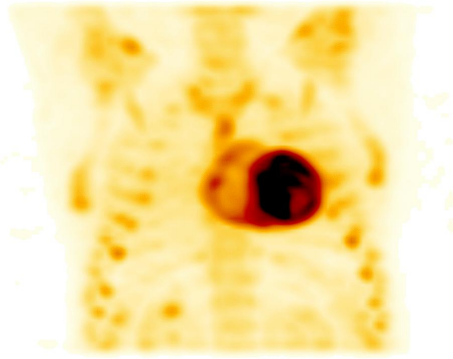


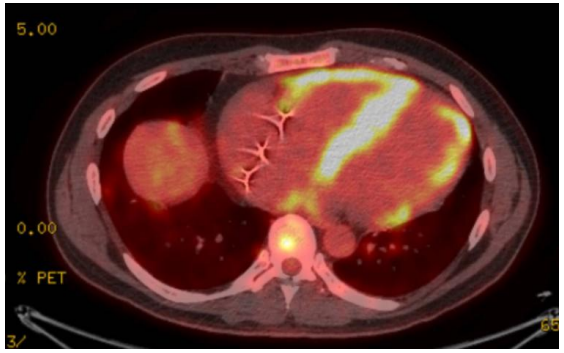
All first-degree relatives of patients with cardiomyopathy should be offered clinical screening with ECG and cardiac imaging (echocardiogram [ECHO] and/or CMR). In families in whom a disease-causing genetic

[a]If no additional affected relatives and no variant identified on genetic testing, consider earlier termination of clinical screening.

2023 ESC Guidelines: CT / nukleární kardiologie doporučení

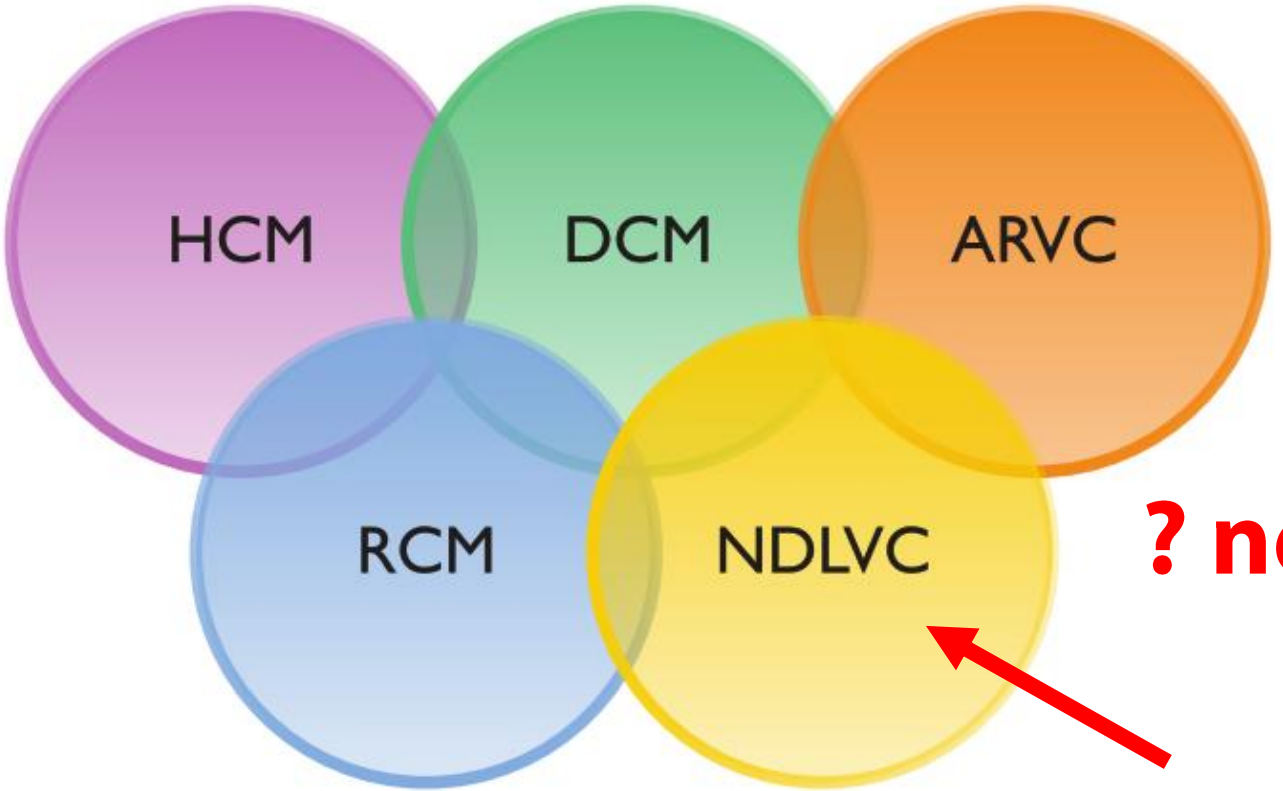






Recommendations	Class[a]	Level[b]
DPD/PYP/HMDP bone-tracer scintigraphy is recommended in patients with suspected ATTR-related cardiac amyloidosis to aid diagnosis.[166–168]	I	B
Contrast-enhanced cardiac CT should be considered in patients with suspected cardiomyopathy who have inadequate echocardiographic imaging and contraindications to CMR.[169,170]	IIa	C
In patients with suspected cardiomyopathy, CT-based imaging should be considered to exclude congenital or acquired coronary artery disease as a cause of the observed myocardial abnormality.[171]	IIa	C
18F-FDG-PET scanning should be considered for the diagnostic work-up in patients with cardiomyopathy in whom cardiac sarcoidosis is suspected.[164,172,173]	IIa	C

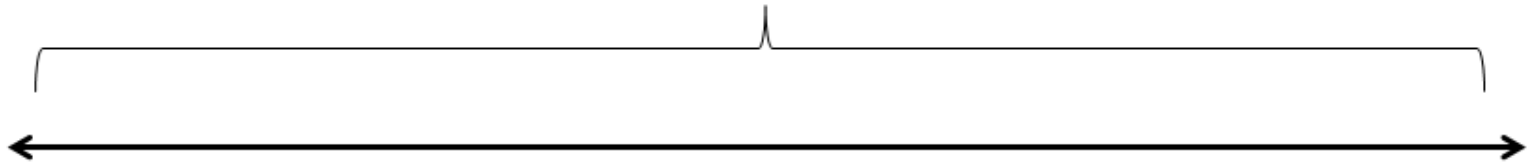
2023 ESC Guidelines: Fenotypy kardiomyopatií



? ne ACM ?

Arytmogenní kardiomyopatie

= geneticky podmíněná fibrózní / fibrolipomatózní náhrada myokardu



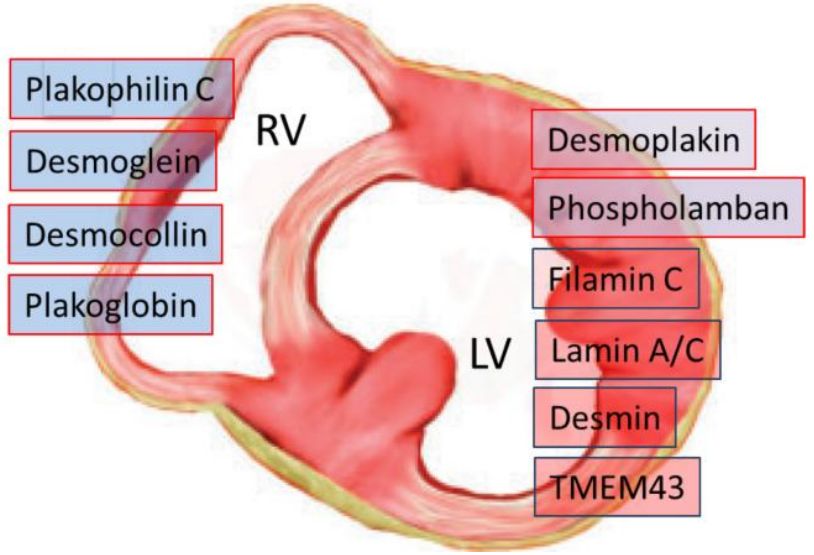
izolované / dominantní postižení levé komory	biventrikulární postižení	izolované / dominantní postižení pravé komory
⇩		⇩
Arytmogenní kardiomyopatie levé komory (ALVC)		Arytmogenní kardiomyopatie pravé komory (ARVC)

Havránek a Paleček, Vnitřní lékařství 2016;9

Arytmogenní kardiomyopatie: definice, Padovská kritéria 2020

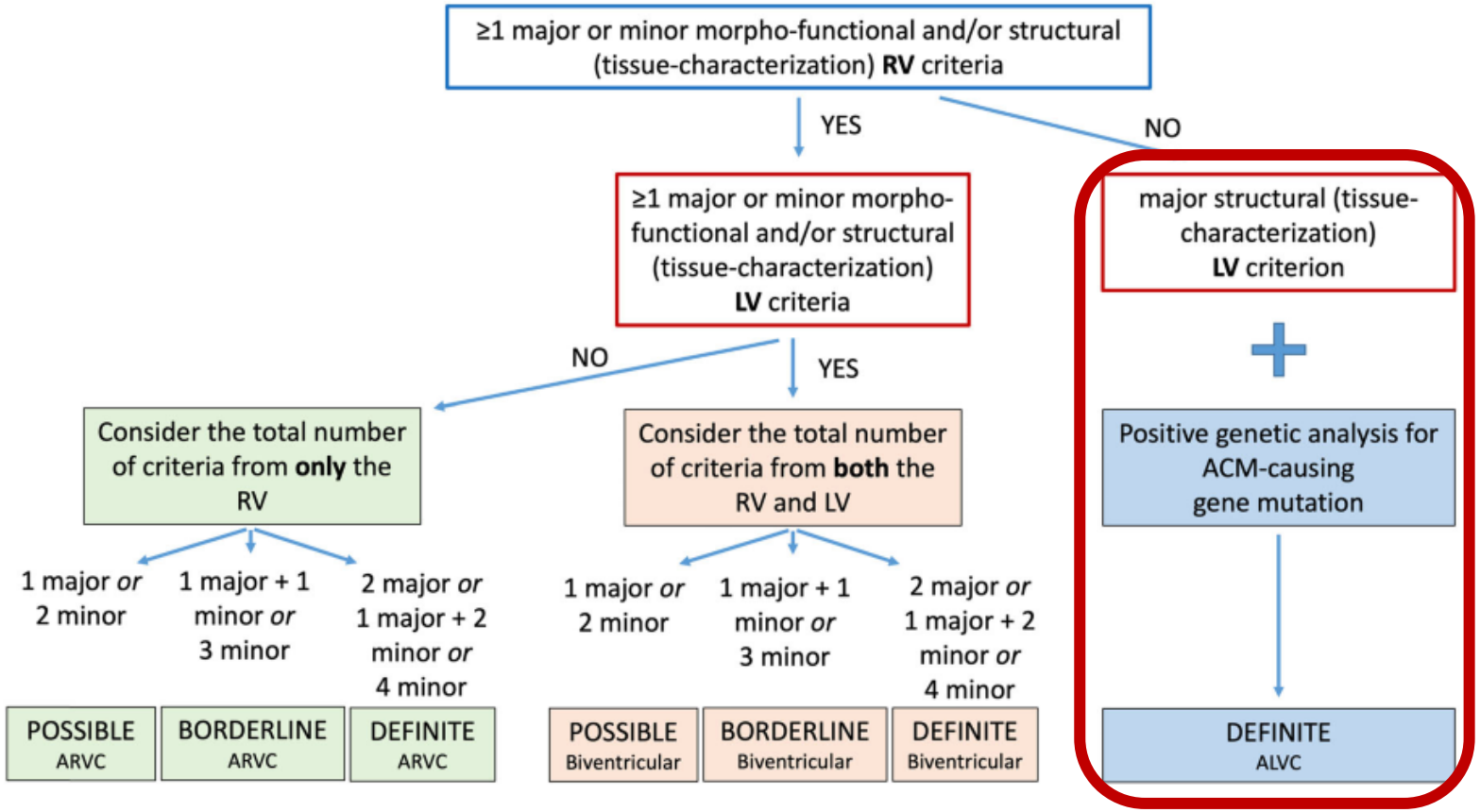
- **geneticky podmíněné** onemocnění srdečního svalu **PK / LK / obou komor**
- charakterizované **náhradou myokardu fibrózní / fibrolipomatózní tkání**
- **predisponující k potenciálně letálním komorovým arytmiím** bez ohledu na systolickou funkci komory

mutace v genech kódující desmosomální a non-desmosmální proteiny



Corrado D et al., Int J Card 2020; 319

Arytmogenní kardiomyopatie: definice, Padovská kritéria 2020



Arytmogenní kardiomyopatie LK:

1) neischemický typ fibrózy LK

(MRI – zásadní úloha !)

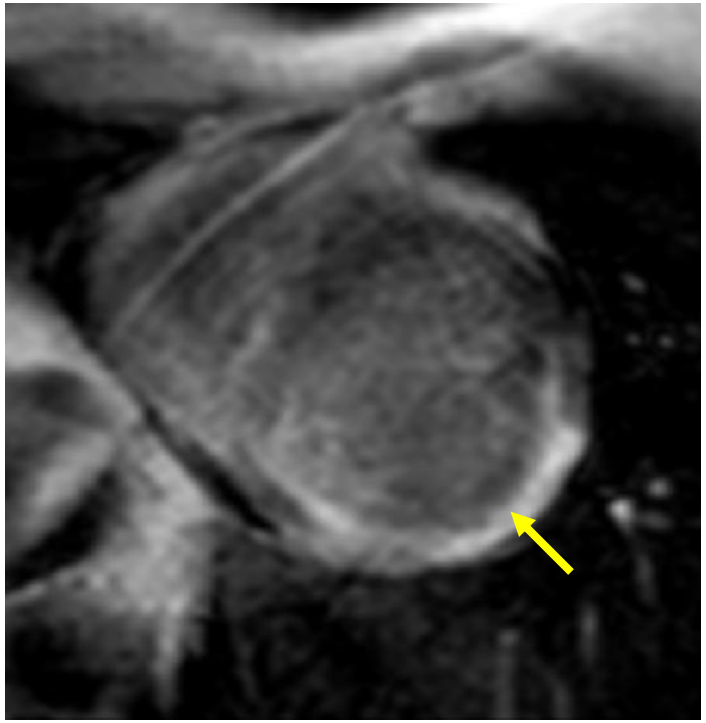
2) detekce kauzální mutace ACM

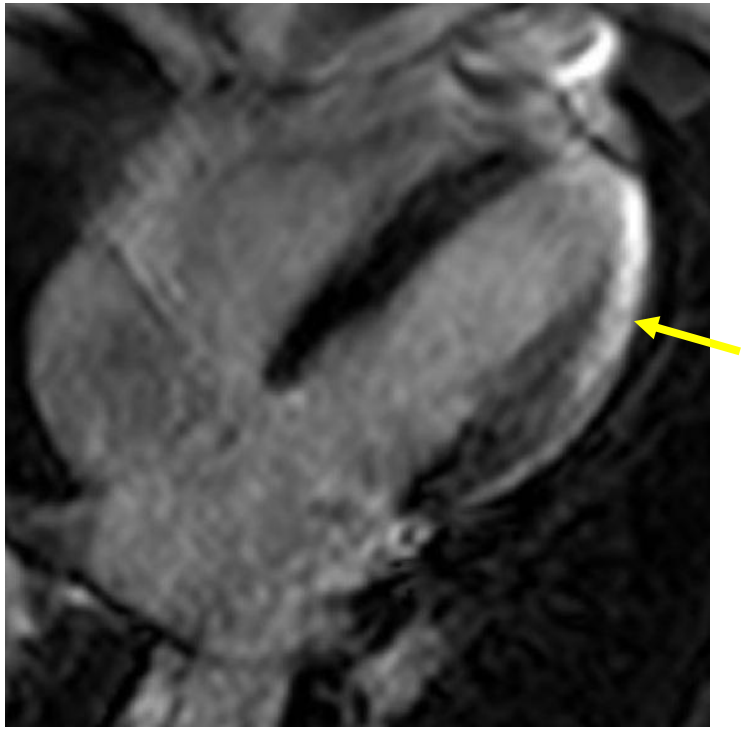
Corrado D et al., Int J Card 2020; 319

Arytmogenní kardiomyopatie LK: zásadní úloha MRI !

- **normální kinetika / regionální porucha kinetiky /**
celková systolická funkce v normě či lehká dysfunkce (těžká až v end-stage fázi) LK

- **průkaz „neischemické“ nahrazující fibrózy (LGE)**
(typicky subepikardiální oblast spodní / inferolaterální stěny → „ring-like“ pattern)





Arytmogenní kardiomyopatie LK: zásadní úloha MRI !

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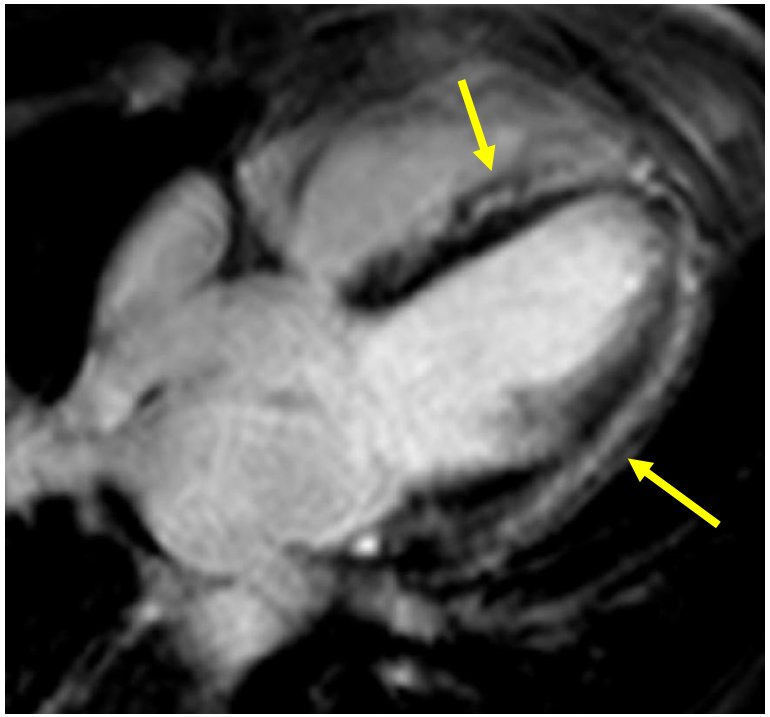
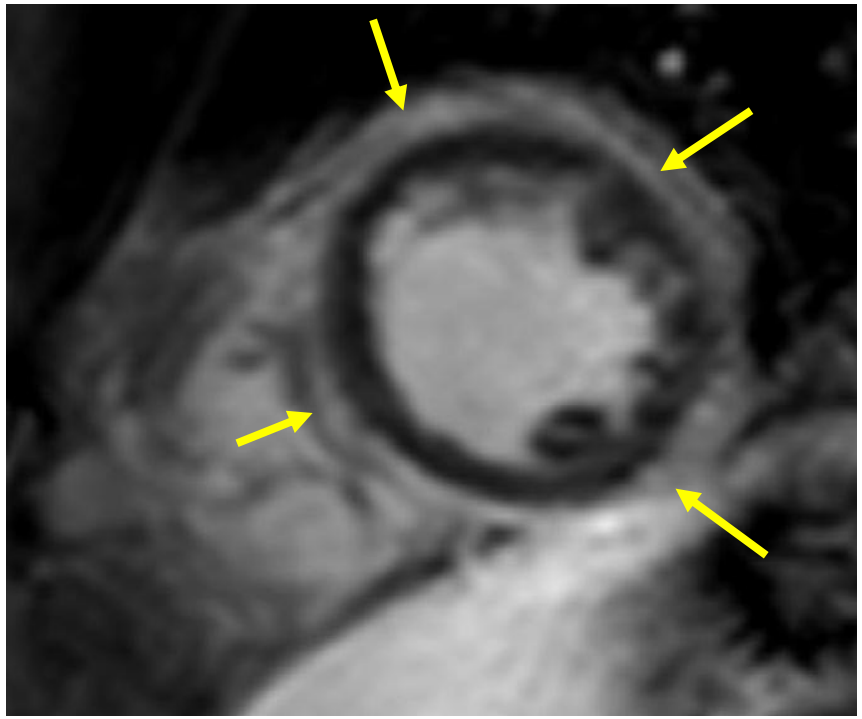
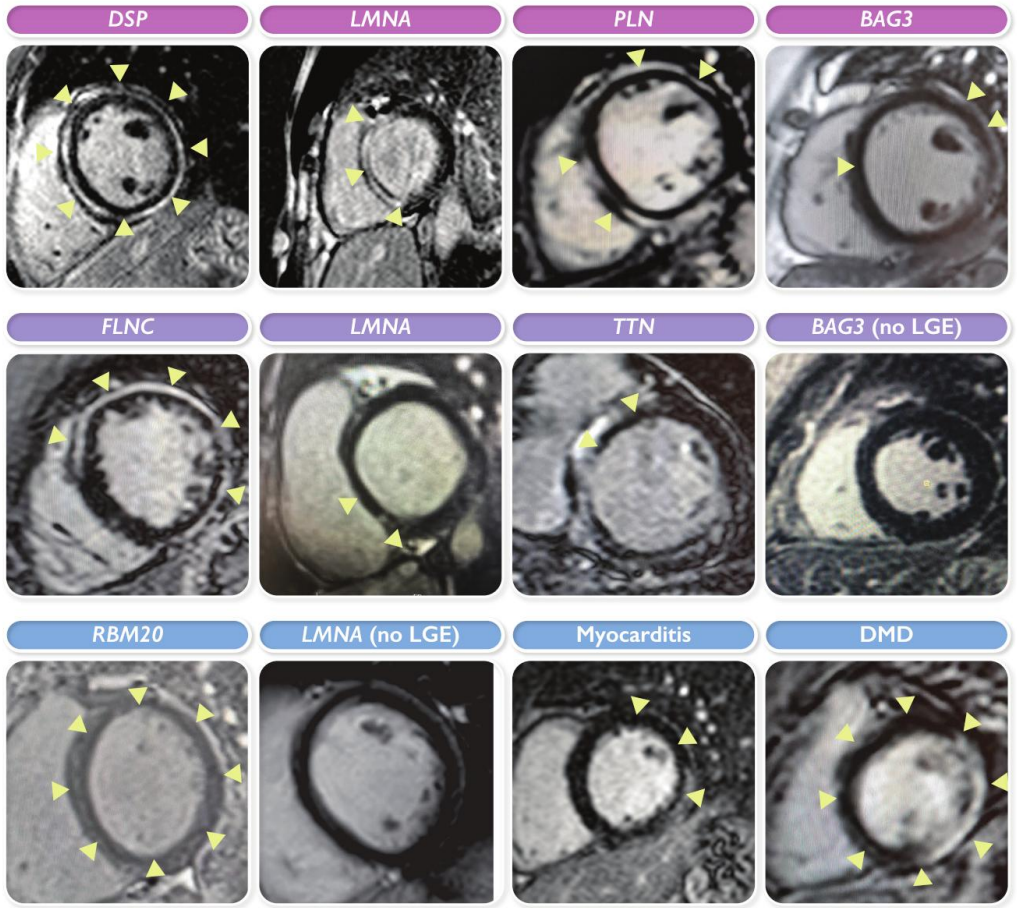


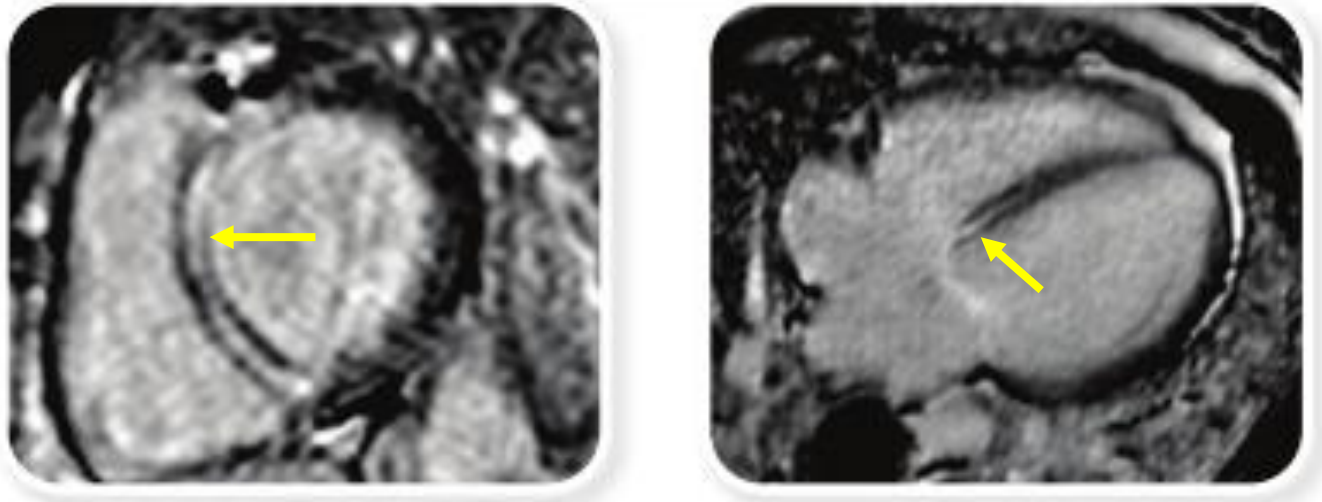


Arytmogenní kardiomyopatie LK: zásadní úloha MRI !



- průkaz „neischemické“ nahrazující fibrózy (LGE)

u non-desmosomálních mutací
i mid-wall LGE septálně (např. laminonopatie)



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Arytmogenní kardiomyopatie LK: zásadní úloha MRI !

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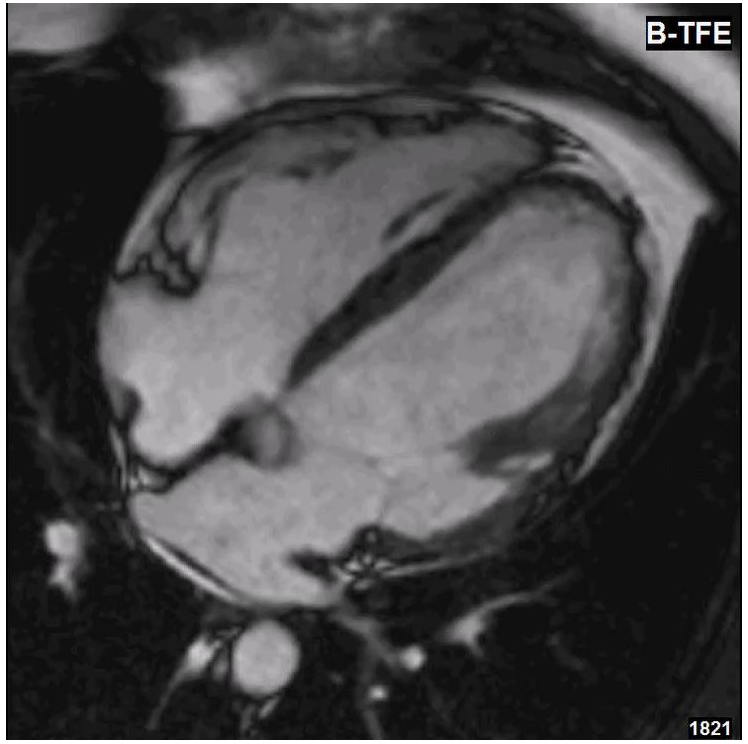

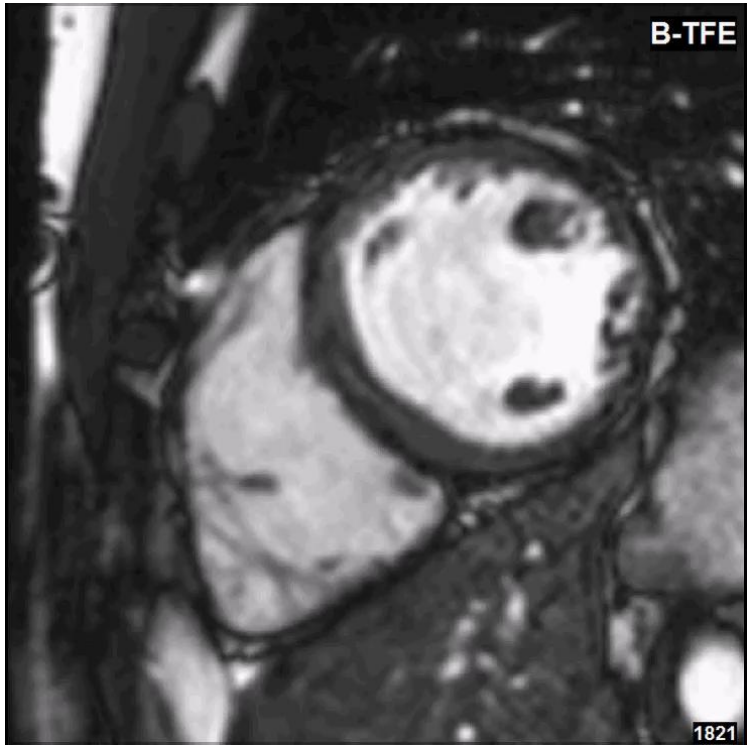

Arytmogenní kardiomyopatie LK: zásadní úloha MRI !

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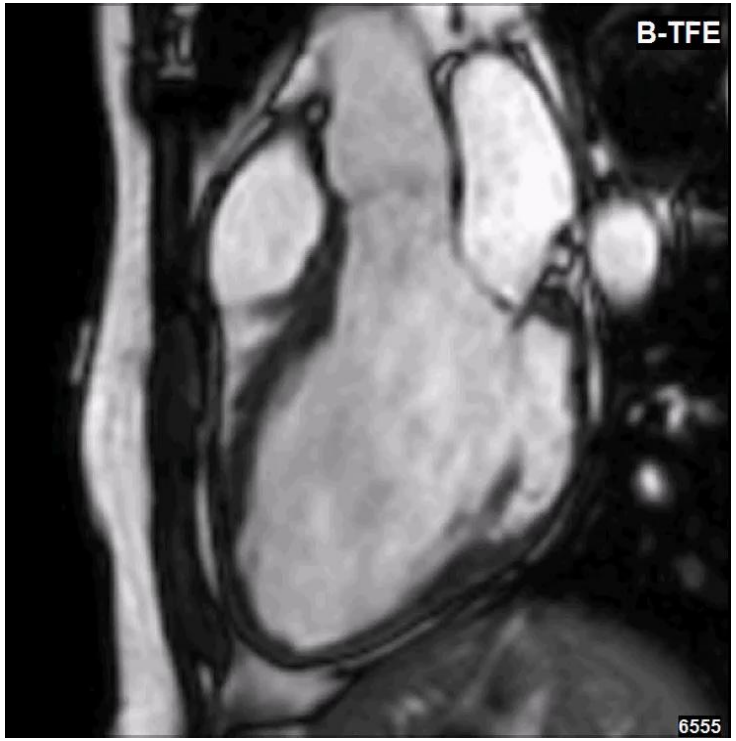
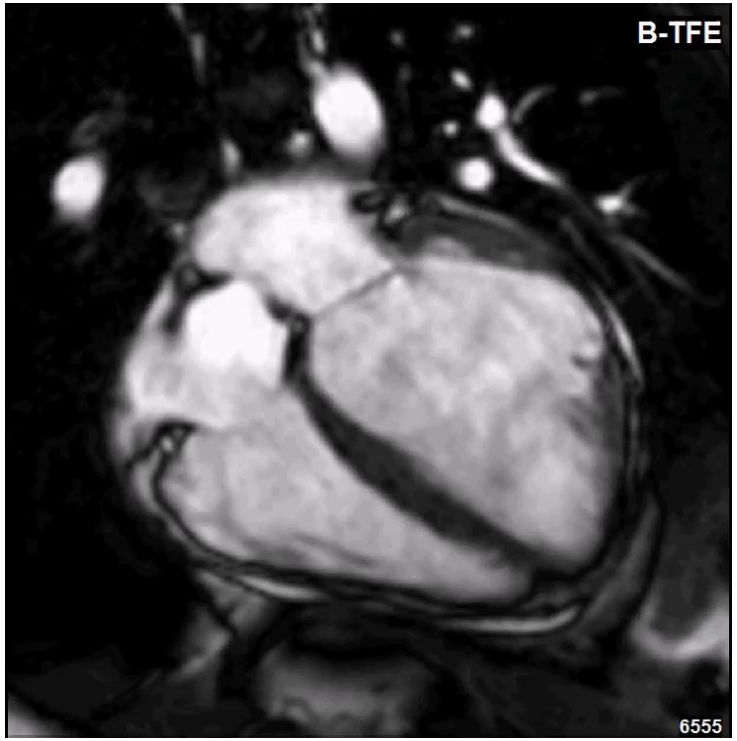




2023 Guidelines: Arytmogenní kardiomyopatie ? NE

contrast-enhancement CMR led to the identification of fibro-fatty replacement of the myocardium as a key phenotypic feature of the disease that affects the myocardium of both ventricles, with LV involvement which may even exceed the severity of RV involvement. This has led to the catch-all term of arrhythmogenic cardiomyopathy (ACM), which represents the evolution of the original term of ARVC.[5] Consistent with its general approach, the Task Force agreed

pathological investigation) and ventricular arrhythmia. This nosology has evolved in response to the recognition of the clinical and genetic overlap between right ventricular (RV) and LV cardiomyopathies, but a lack of a generally accepted definition has meant that the term encompasses a broad range of diverse pathologies and has introduced a number of inconsistencies and contradictions when applied in a clinical

and prognostic marker across a range of clinical phenotypes, but did not recommend the use of the term ACM as a *distinct* cardiomyopathy subtype as it lacks a morphological or functional definition consistent with the existing classification scheme. While acknowledging that

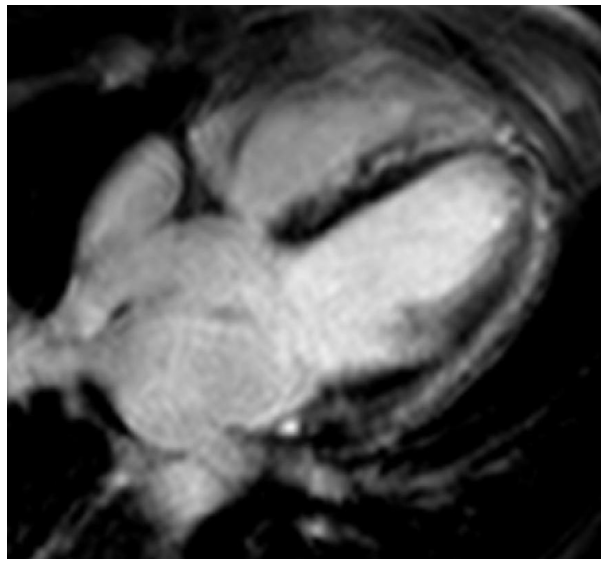
Nedilatovaná kardiomyopatie levé komory

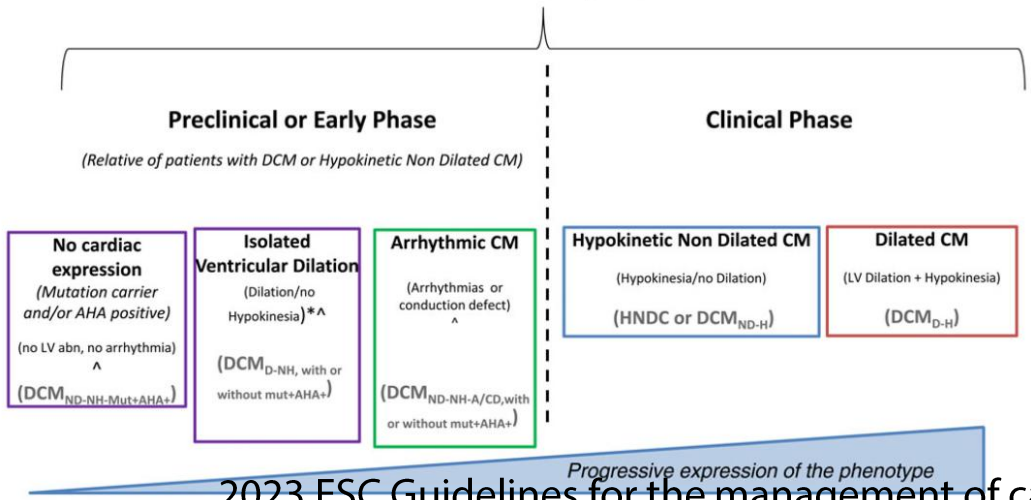
1) přítomnost neischemické fibrózy/jizvy či tukové náhrady myokardu LK, bez ohledu na přítomnost globální či regionální systolické dysfunkce LK

2) izolovaná difuzní hypokineza

arytmogenní kardiomyopatie LK

hypokinetická nedilatovaná KMP





2023 ESC Guidelines for the management of cardiomyopathies

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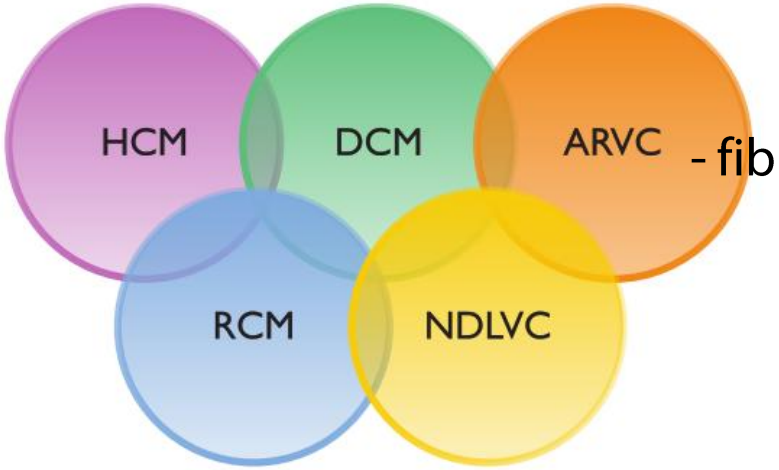
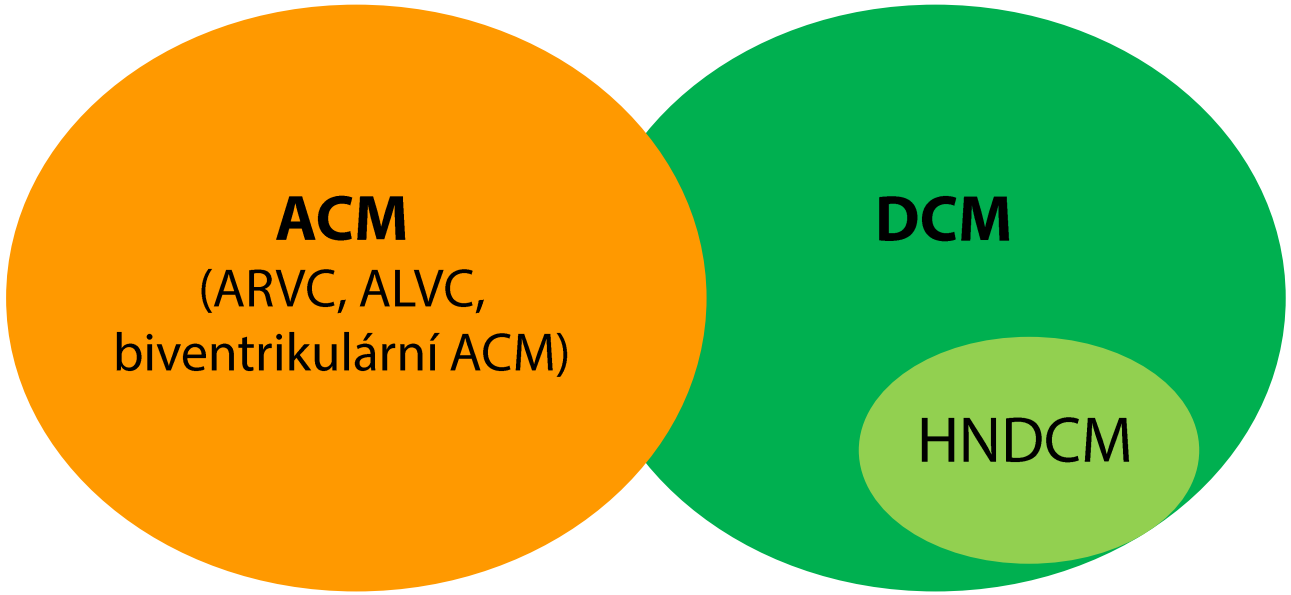


Co takto?:

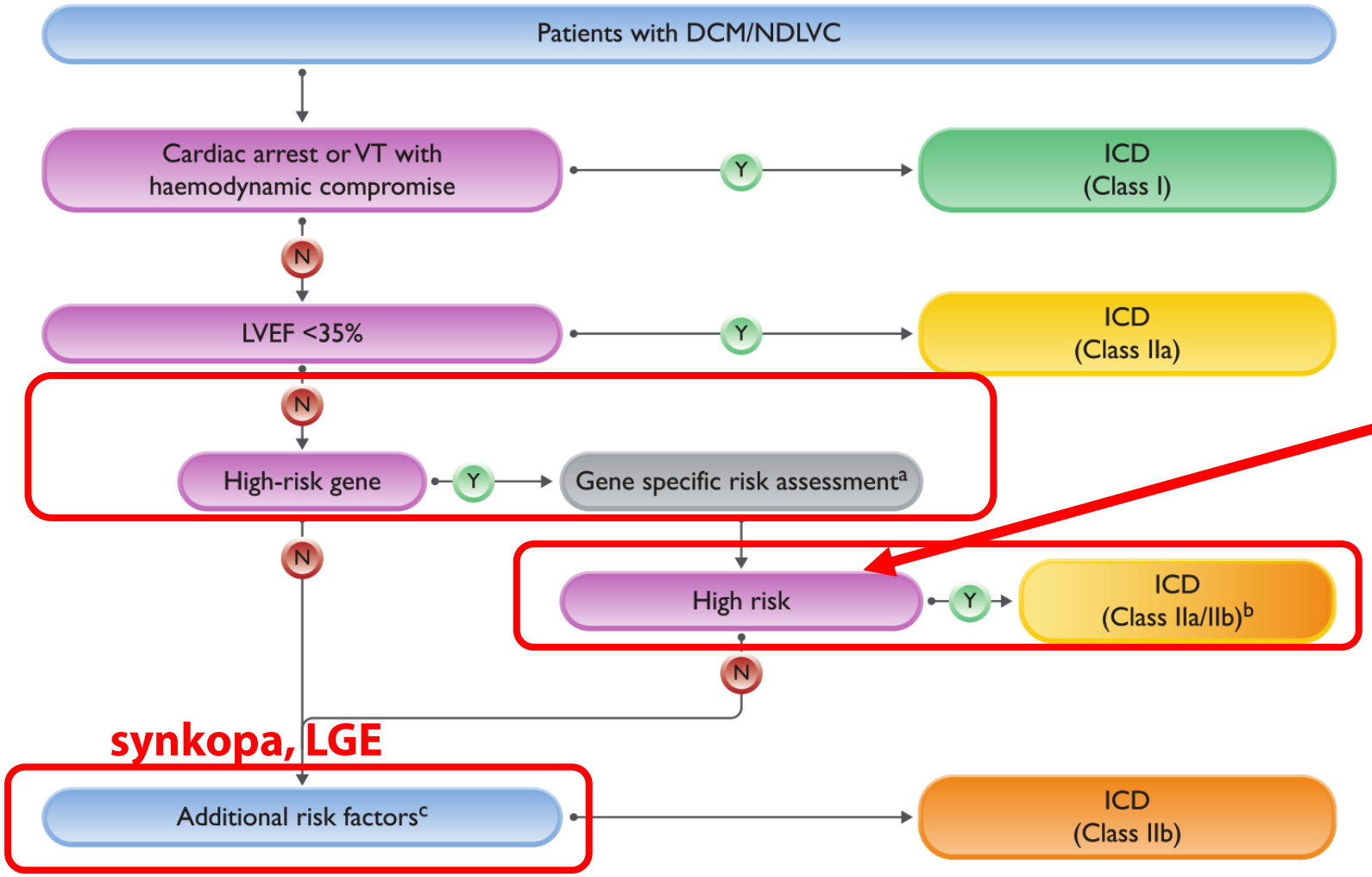
ACM vs. DKMP

- geneticky podmíněná
- fibróza/jizva vždy
- dominantně arytmická prezentace

- hereditární i získaná forma
- absence/minimální množství fibrózy (většinou typická lokalizace)
- dominantně prezentace selháním



Riziková stratifikace náhlé smrti u NDLVC a DKMP



Genetika + LGE + EF

Gene	Annual SCD rate	Predictors of SCD
LMNA[185,186,438,541,865,878,879]	5–10%	Estimated 5-year risk of life-threatening arrhythmia using *LMNA* risk score (https://lmna-risk-vta.fr)
FLNC-truncating variants[866,867,880]	5–10%	LGE on CMR LVEF < 45%
TMEM43[868,881]	5–10%	Male Female and any of the following: LVEF <45%, NSVT, LGE on CMR, >200 VE on 24h Holter ECG
PLN[542,882,883]	3–5%	Estimated 5-year risk of life-threatening arrhythmia using *PLN* risk score (https://plnriskcalculator.shinyapps.io/final_shiny) LVEF < 45% LGE on CMR NSVT
DSP[185,186]	3–5%	LGE on CMR LVEF < 45%
RBM20[869]	3–5%	LGE on CMR LVEF < 45%

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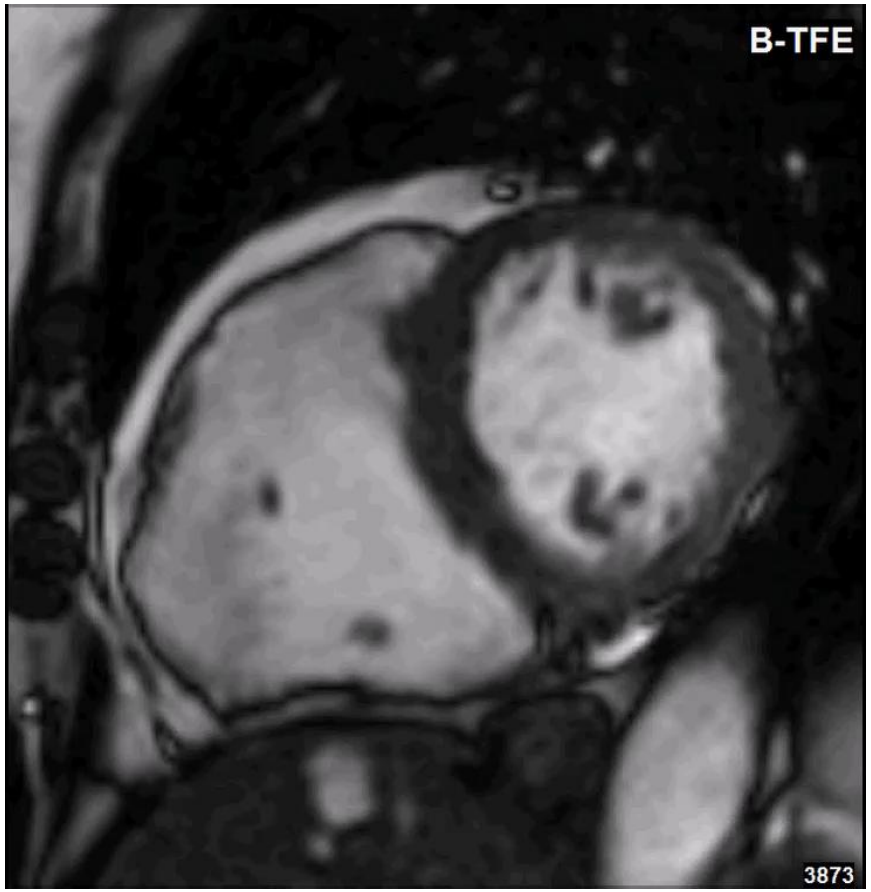
Arytmogenní kardiomyopatie PK: MRI

regionální akineze / dyskineze / aneuryzma PK (! ne hypokineza)

dilatace PK, snížená EF PK



MRI tkáňová charakteristika PK:

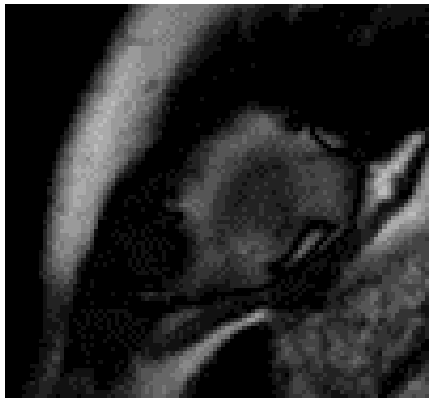
- ne průkaz tukové tkáně (obě klasifikace)
- ne LGE v 2010 klasifikaci /v Padovské ano

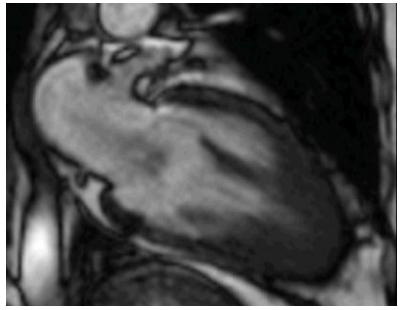
Minor

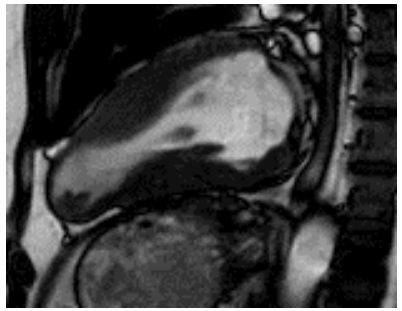
- Regional RV akinesia or dyskinesia or dyssynchronous RV contraction
- *and* 1 of the following:
  - Ratio of RV end-diastolic volume to BSA ≥100 to <110 mL/m² (male) or ≥90 to <100 mL/m² (female)
  - *or* RV ejection fraction >40% to ≤45%

Marcus FI et al., Circulation 2010;121

Hypertrofická kardiomyopatie: MRI





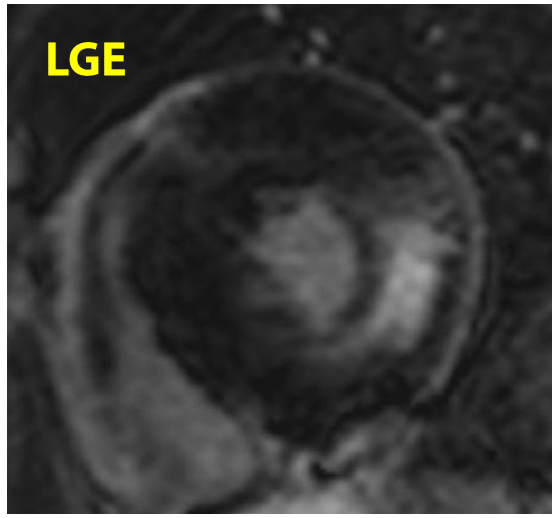


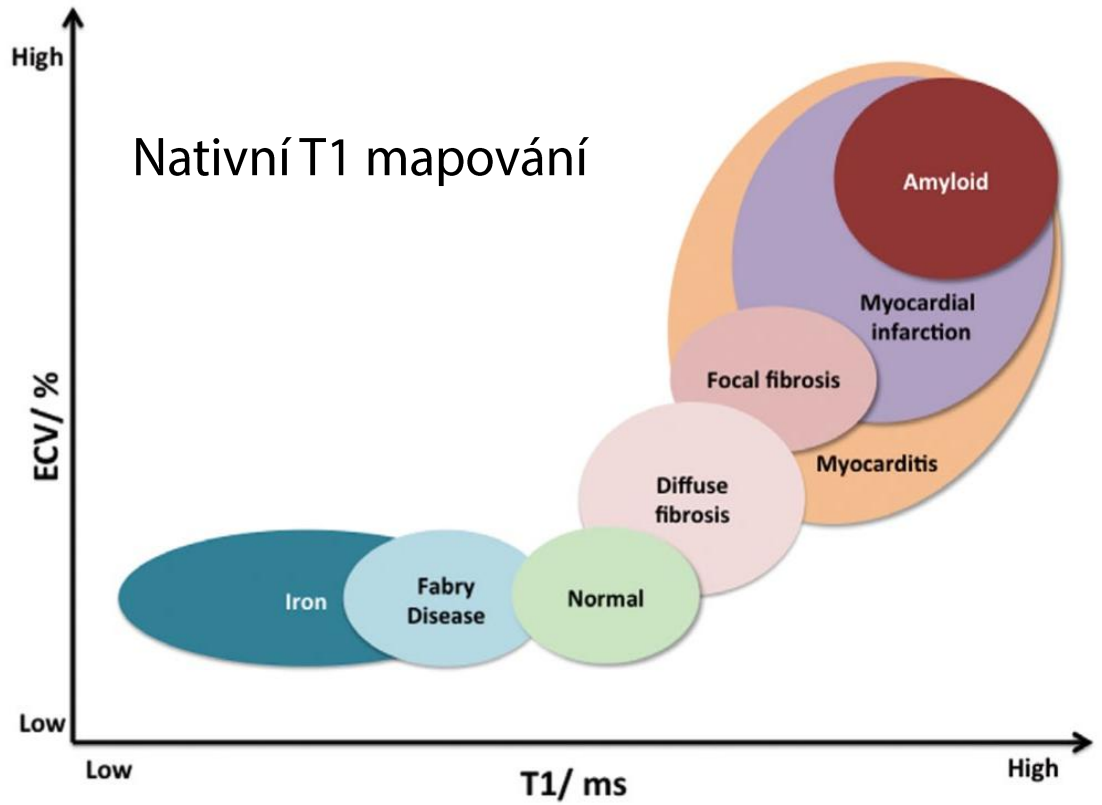
Item to assess	Primary imaging modality	Comments
LV wall thickness	ECHO/CMR	• All LV segments from base to apex examined in end-diastole, preferably in the 2D short-axis view, ensuring that the wall thickness is recorded at mitral, mid-LV, and apical levels. • CMR is superior in the detection of LV apical and anterolateral hypertrophy, aneurysms,[580] and thrombi,[581] and is more sensitive in the detection of subtle markers of disease in patients with sarcomeric protein gene variants (e.g. myocardial crypts, papillary muscle abnormalities).[159,582,583]
Systolic function (global and regional)	ECHO/CMR	• Ejection fraction is a suboptimal measure of LV systolic performance when hypertrophy is present. • Doppler myocardial velocities and deformation parameters (strain and strain rate) are typically reduced at the site of hypertrophy despite a normal EF and may be abnormal before the development of increased wall thickness in genetically affected patients.
Diastolic function	ECHO	• Routine examination should include mitral inflow assessment, tissue Doppler imaging, pulmonary vein flow velocities, pulmonary artery systolic pressure, and LA size/volume.
Mitral valve	ECHO	• Assess presence and degree of SAM and mitral regurgitation. The presence of a central- or anteriorly directed jet of mitral regurgitation should raise suspicion of an intrinsic/primary mitral valve abnormality and prompt further assessment.
LVOT	ECHO	• See *Figure 12*.
LA dimensions	ECHO/CMR	• Provides important prognostic information.[365,525,584] • Most common mechanisms of LA enlargement are SAM-related mitral regurgitation and elevated LV filling pressures.
Myocardial fibrosis/LGE	CMR	• The distribution and severity of interstitial expansion can suggest specific diagnoses. Anderson–Fabry disease is characterized by a reduction in non-contrast T1 signal and the presence of posterolateral LGE.[134,155] In cardiac amyloidosis, there is often global, subendocardial or segmental LGE and a highly specific pattern of myocardial and blood-pool gadolinium kinetics caused by similar myocardial and blood T1 signals.[585,586]

2023 ESC Guidelines for the management of cardiomyopathies

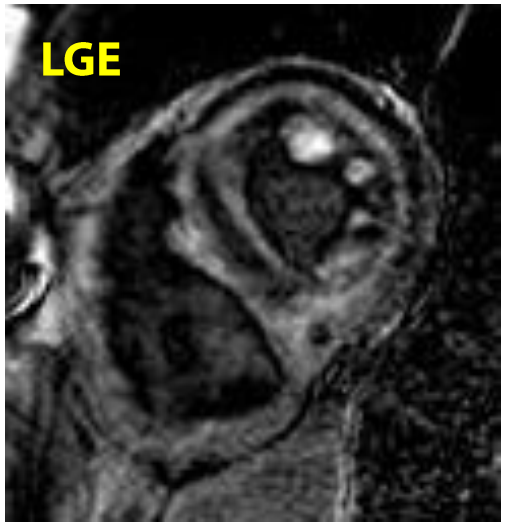
Hypertrofická kardiomyopatie: MRI a specifické diagnózy

Fabryho choroba





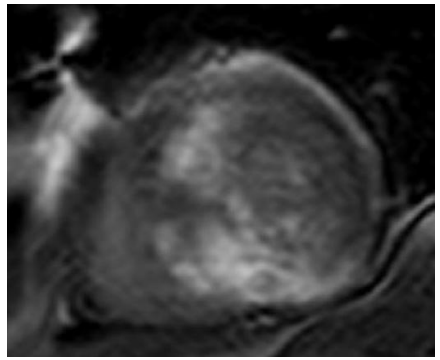
Amyloidóza



2023 ESC Guidelines for the management of cardiomyopathies

Hypertrofická kardiomyopatie: ICD - primární prevence SCD

For patients who are in the low-risk category (<4% estimated 5-year risk of SCD), the presence of extensive LGE (≥15%) on CMR may be considered in shared decision-making with patients about prophylactic ICD implantation, acknowledging the lack of robust data on the impact of scar quantification on the personalized risk estimates generated by HCM Risk-SCD or a validated paediatric model (e.g. HCM Risk-Kids).[141,796,797,834–841]	IIb	B
For patients who are in the low-risk category (<4% estimated 5-year risk of SCD), the presence of LVEF <50% may be considered in shared decision-making with patients about prophylactic ICD implantation, acknowledging the lack of robust data on the impact of systolic dysfunction on the personalized risk estimates generated by HCM Risk-SCD or a validated paediatric model (e.g. HCM Risk-Kids).[89,315,841–844]	IIb	B



2023 ESC Guidelines for the management of cardiomyopathies

Restriktivní kardiomyopatie

Intrinsic myocyte dysfunction

Genetic
- Primary RCM
- Variants in sarcomeric, cytoskeletal, nuclear envelope, filamin, titin genes

Storage
- Desmin
- AFD
- Danon
- Glycogenoses
- *PRKAG2* variants
- Iron overload/storage disorders

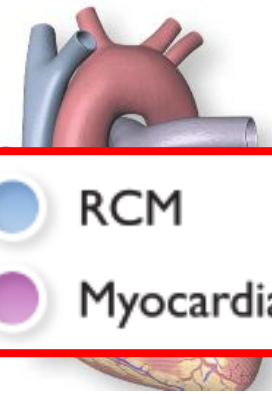
Non-genetic
- Drugs (e.g. chloroquine)

Endomyocardial disorders
- Endomyocardial fibrosis
- Hypereosinophilia
- Carcinoid
- Endocardial fibroelastosis
- Endocardial neoplasms
- Iatrogenic/drug toxicity

Myocardial extracellular matrix disorders

Infiltrative
- Hyperoxaluria
- Amyloidosis
- Sarcoidosis

Fibrosis
- Radiation
- Chemotherapy
- Systemic sclerosis
- Inflammatory/granulomatous
- Diabetic heart disease



- RCM
- Myocardial diseases with occasional restrictive physiology, often in the context of LVH

RKMP

patologie myokardu | **patologie endokardu**

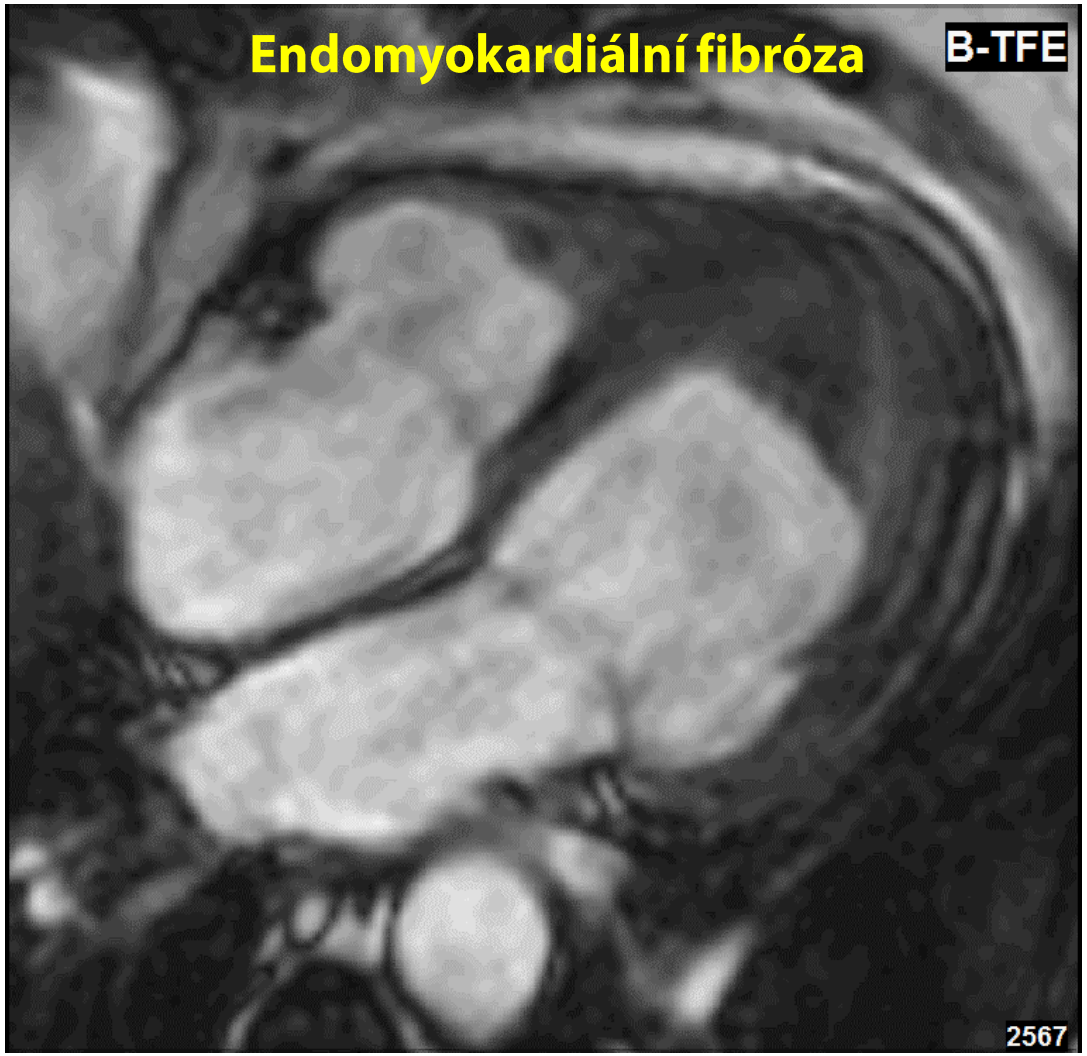
- afekce myocytu:

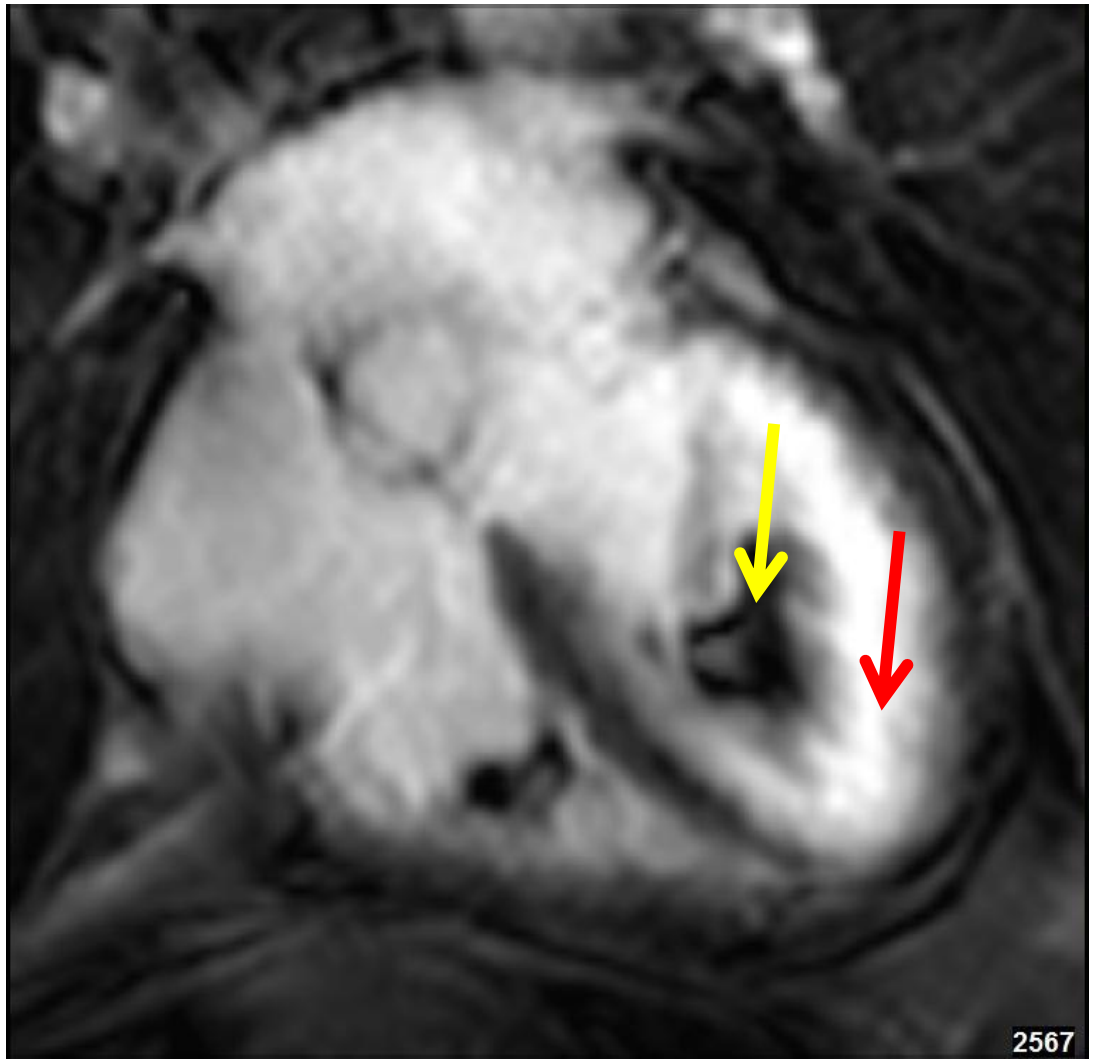
a) hereditární primární RKMP
b) střádavé choroby (intracelulárně)
c) non-genetická: toxicita léků

- afekce extracelulárního prostoru:

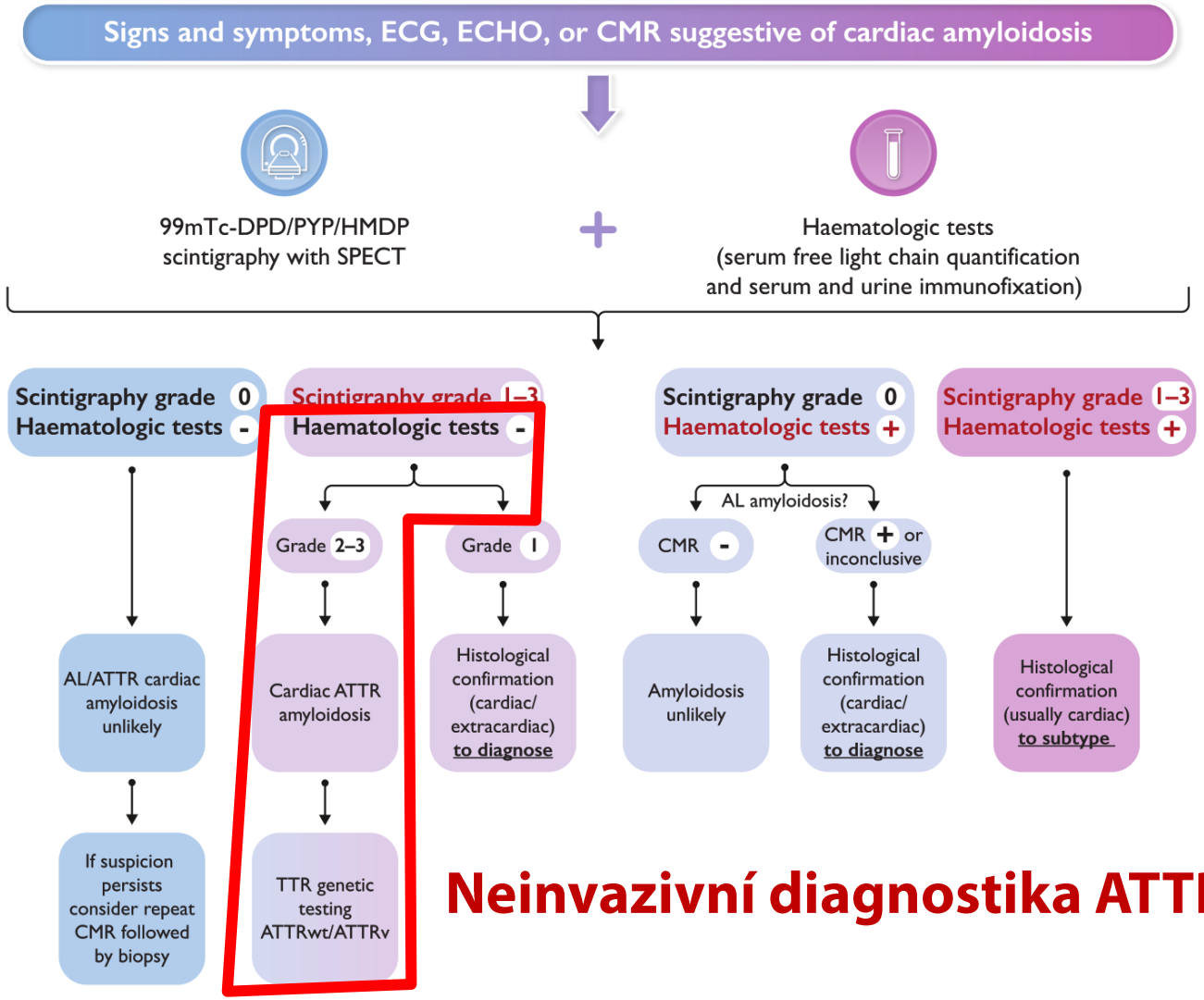
2023 ESC Guidelines for the management of cardiomyopathies

RKMP v důsledku patologie endokardu

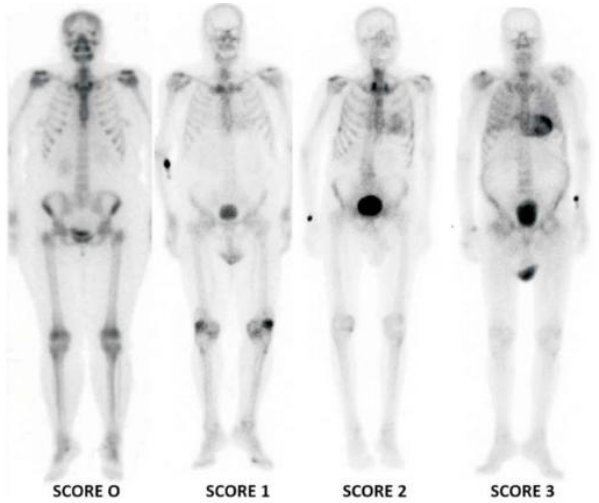




Diagnostika amyloidózy srdce



DPD scintigrafie



SCORE	DESCRIPTION
0	No cardiac uptake and normal bone uptake
1	Cardiac uptake which is less than bone uptake
2	Cardiac uptake with intensity similar to or greater than bone uptake
3	Cardiac uptake with much reduced or absent bone signal

Skóre dle Peruginiové

Neinvazivní diagnostika ATTR srdce možná u většiny jedinců

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Pozor !!!

Tc-99m labelled bone scintigraphy in suspected cardiac amyloidosis

multicentrická studie 3354 pts se suspektní či histologicky verifikovanou amyloidovou kardiomyopatií, Tc-99m scany

The NBDC for ATTR-CM are highly specific [97% (95% CI 0.91-0.99)] in clinical setting, and diagnostic performance was further refined here using new cut-offs for sFLC ratio in patients with CKD. A grade 0 radionuclide scan all but excludes ATTR-CM but occurs in most patients with AL-CA. Grade 1 scans in patients with CA and no MG are strongly suggestive of early ATTR-type, but require urgent histologic corroboration.

Table 3 Patients with Perugini grade 2/3 radionuclide bone scan

	N	Amyloid type by histology +/– proteomics				
		ATTR amyloid	AL amyloid	Other amyloid	No amyloid	No bi
Patients with no monoclonal gammopathy	1636[a]	403	0	0	428	
Endomyocardial biopsy	134	132	0	0	2[b]	
Extra-cardiac biopsy	697	271	0	0	426[c]	
Patients with monoclonal gammopathy	444	199	40	0	126	
Endomyocardial biopsy	101	85	15	0	1[b]	
Extra-cardiac biopsy	264	114	25	0	125	
Total	**2080**	**602**	**40**	**0**	**554**	

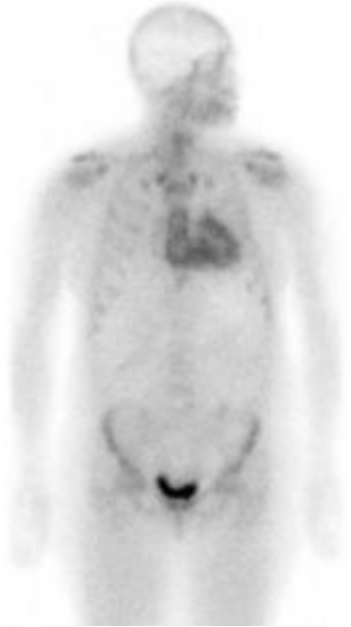
Table 5 Patients with Perugini grade 1 radionuclide bone scan

	N	Amyloid type by histology +/– proteomics					
		ATTR amyloid	AL amyloid	AApoAIV amyloid	AApoAI amyloid	No amyloid	No biopsy taken
Patients with no monoclonal gammopathy	61	25	0	0	0	19	17
Endomyocardial biopsy	1	1	0	0	0	0	-
Extra-cardiac biopsy	43	24	0	0	0	19	-
Patients with monoclonal gammopathy	122	9	83	1	0	14	15
Endomyocardial biopsy	20	3	15	0	0	2*	-
Extra-cardiac biopsy	87	6	68	1	0	12	-
Total	**183**	**34**	**83**	**1**	**0**	**33**	**32**

Rauf UM et al., Eur Heart J 2023;44

^{99m}Tc-DPD scintigraphy in immunoglobulin light chain (AL) cardiac amyloidosis

Scintigrafie pozitivní u 114 pts s AL amyloidózou (39%):
grade 1 u 75%, **grade 2 u 17% a grade 3 u 8%**



Neinvazivní diagnostika ATTR srdce:
<u>nutnost kombinace</u>
1) klinické příznaky
+ echokg/MRI suspektní z amyloidózy
+2) pozitivní scan (skóre 2 či 3)
+ 3) normální poměr FLC a normální IELFO !

Quarta CC. et al. EHJ-CV Imaging 2021;22

Signs and symptoms, ECG, ECHO, or CMR suggestive of cardiac amyloidosis

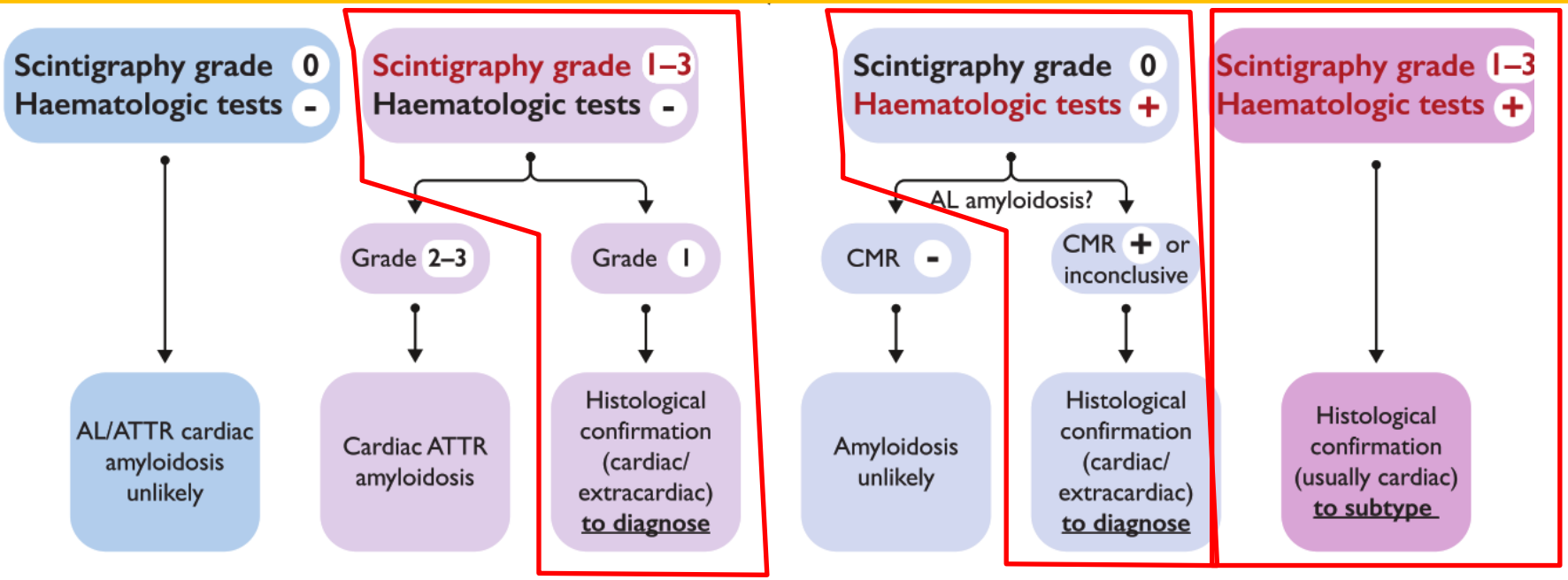
Pokud není splněno:

příznaky/echo/MRI

+ pozitivní scan (skóre 2 či 3) + normální poměr FLC a normální IELFO

⇓

nutná histologická verifikace přítomnosti a typu amyloidu



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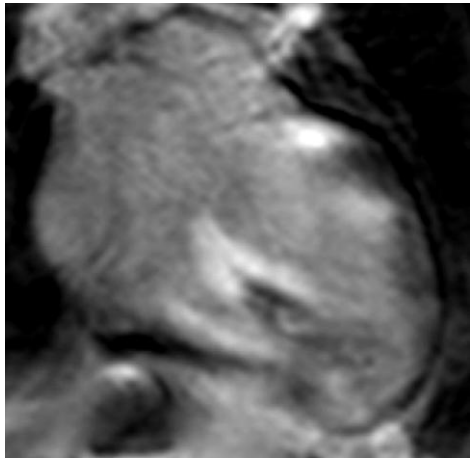
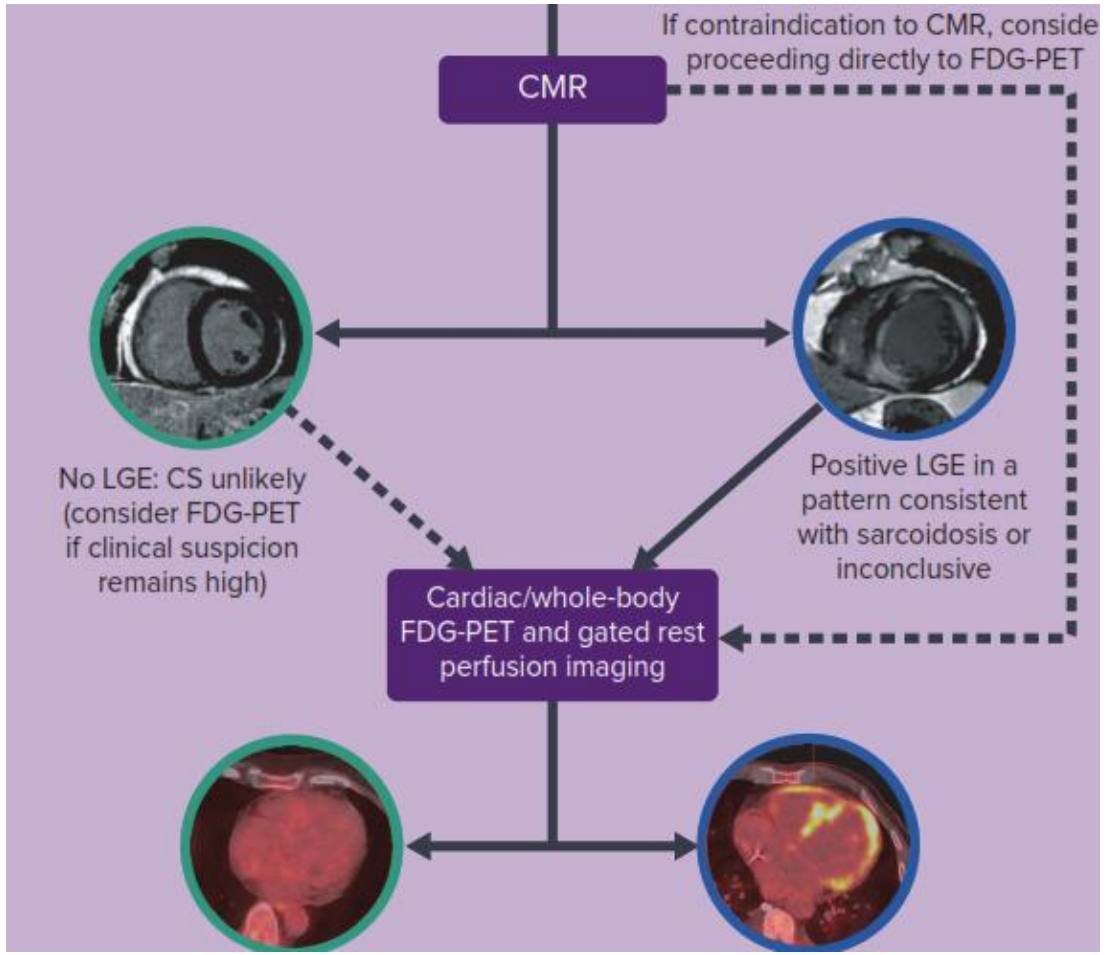
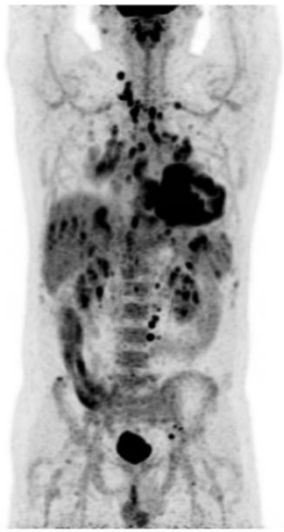
Sarkoidóza srdce

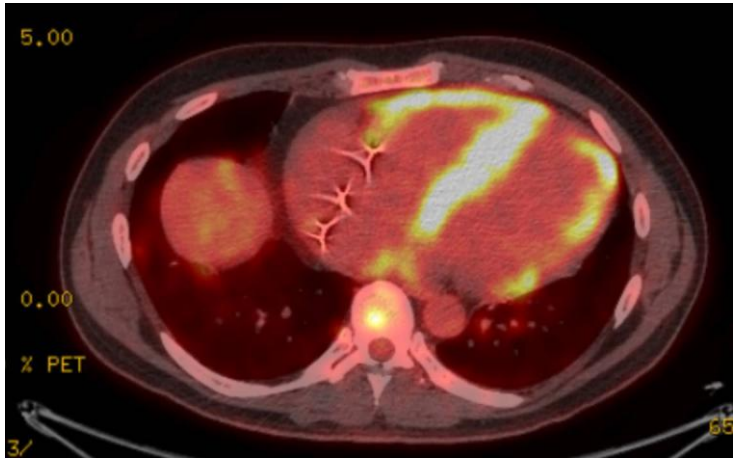
MRI







PET/CT



Giblin GT et al., Cardiac Failure Review 2021;7,e17

Sarkoidóza srdce

perfúze myokardu+ metabolizmus:

⇓

aktivita onemocnění

odlišení:

aktivního zánětu myokardu

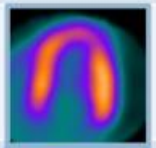
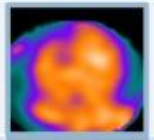
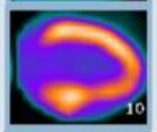
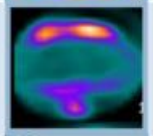
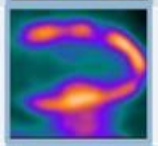
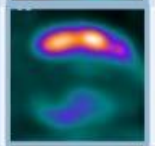
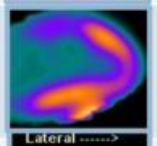
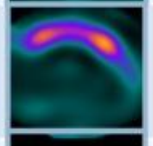
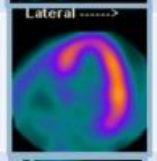
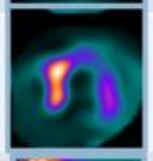
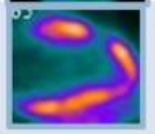
(↑ FDG uptake, perfuzní defekt)

od jizvy

(↓ FDG uptake, těžký defekt perfúze)

⇓

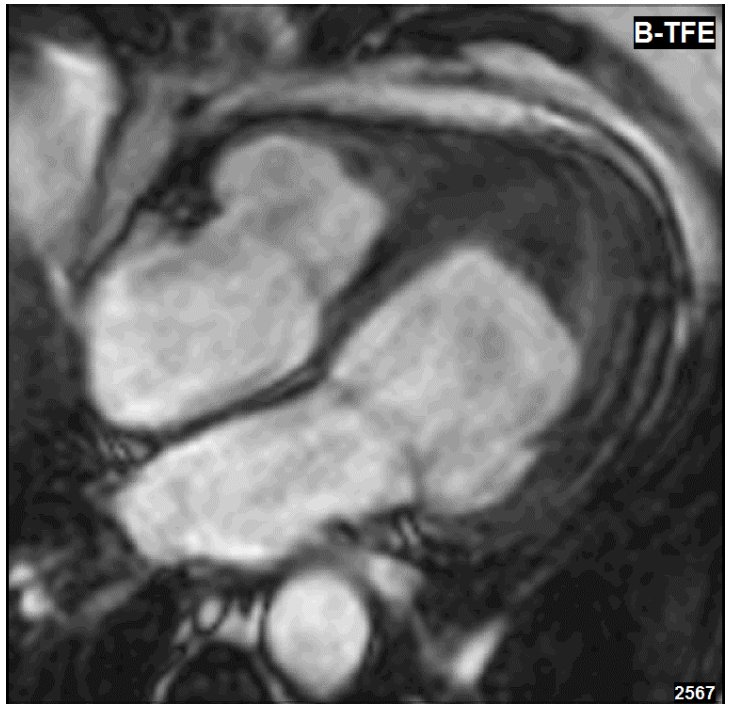
terapeutické konsekvence

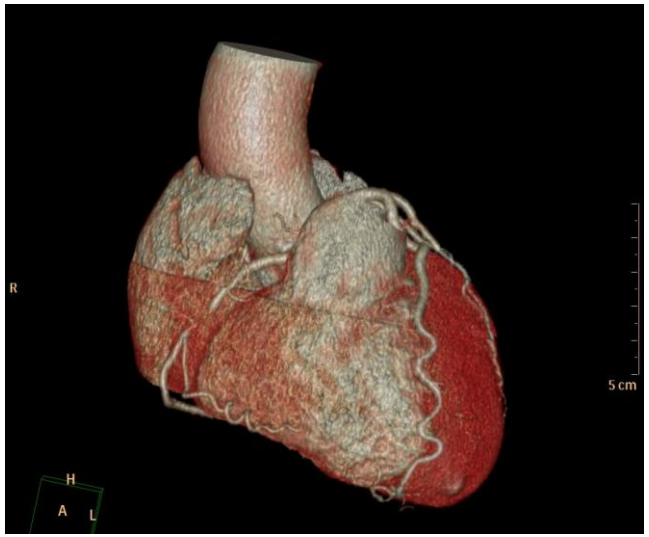
STAGES	Perfusion / FDG Patterns			
	Perfusion Defect		FDG-Uptake	
Normal	None		No / Low	
Early	None		FDG uptake high	
Progressive	Mild			
Peak active	Moderate			
Progressive myocardial impairment	Severe			
Fibrosis	Severe		Low	

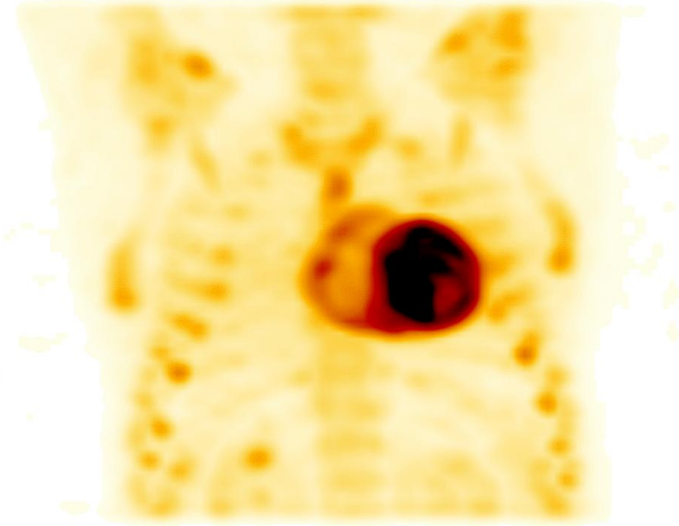
Skali H. et al. Curr Cardiol Rep 2013; 15

Závěr

Multimodalitní zobrazovací přístup k morfologicko-funkční charakteristice srdce je zásadní součástí diagnostického procesu i následného sledování jedinců s kardiomyopatiemi





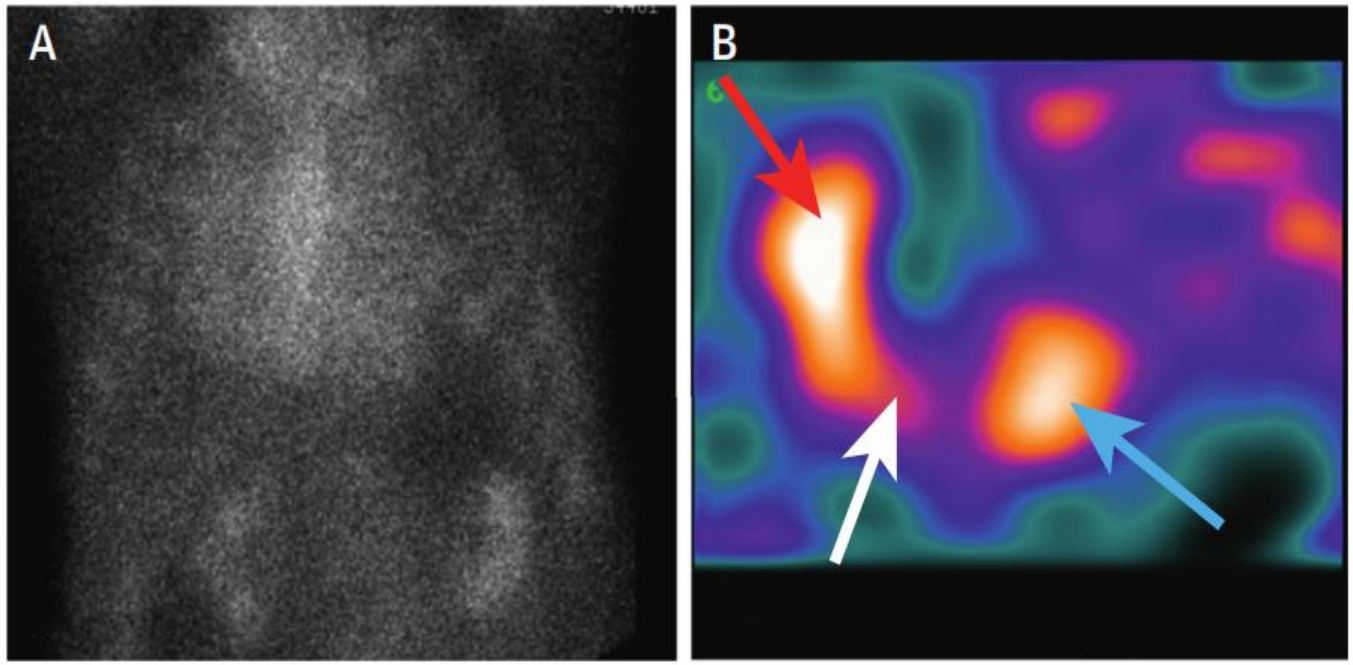


KOMPLEXNÍ KARDIO VASKULÁRNÍ CENTRUM VFN Praha

Děkuji za pozornost !

Diagnosing Transthyretin Cardiac Amyloidosis by Scintigraphy

unicentrická retrospektivní studie 753 pacientů se susp. amyloidovou kardiomyopatií,
Planární scinti provedena za 1 hodinu po aplikaci radiofarmaka; SPECT proveden u 257 pacientů



- význam skanování **2-3 hodiny po podání radiofarmaka**

- **konfirmace** pozitivního planárního skenování **pomocí SPECTu**

SPECT vs. planární scan: krev pouze v dutinách komor, ne v myokardu !

Poterucha TJ et sl., JACC CV Imag 2021;14

Cardiac Scintigraphy and Screening for Transthyretin Cardiac Amyloidosis

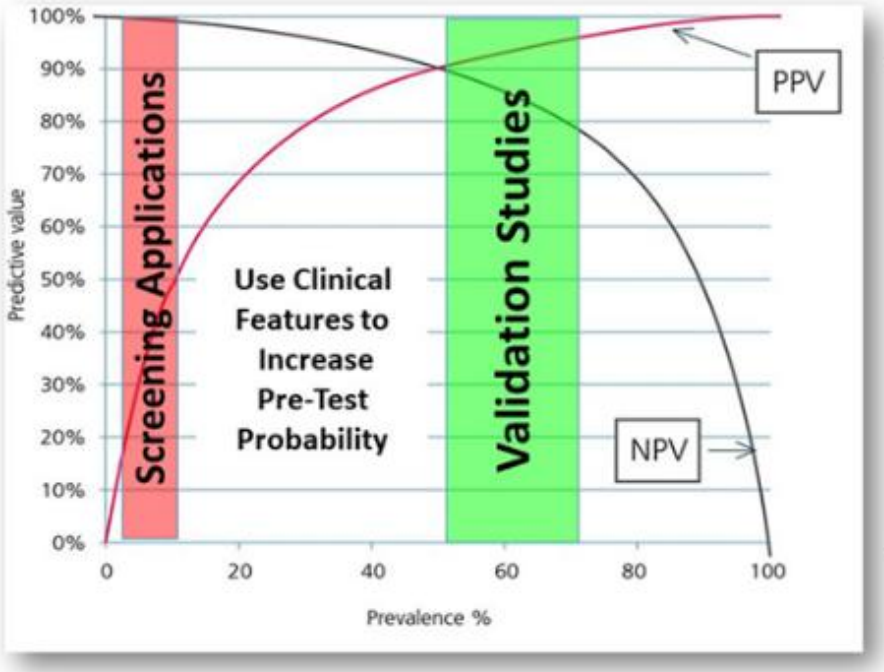
Caveat Emptor

Mathew S. Maurer, MD; Frederick L. Ruberg, MD

Clinical "Screening" Features to Enhance Pre-Test Probability

- **Age > 60 years**
- **Cardiac Features**
  - Increased wall thickness
  - Non-dilated left ventricle
  - High relative wall thickness
  - Apical sparing longitudinal systolic strain pattern
  - Low Tissue Doppler Velocities
  - Persistently positive troponin
  - AV Block in Older Adults
- **Extra-cardiac features**
  - Orthopedic manifestations
    - Carpal tunnel syndrome
    - Lumbar spinal stenosis
    - Biceps tendon rupture
  - Polyneuropathy
  - Autonomic neuropathy

Cardiac Scintigraphy Test Performance Differs in Screening and Validation Cohort: For optimal test performance the "right" population should be tested



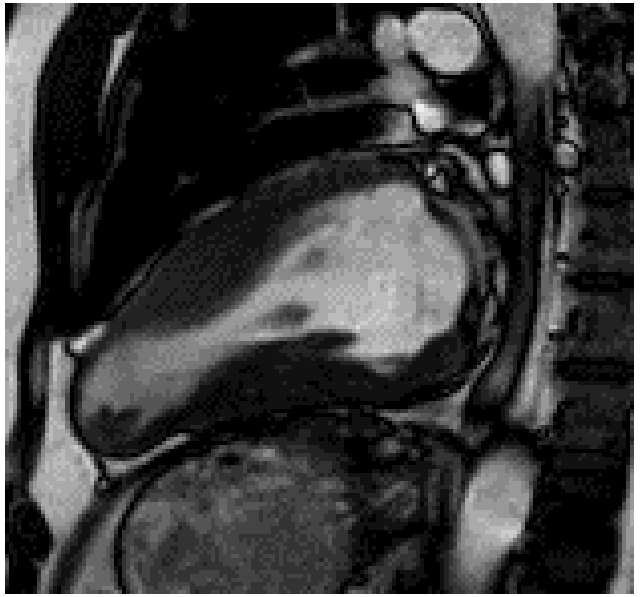
Best Practices for Cardiac Scintigraphy to Validate the Diagnosis of TTR Cardiac Amyloidosis:

1. Assess for AL Amyloidosis with serum free light chains and immunofixation electrophoresis.
2. SPECT imaging to confirm myocardial retention of isotope.
3. Delayed (e.g. 3 hour) imaging to minimize impact of blood pooling.

Circulation 2021;144

Hypertrofická kardiomyopatie: primární prevence SCD

In patients with LV apical aneurysms, decisions about primary prevention ICD based on an assessment of risk using the HCM Risk-SCD or a validated paediatric risk-prediction (e.g. HCM Risk-Kids) tool and not solely on the presence of the aneurysm should be considered.[580,728,737,791,792]	IIa	B



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