Fulminantní myokarditida

Jan Krejčí

FAKULTNÍ NEMOCNICE U SV. ANNY V BRNĚ

I. INTERNÍ KARDIOANGIOLOGICKÁ KLINIKA FNUSA A LF MU

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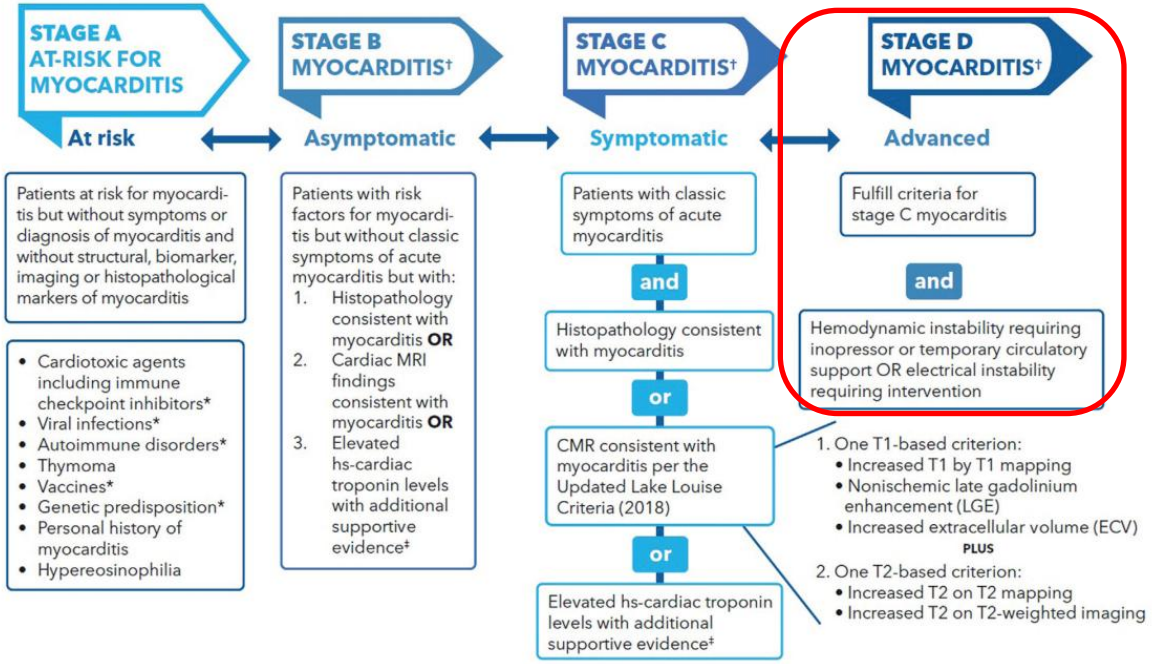
Fulminantní myokarditida v ACC consensusu 2024

2024 ACC Expert Consensus Decision Pathway on Strategies and Criteria for the Diagnosis and Management of Myocarditis

FIGURE 5 Proposed Stages of Myocarditis



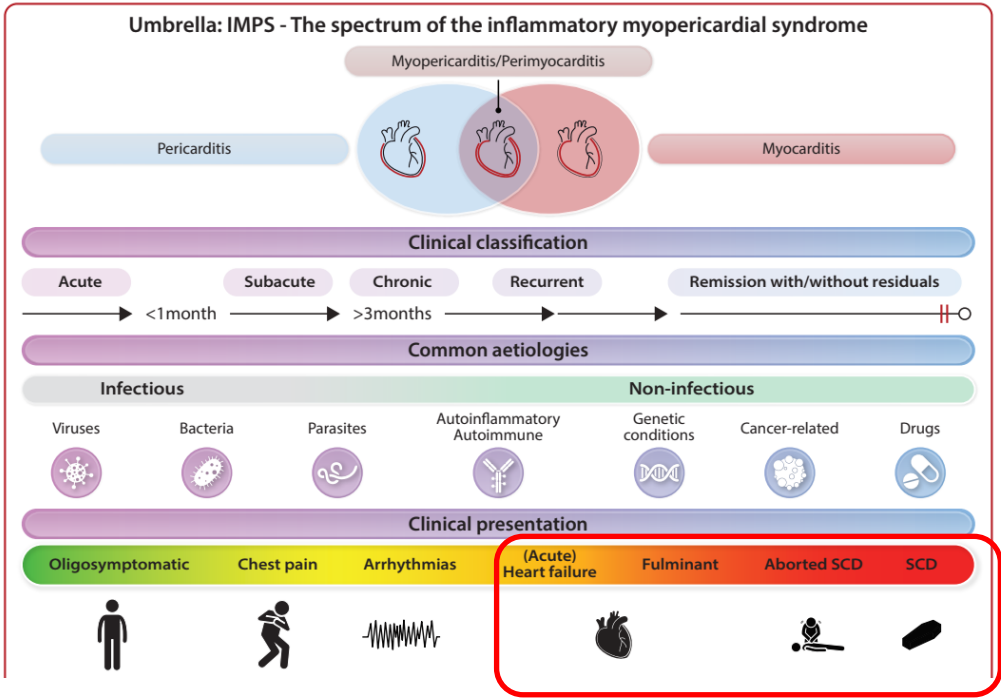
JACC VOL. 85, NO. 4, 2025
FEBRUARY 4, 2025:391-431

Fulminantní myokarditida v ESC Guidelines 20525

2025 ESC Guidelines for the management of myocarditis and pericarditis

Developed by the task force for the management of myocarditis and pericarditis of the European Society of Cardiology (ESC)

Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC) and the European Association for Cardio-Thoracic Surgery (EACTS)



European Heart Journal (2025) **00**, 1–90
https://doi.org/10.1093/eurheartj/ehaf192

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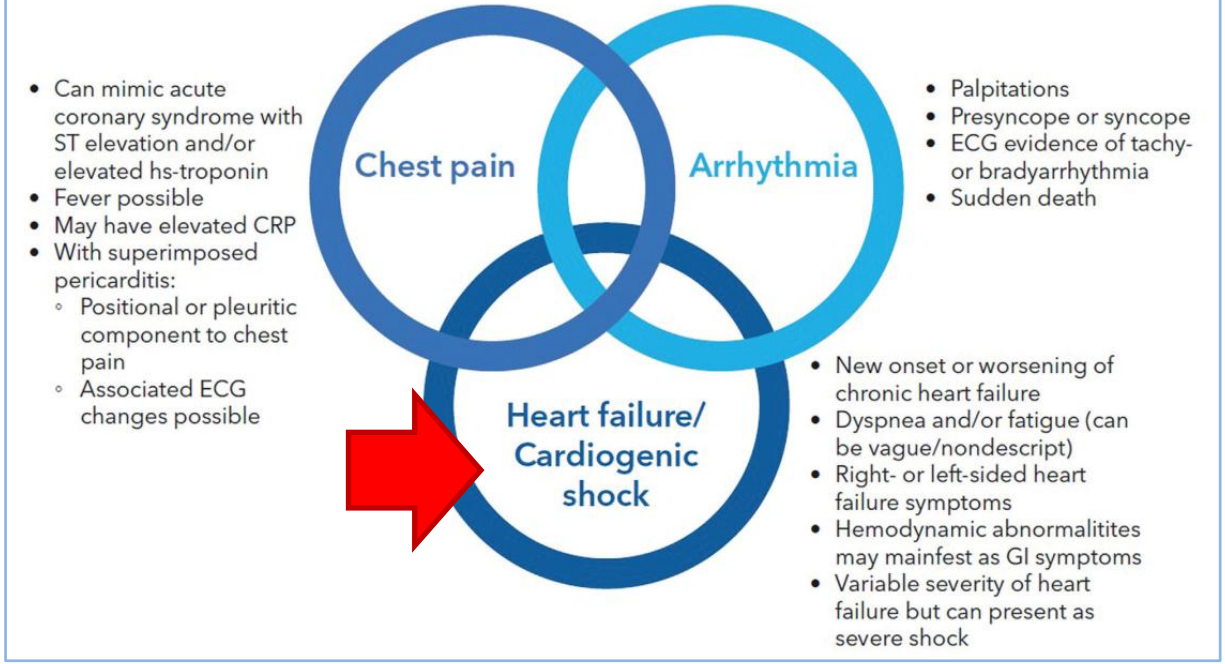
Myokarditididy – klinický obraz

2024 ACC Expert Consensus Decision Pathway on Strategies and Criteria for the Diagnosis and Management of Myocarditis

FIGURE 2 Three Classic Presentations of Myocarditis



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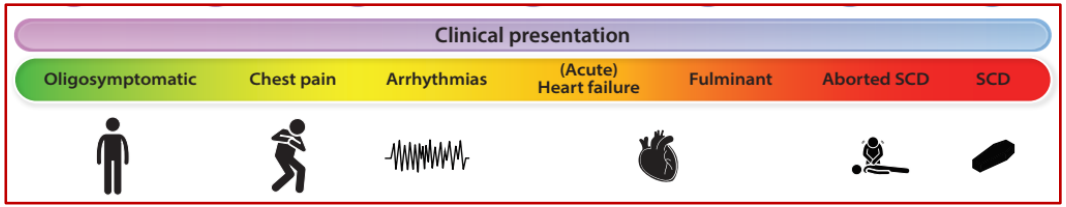
4.2.2. Fulminant myocarditis

Fulminant myocarditis (occurring in 3%–9%) is characterized by cardiogenic shock at presentation for which haemodynamic support is needed.[28] Isolated right ventricle (RV) dysfunction is uncommon; however, biventricular failure occurs frequently in FM. Sustained ventricular arrhythmias (VA) may also occur in these patients (46.9%) and some present with sudden cardiac death (SCD) (25.8%).[28,56,57]



European Heart Journal (2025) **00**, 1–90
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Diagnostický algoritmus – akutní HF se susp. akutní MC

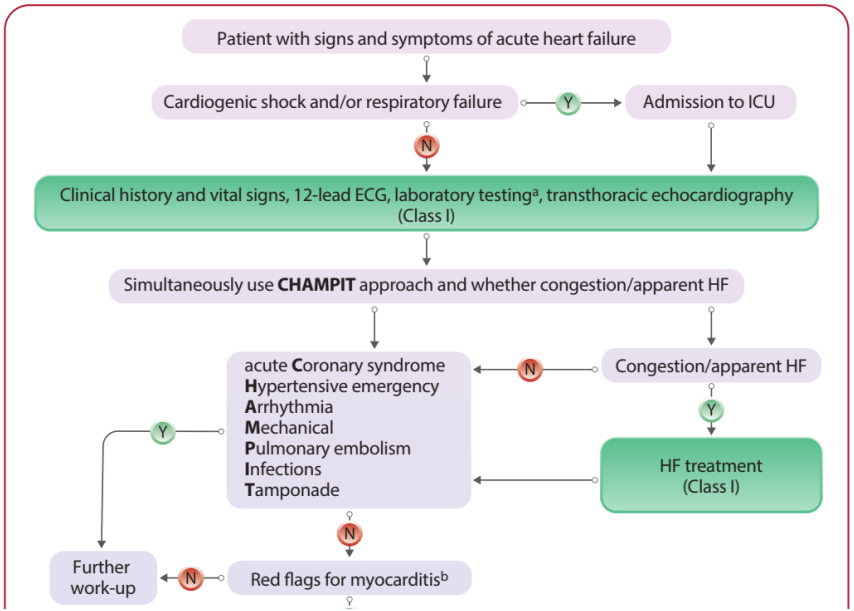

Table 6 **Red flags for the clinical diagnosis of myocarditis**

Myocarditis
Recent or concomitant flu-like syndrome or gastroenteritis
Infarct-like chest pain
Palpitations
HF symptoms
ECG changes[a]
Ventricular arrhythmias (isolated, complex)
Syncope
Haemodynamic instability
Elevated markers of myocardial lesion (hs-Tn, CK-MB elevation)
Elevated markers of HF (NT-proBNP)
Abnormal wall motion, increased wall thickness and/or impaired systolic function on imaging
CMR imaging with myocardial oedema and/or LGE

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Diagnostický algoritmus – klíčová role EMB

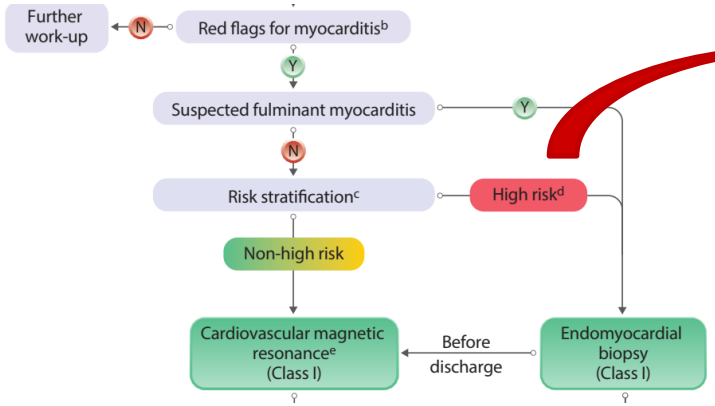

Table 7 Clinical risk stratification to guide

Risk	High risk
Myocarditis	• Acute HF/cardiogenic shock • Dyspnoea NYHA III–IV refractory to medical therapy • Cardiac arrest/syncope[a] • Ventricular fibrillation/sustained ventricular tachycardia[a] • High-level AV block[a]
	Imaging criteria:
	• Newly reduced LVEF (<40%)[a] • Extensive LGE on CMR[a]

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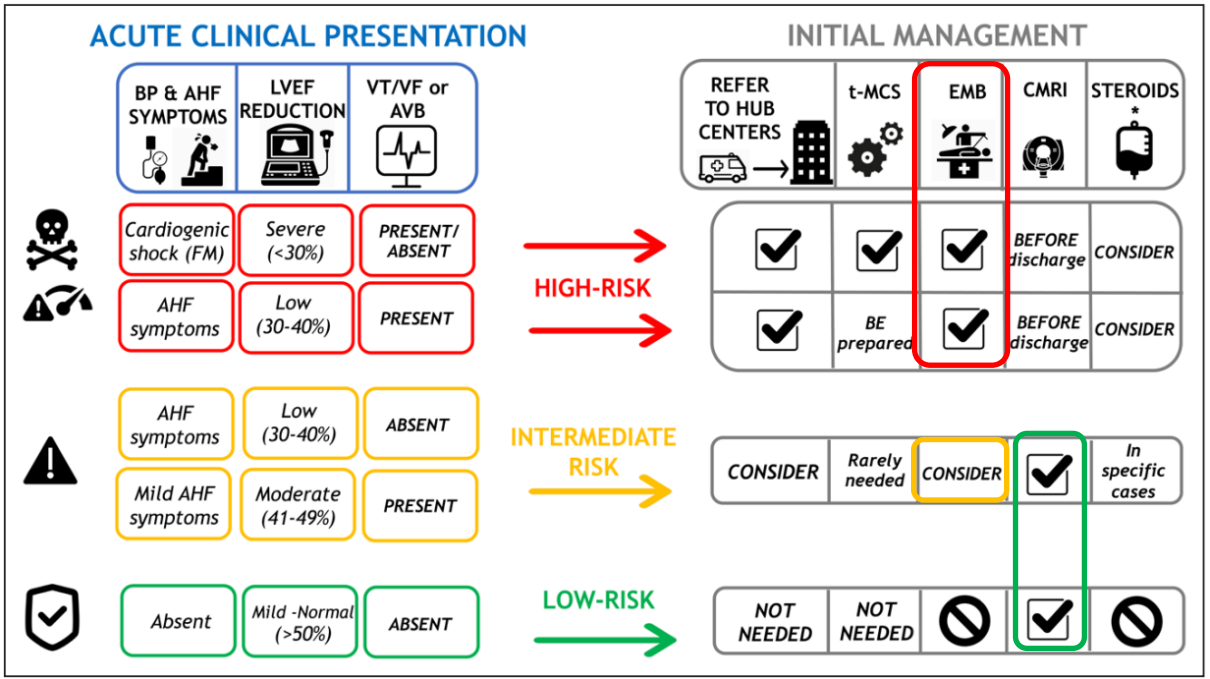
Kdy indikovat EMB u nemocných s podezřením na myokarditidu?

Management of Acute Myocarditis and Chronic Inflammatory Cardiomyopathy

An Expert Consensus Document



Circ Heart Fail. 2020 Nov;13(11):e007405.

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EKG a riziková stratifikace u akutní myokarditidy

2024 ACC Expert Consensus Decision Pathway on Strategies and Criteria for the Diagnosis and Management of Myocarditis

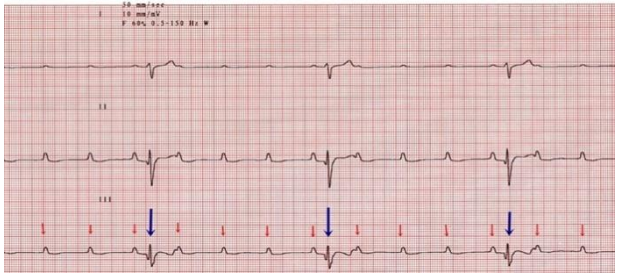
4.2.1. Electrocardiogram

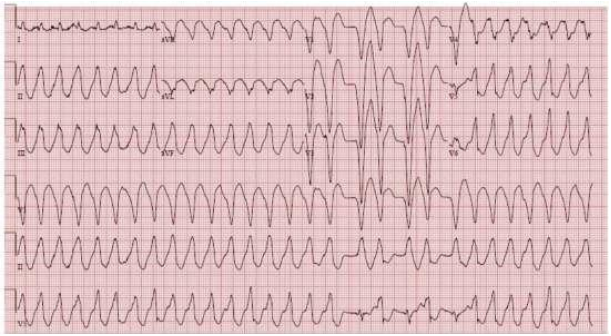
Electrocardiogram (ECG) is widely used as an initial screening tool for diagnosis of myocarditis, despite its low sensitivity of 47%.[9] ECGs of patients with myocarditis

Table 7 Clinical risk stratification to guide work-up in inflammatory myoper

Risk	High risk	Intermediate risk
Myocarditis	• Acute HF/cardiogenic shock • Dyspnoea NYHA III–IV refractory to medical therapy • Cardiac arrest/syncope[a] • Ventricular fibrillation/sustained ventricular tachycardia[a] • High-level AV block[a]	• New/progressive dyspnoea • Non-sustained ventricular arrhythmias • Persistent release or relapsing troponin

of the conduction system also raises the suspicion for sarcoidosis, GCM, or Lyme disease. Ongoing research,





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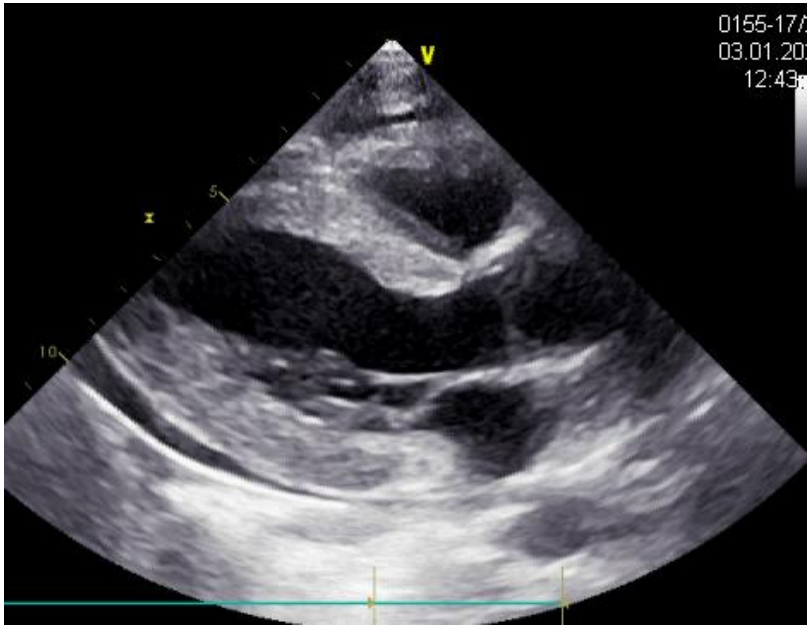
Echokardiografie v akutní fázi myokarditidy



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Fulminantní myokarditida je jasná indikace k časné EMB!

Recommendation Table 6 — Recommendations for endomyocardial biopsy (see Evidence Table 6)

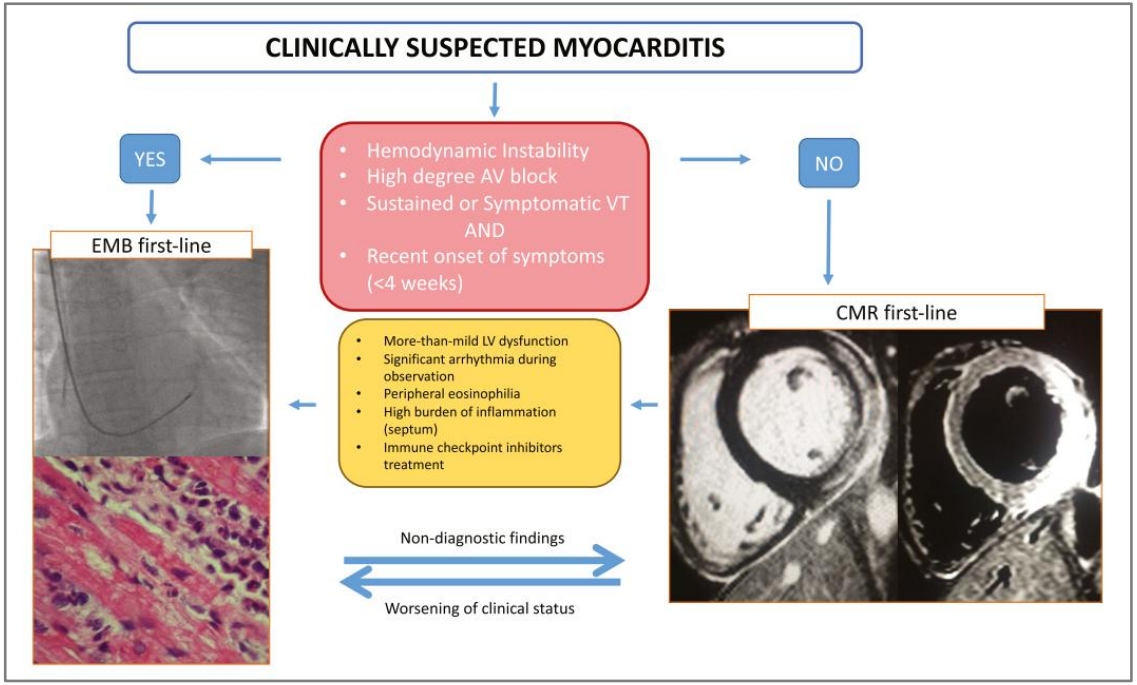
Recommendations	Class[a]	Level[b]
EMB[c] is recommended in patients with high-risk myocarditis[d], and/or haemodynamic instability, and/or in patients with intermediate-risk myocarditis not responding to conventional therapy in order to detect a specific histologic subtype and to assess the presence of viral genome for treatment.[34,63,73,131]	I	C

Table 7 Clinical risk stratification to guide work-up in inflammatory myopericardial syndrome

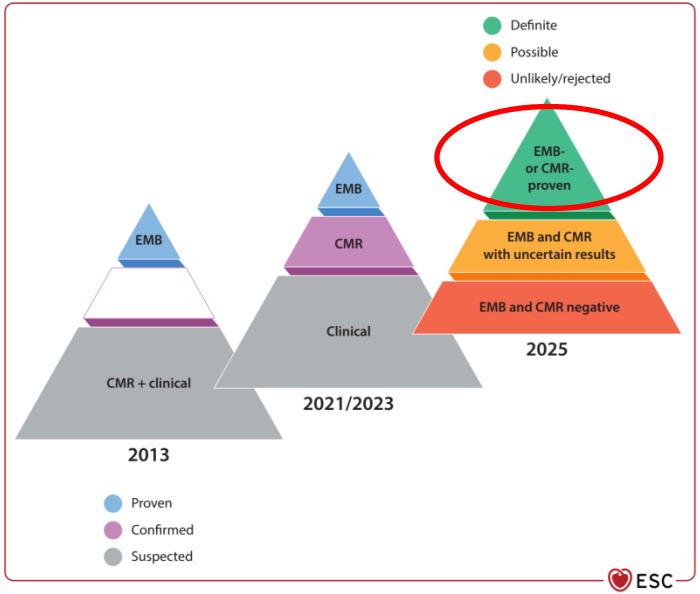
Risk	High risk	Intermediate risk	Low risk
Myocarditis	• Acute HF/cardiogenic shock • Dyspnoea NYHA III–IV refractory to medical therapy • Cardiac arrest/syncope[a] • Ventricular fibrillation/sustained ventricular tachycardia[a] • High-level AV block[a]	• New/progressive dyspnoea • Non-sustained ventricular arrhythmias • Persistent release or relapsing troponin	Stable symptoms or oligosymptomatic
	Imaging criteria:	**Imaging criteria:**	**Imaging criteria:**
	• Newly reduced LVEF (<40%)[a] • Extensive LGE on CMR[a]	• Newly mildly reduced LVEF (41%–49%) and/or WMA • Preserved LVEF (≥50%) and LGE ≥2 segments on CMR	• Preserved LVEF (≥50%) without LGE or limited LGE (<2 segments) on CMR

Invazivní a neinvazivní dg nestojí proti sobě, ale doplňují se!

State-of-the-Art of Endomyocardial Biopsy on Acute Myocarditis and Chronic Inflammatory Cardiomyopathy



Current Cardiology Reports
https://doi.org/10.1007/s11886-022-01680-x



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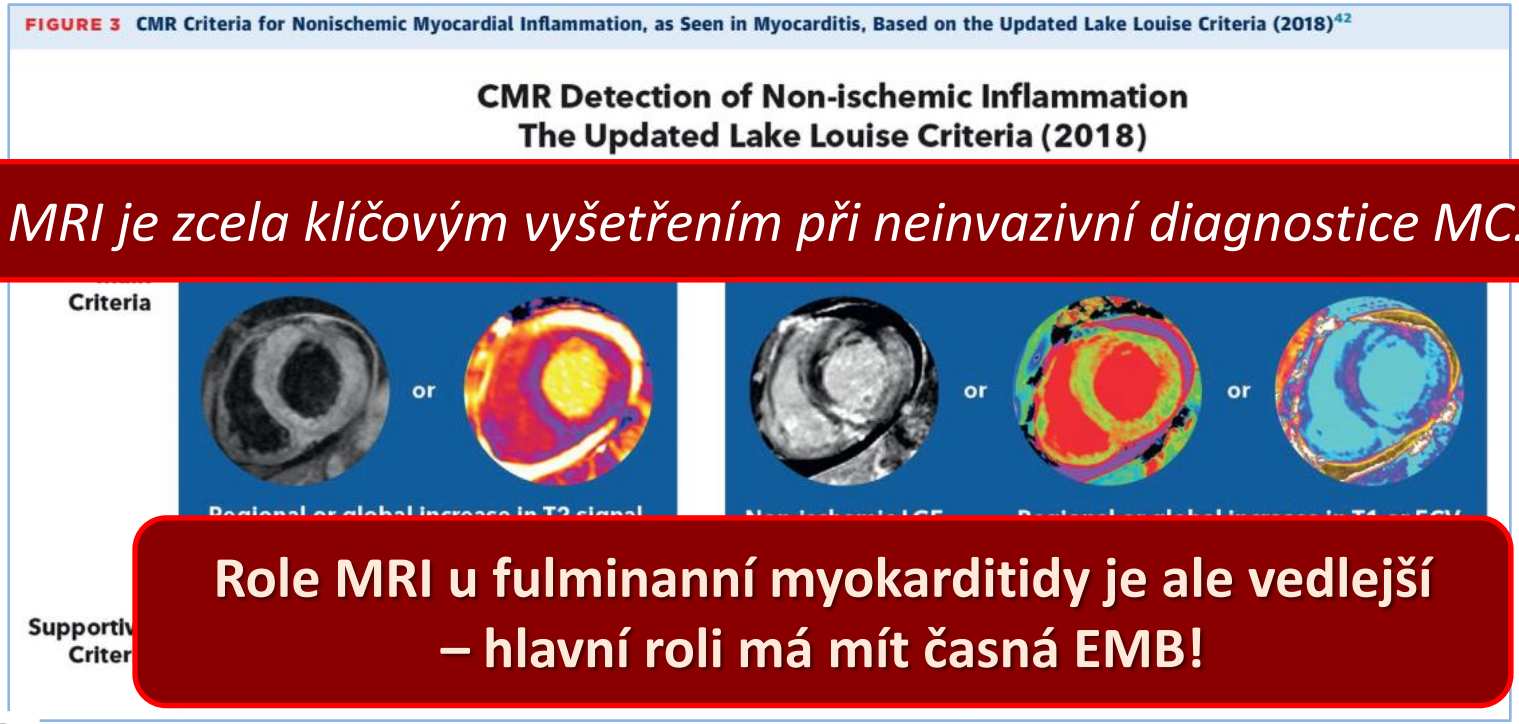
Fulminantní myokarditidida – neinvazivní diagnostika – MRI



MRI je zcela klíčovým vyšetřením při neinvazivní diagnostice MC.

Role MRI u fulminanní myokarditidy je ale vedlejší – hlavní roli má mít časná EMB!

IS/IM terapie u susp. fulminantní myokarditidy

Immunomodulating Therapies in Acute Myocarditis and Recurrent/Acute Pericarditis

…doporučení zahájit pulsní léčbu kortikoidy i před provedením EMB!

SUSPECTED FULMINANT OR COMPLICATED ACUTE MYOCARDITIS

↓

i.v. pulse methylprednisolone 7–14 mg/kg/day for 3 d, then 1 mg/kg/day

	LYMPHOCYTIC	ICI-ASSOCIATED	GIANT CELL	EOSINOPHILIC	SARCOIDOSIS
FIRST-LINE	- If associated systemic autoimmune disorders (eg. SLE and APS): add aggressive treatment of associated conditions	**Hold ICI** therapy Confirm ICI-myocarditis via definitive imaging and/or endomyocardial biopsy	- If hemodynamically unstable pts: **ATG**, from 1 mg/kg, usually single-dose to 300 mg in 3 days or (alternative) i.v. **alemtuzumab** (anti-CD52 antibody) single dose of 30 mg plus oral **CyA**, BID, target through levels 150–250 ng/mL - If hemodynamically stable pts: only oral **CyA**, BID, target trough levels 150–250 ng/mL	- If EGPA: consider i.v. **cyclophosphamide** (especially in ANCA-positive pts), 600 mg*m² at days 1, 15, and 30 - If clonal (myeloproliferative) HES: **imatinib** 100–400 mg OD - If helminthic infection: **albendazole** 400 mg BID for 2–4 wk - If hypersensitivity reaction: **withdraw suspected drug**	
SECOND-LINE	**IVIG** (2 g/kg), single continuous infusion in 24–48 h or divided in 4 d or **plasmapheresis**, 3–5 sessions in 5–10 d	i.v. **abatacept** (a CTLA- 4 agonist) or **ATG**, 1 mg/kg, usually single dose or i.v. **alemtuzumab** (anti-CD52 antibody), 30 mg, single dose	i.v. **rituximab** 375 mg×m² (BSA) mg (once a wk for 4 wk and then every 4 mo as maintenance therapy) for 1 yr	- If DRESS, EGPA or idiopathic HES: anti-IL5 agents (e.g., **benralizumab** 30 mg s.c./4–8wk or **mepolizumab** 100-300 mg/4wk)	s.c. **methotrexate** 15–20 mg/wk or i.v. **infliximab** 5 mg/kg (up to 500 mg) at time 0 and after 2 and 4 wk and then every 6–8 wk or s.c. **adalimumab** 40 mg/2wk

Front Med (Lausanne). 2022 Mar 7;9:838564.

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Fulminantní myokarditida - IS léčba

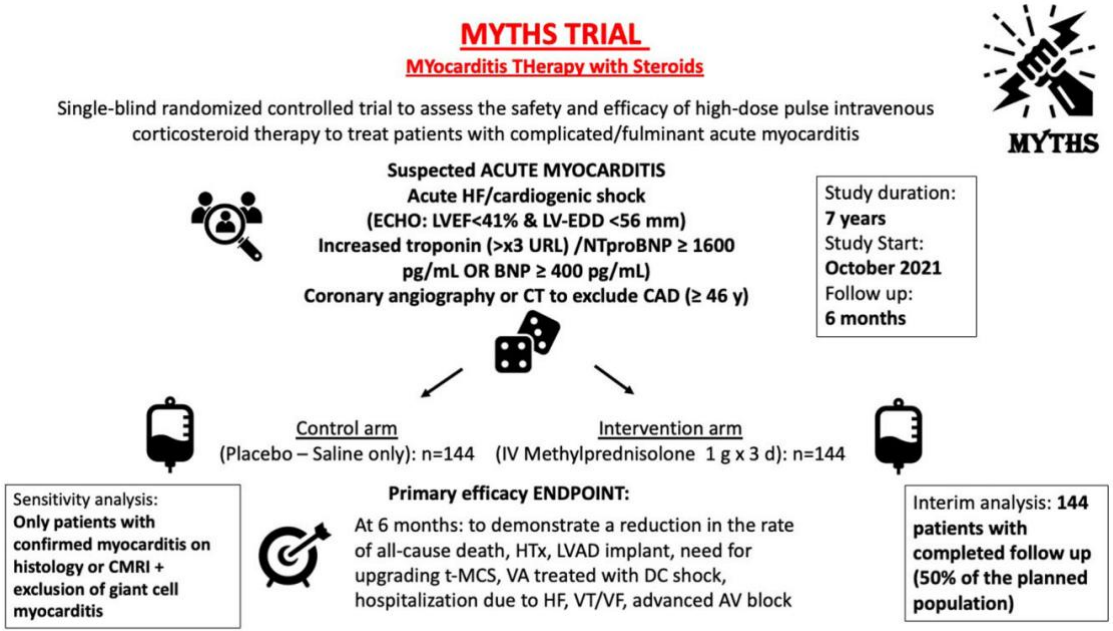
JOURNAL ARTICLE

Rationale and study design of the international randomized control trial MYocarditis THerapy with Steroids: the MYTHS trial

E Ammirati, N Conti, S Frea, A Uribarri, A Grosu, F Loffredo, D Corsi, D Tomasoni, F Cappelli, M Marini, A Garascia, C M Van De Heyning, M Crespo-Leiro, E D Adler, L Potena MYTHS trial investigators

Author Notes

European Heart Journal, Volume 45, Issue Supplement_1, October 2024, ehae666.1239, https://doi.org/10.1093/eurheartj/ehae666.1239



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Léčba fulminantní MC v Guidelines 2025

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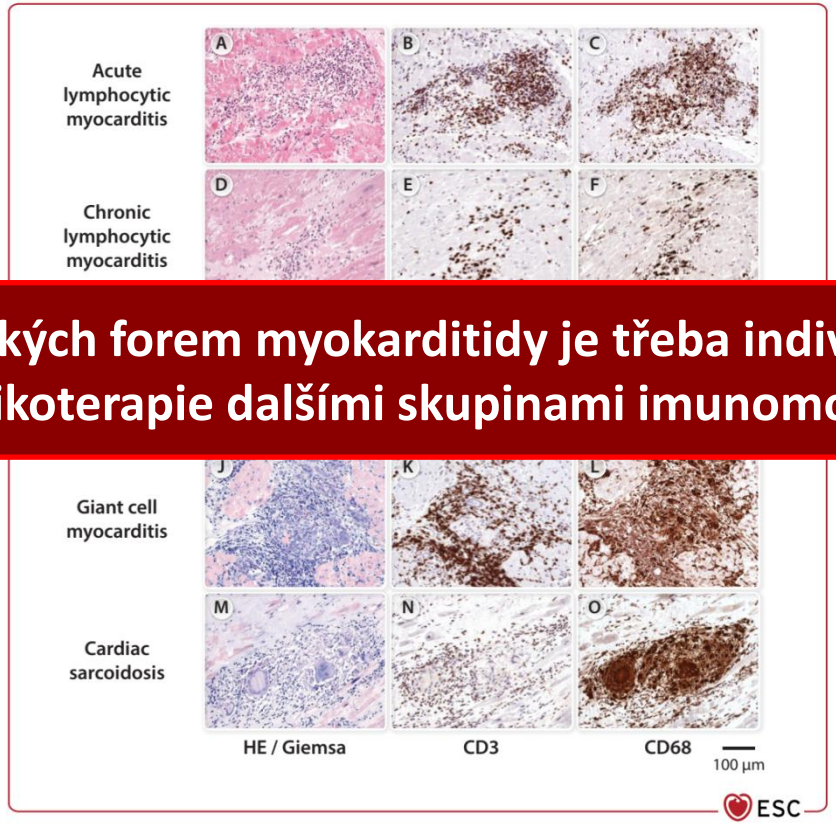
Immunosuppressive therapy		
Corticosteroids should be considered in patients with fulminant, non-infectious forms of myocarditis to stabilize the patients.	IIa	C
Corticosteroids may be considered in patients with acute myocarditis with impaired LVEF if refractory to standard HF therapy to stabilize patients.	IIb	C
Routine use of immunosuppressive therapy is not recommended in acute myocarditis with preserved LV function because no outcome benefit has been shown.	III	C

Jen EMB s (imuno)histologií určí podtyp myokarditidy…



…u specifických forem myokarditidy je třeba individualizace a doplnění kortikoterapie dalšími skupinami imunomodulačních léků

IS/IM terapie u fulminantní myokarditidy

Immunomodulating Therapies in Acute Myocarditis and Recurrent/Acute Pericarditis

…zde už je EMB nezastupitelná!

SUSPECTED FULMINANT OR COMPLICATED ACUTE MYOCARDITIS

↓

i.v. pulse methylprednisolone 7–14 mg/kg/day for 3 d, then 1 mg/kg/day

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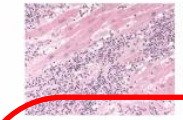
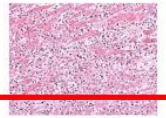
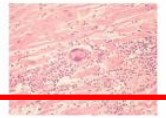
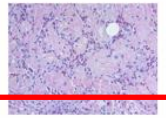
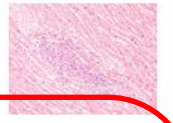
FIRST-LINE					
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Front Med (Lausanne). 2022 Mar 7;9:838564.

Časná invazivní strategie a IS/IM th je lepší!

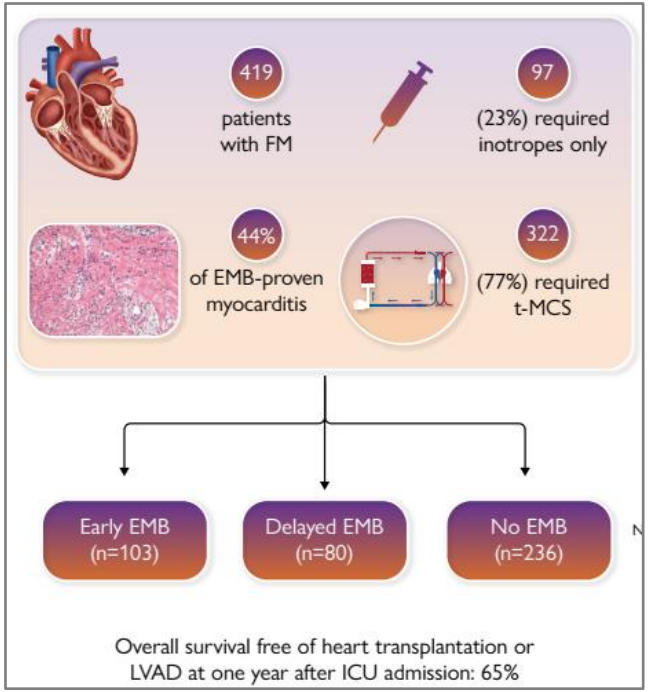
ESC European Society of Cardiology
European Heart Journal (2023) **44**, 5110–5124
https://doi.org/10.1093/eurheartj/ehad707

CLINICAL RESEARCH
Acute cardiovascular care

Fulminant myocarditis proven by early biopsy and outcomes

Background and Aims While endomyocardial biopsy (EMB) is recommended in adult patients with fulminant myocarditis, the clinical impact of its timing is still unclear.

Methods Data were collected from 419 adult patients with clinically suspected fulminant myocarditis admitted to intensive care units across 36 tertiary centres in 15 countries worldwide. The diagnosis of myocarditis was histologically proven in 210 (50%) patients, either by EMB ($n = 183$, 44%) or by autopsy/explanted heart examination ($n = 27$, 6%), and clinically suspected cardiac magnetic resonance imaging confirmed in 96 (23%) patients. The primary outcome of survival free of heart transplantation (HTx) or left ventricular assist device (LVAD) at 1 year was specifically compared between patients with early EMB (within 2 days after intensive care unit admission, $n = 103$) and delayed EMB ($n = 80$). A propensity score-weighted analysis was done to control for confounders.



Huang et al, EHJ 2023

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Histologická charakteristika

Table 1 Baseline characteristics, clinical, echocardiography, and biological findings at intensive care unit admission according to endomyocardial biopsy timing after intensive care unit admission

	Available data, *N*	All patients (*N* = 419)	EMB ≤ 2 days (*n* = 103)	EMB > 2 days (*n* = 80)	No EMB (*n* = 236)	*P*-value
Age, years	419	40 (29–52)	44 (31–55)	41 (28–52)	38 (28–49)	.091
Woman, *n* (%)	419	220 (53)	58 (56)	33 (41)	129 (55)	.078
EMB finding consistent with myocarditis[b]	183	183 (44)				
Lymphocytic infiltrate		125 (68)	71 (69)	54 (68)	-	.836
Giant cell infiltrate		20 (11)	11 (11)	9 (11)	-	.902
Eosinophilic infiltrate		20 (11)	11 (11)	9 (11)	-	.902
Other infiltrate[c]		18 (10)	10 (10)	8 (10)	-	.948
Histologic demonstration of myocarditis on autopsy/explanted heart/myocardial specimen after LVAD	419	27 (6)	0 (0)	0 (0)	27 (11)	**<.001**
Myocarditis proven by CMRI	419	158 (38)	36 (35)	22 (28)	100 (42)	**.048**

Huang et al, EHJ 2023

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Časná invazivní strategie a časná IS/IM th zlepšuje prognózu!

ESC European Society of Cardiology
European Heart Journal (2023) 44, 5110–5124
https://doi.org/10.1093/eurheartj/ehad707

CLINICAL RESEARCH
Acute cardiovascular care

Fulminant myocarditis proven by early biopsy and outcomes

Table 5 Immunomodulatory therapy and one-year outcome in the group of endomyocardial biopsy-proven myocarditis ($n = 183$) according to main histologic subtypes

	One-year outcome		*P*-value
	Alive without HTx or LVAD	Death, HTx or LVAD	
Lymphocytic myocarditis ($n = 125$)	**$n = 78$**	**$n = 47$**	
Any IMT	54 (69)	26 (55)	.117
Early use of IMT[a]	50 (64)	16 (34)	**.001**
Corticosteroids	54 (69)	23 (49)	**.024**
Pulse therapy	50 (64)	18 (38)	**.005**
Other IMT[b]	10 (13)	6 (13)	.993
Intravenous immunoglobulins	9 (12)	6 (13)	.838
Multiple IMT	15 (19)	8 (17)	.757
Intravenous immunoglobulins	2 (40)	4 (27)	.573
Multiple IMT	4 (80)	11 (73)	.766

Huang et al, EHJ 2023

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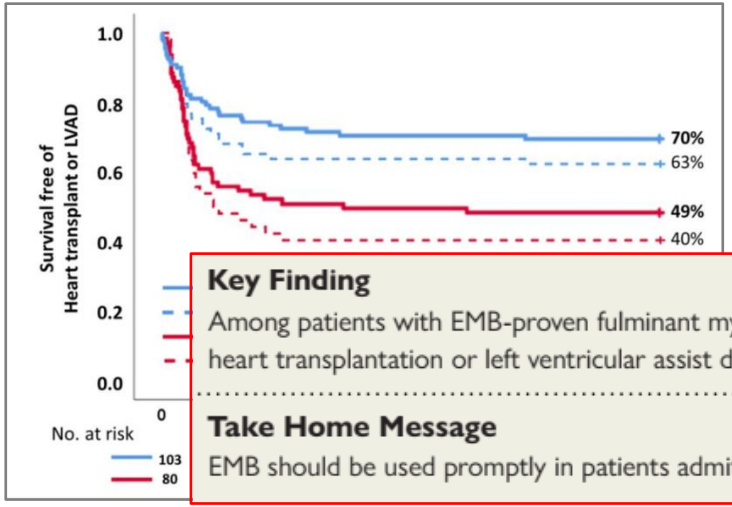
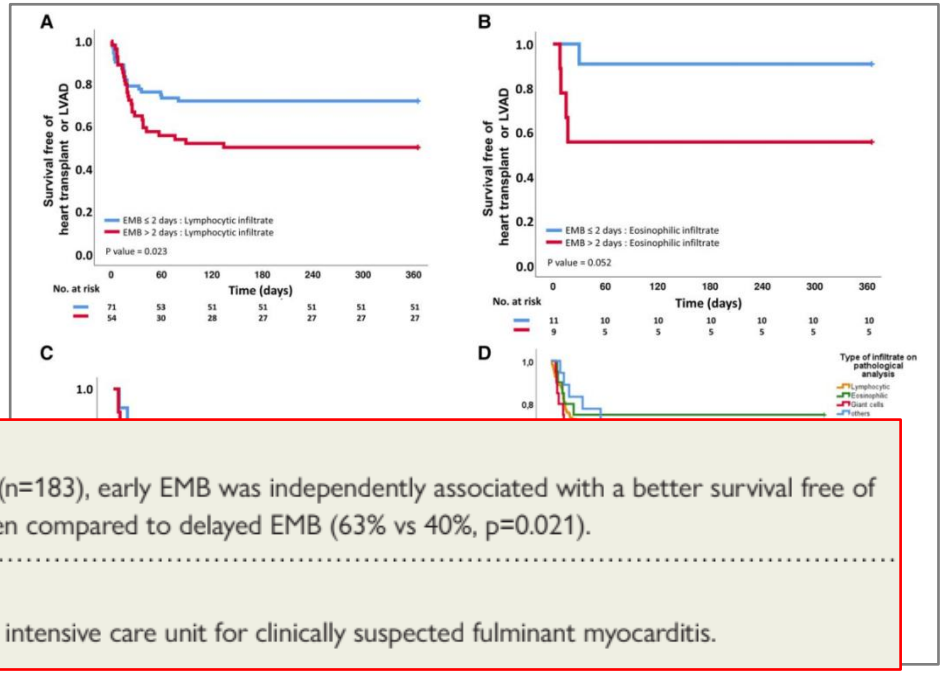
Acute cardiovascular care

Fulminant myocarditis proven by early biopsy and outcomes





Key Finding

Among patients with EMB-proven fulminant myocarditis (n=183), early EMB was independently associated with a better survival free of heart transplantation or left ventricular assist device, when compared to delayed EMB (63% vs 40%, p=0.021).

Take Home Message

EMB should be used promptly in patients admitted to an intensive care unit for clinically suspected fulminant myocarditis.

Huang et al, EHJ 2023

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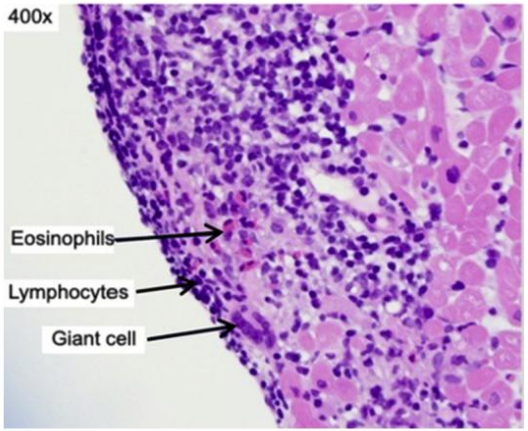
GCM – nejnebezpečnější forma myokarditidy!

Management of Patients With Giant Cell Myocarditis

JACC Review Topic of the Week

- **Přítomnost multinukleárních obrovských buněk spolu s výraznou smíšenou celulární inflamatorní infiltrací včetně eozinofilů a také přítomnost rozsáhlé nekrózy myocytů jsou typické pro GCM.**

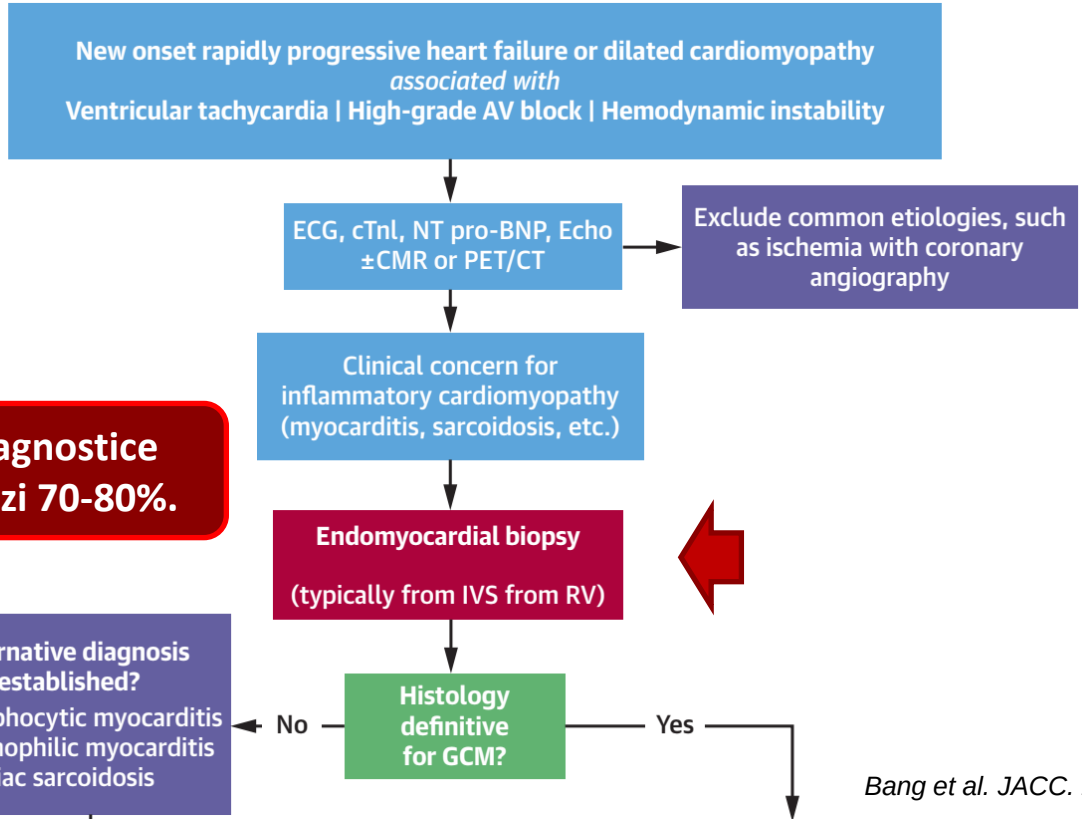
FIGURE 3 Histopathology of Giant Cell Myocarditis



Courtesy of Dr. Juan Vilaro, University of Florida Medical Center. This is a high-power magnification of eosin and hematoxylin staining of cardiac myocytes affected by giant cell myocarditis. Multifocal inflammatory infiltrates consisting of lymphocytes with multinucleated giant cells and eosinophils are seen.

J Am Coll Cardiol 2021;77:1122-34

Diagnostika GCM



Senzitivita EMB v diagnostice GCM se pohybuje mezi 70-80%.

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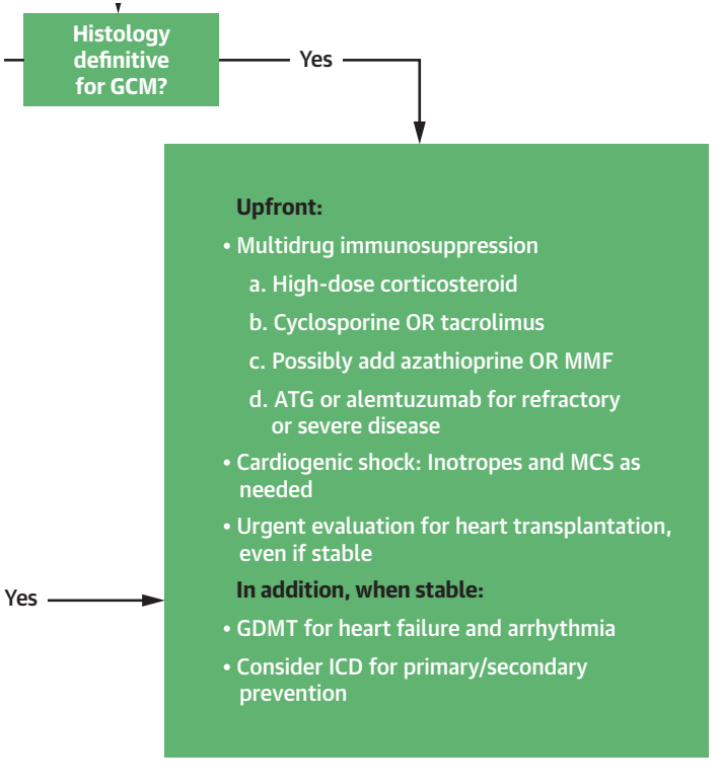
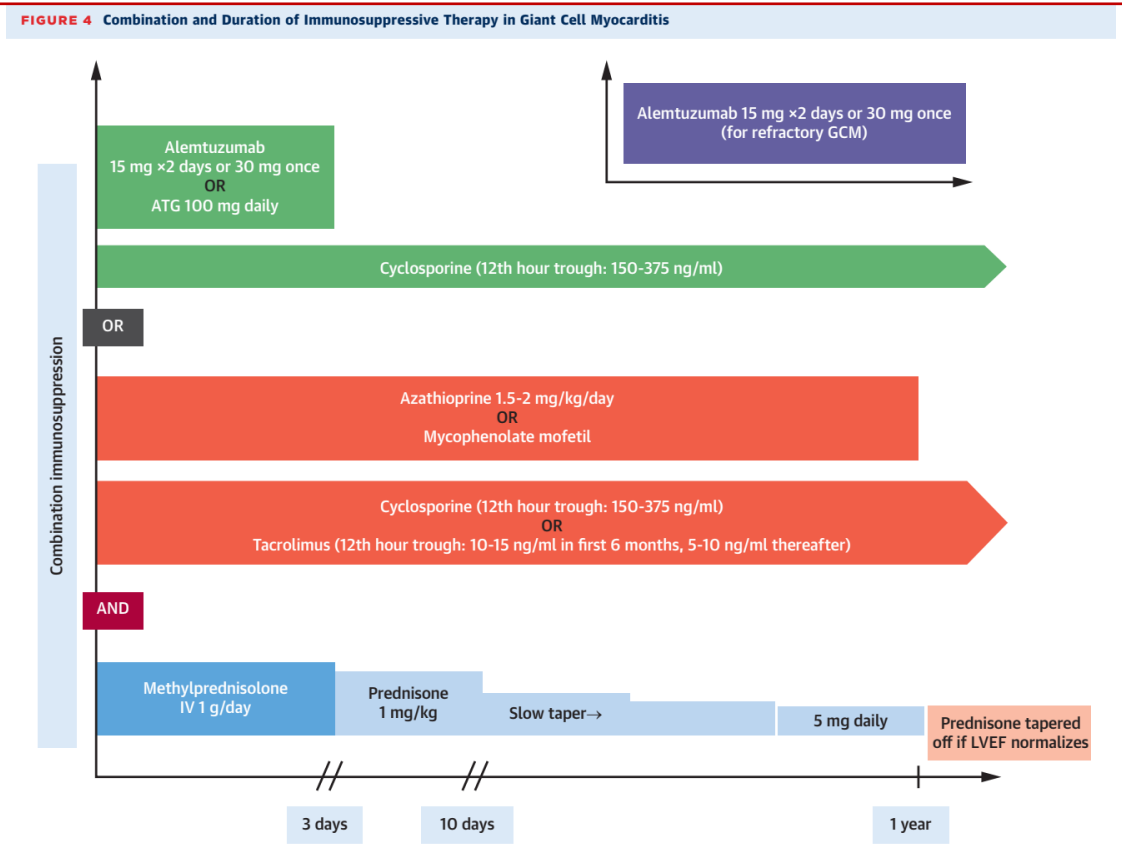
Bang et al. JACC. 2021 Mar, 77 (8) 1122–1134.

Je-li dg GCM potvrzena, začni okamžitě s léčbou!

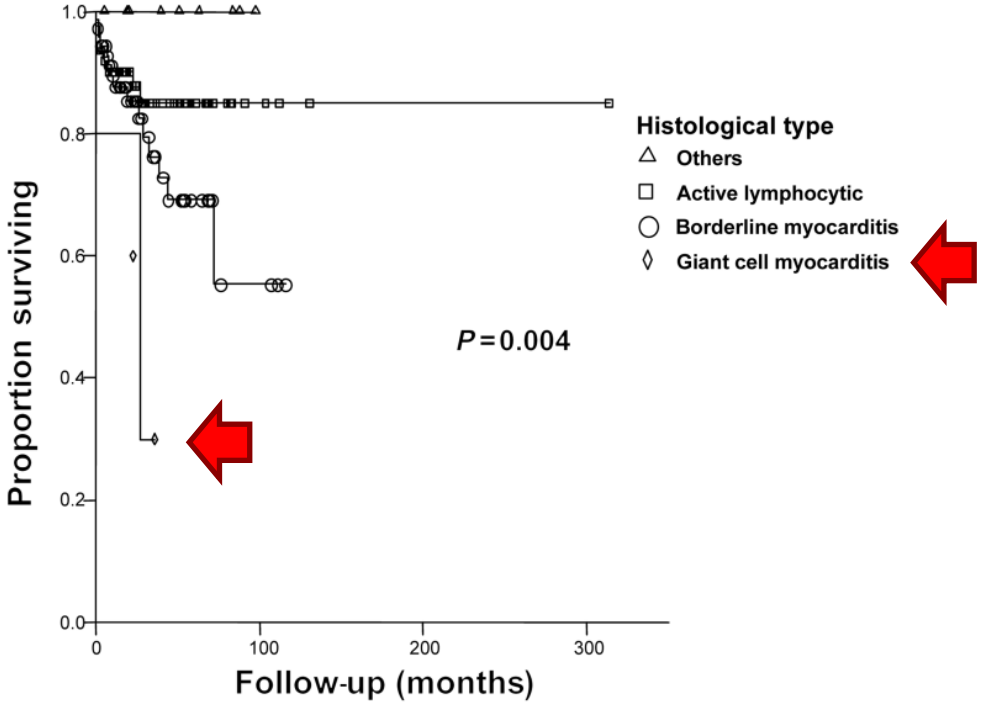




Bang et al. JACC. 2021 Mar, 77 (8) 1122–1134.

Prognóza GCM ve srovnání s jinými typy myokarditid

A prospective study of biopsy-proven myocarditis: prognostic relevance of clinical and aetiopathogeneti features at diagnosis



Neléčená GCM prakticky vždy končí fatálně!

European Heart Journal (2007) **28**, 1326–1333

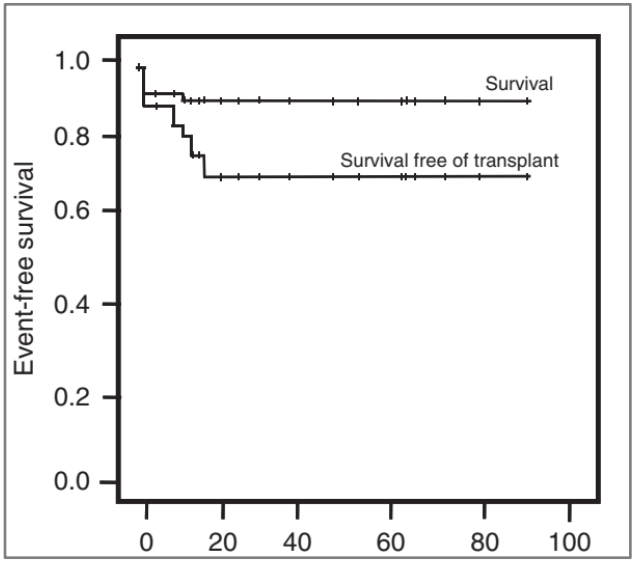
Efekt včasné diagnostiky a IS léčby u GCM

Diagnosis, Treatment, and Outcome of Giant-Cell Myocarditis in the Era of Combined Immunosuppression

Riina Kandolin, MD; Jukka Lehtonen, MD; Kaisa Salmenkivi, MD; Anne Räisänen-Sokolowski, MD; Jyri Lommi, MD; Markku Kupari, MD

Table 1. Immunosuppressive Treatment of the 26 Patients With Biopsy-Diagnosed GCM

Corticosteroid + Azathioprine + Cyclosporine 17 (65%)
Corticosteroid + Azathioprine 4 (15%)
Corticosteroid + Azathioprine + Muromonab + Gammaglobulin 1 (4%)
Corticosteroid + Azathioprine + Myocophenolate mofetil 1 (4%)
Corticosteroid + Cyclosporine+ Myocophenolate mofetil 2 (8%)
Corticosteroid + Cyclosporine + Azathioprine/Methotrexate* 1 (4%)



Conclusions—Repeat endomyocardial biopsies are frequently needed to diagnose giant-cell myocarditis. On contemporary immunosuppession, two thirds of patients reach a partial clinical remission characterized by freedom from severe heart failure and need of transplantation but continuing proneness to ventricular tachyarrhythmias. **(*Circ Heart Fail*. 2013;6:15-22.)**

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Praktický přístup k terapii u GCM

- Iniciálně Solumedrol - 1g i.v. /den po 3 dny
- U stabilních pacientů - CyA nebo Tac + MMF + Pre
- U nestabilních pacientů
  - ATG 1mg/kg i.v. po 3 dny
  - alemtuzumab (anti-CD52) + CyA / Tac
  - rituximab (anti-CD20) i.v. 1x týdně 375mg/m2
- Dostupnost MCS a došetření k transplantaci

GIANT CELL

- If hemodynamically unstable pts: **ATG**, from 1 mg/kg, usually single-dose to 300 mg in 3 days or (alternative) i.v. **alemtuzumab** (anti-CD52 antibody) single dose of 30 mg plus oral **CyA**, BID, target through levels 150–250 ng/mL
- If hemodynamically stable pts: only oral **CyA**, BID, target trough levels 150–250 ng/mL

i.v. **rituximab** 375 mg×m^2 (BSA) mg (once a wk for 4 wk and then every 4 mo as maintenance therapy) for 1 yr

Front Med (Lausanne). 2022 Mar 7;9:838564.

Přístrojová léčba fulminantní myokarditidy

Recommendations	Class[a]	Level[b]
A timely and dedicated Shock Team discussion is recommended in patients with myocarditis in the presence of haemodynamic compromise, to decide on the need for escalation to MCS and to determine a long-term management plan.	I	C
Temporary MCS[c] should be considered in patients with myocarditis and cardiogenic shock or acute decompensation in chronic myocarditis to stabilize the patients.	IIa	C

6.3. Interventional techniques including circulatory support

6.3.1. Myocarditis

6.3.1.1. Short-term mechanical circulatory support

Myocarditis patients who present with rapid deterioration in haemodynamic status and rapidly progressive myocardial dysfunction are amongst those who respond best to temporary MCS.[293] Among temporary MCS, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) represents the most frequently applied or recommended approach, ranging from 75% to 85% of AM cases.[75,294–296] Despite the

Přístrojová léčba fulminantní myokarditidy

Diagnosis and management of patients with fulminant myocarditis

Nicoletta D'Ettore [1]*, Kaveh Eghbalzadeh[2], Mehmet Oezkur [3], Letizia F. Bertoldi[4], Matthias Bossard[5], and Federico Pappalardo [6]

Ventricular unloading via MCS devices can play a crucial role in mitigating the adverse effects of viral injury and autoimmune responses in myocarditis. The benefits of ventricular unloading include the following:

(1) Decreased workload of the heart: Ventricular unloading reduces myocardial stress and oxygen demand, which can limit further myocyte damage caused by the inflammatory response and preserve myocardial function.

(2) Improved coronary perfusion: Devices like microaxial flow pumps enhance coronary blood flow, ensuring better oxygen and nutrient delivery to the myocardium, which aids in the repair of damaged myocardial tissue, and reduces the extent of injury.

(3) Modulation of the immune response: Reducing myocardial stress and improving perfusion can indirectly modulate the immune response by decreasing the levels of stress-related inflammatory cytokines, mitigating the autoimmune component of myocarditis, and preventing further myocardial damage.

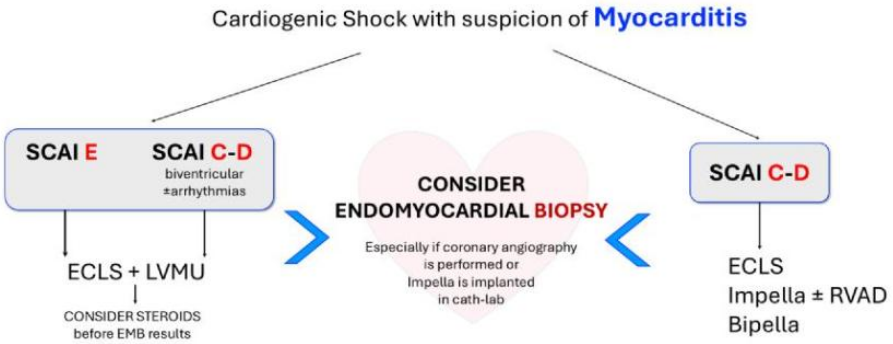
(4) Enhanced recovery environment: Ventricular unloading creates a more favourable environment for myocardial recovery by minimizing further injury and providing the heart with a chance to heal. This can be particularly beneficial in the context of viral myocarditis, where ongoing viral replication and immune-mediated injury are common.

European Heart Journal Supplements (2025) **27** (Supplement 4), iv23-iv30

Přístrojová léčba fulminantní myokarditidy – kterou st-MCS použít?

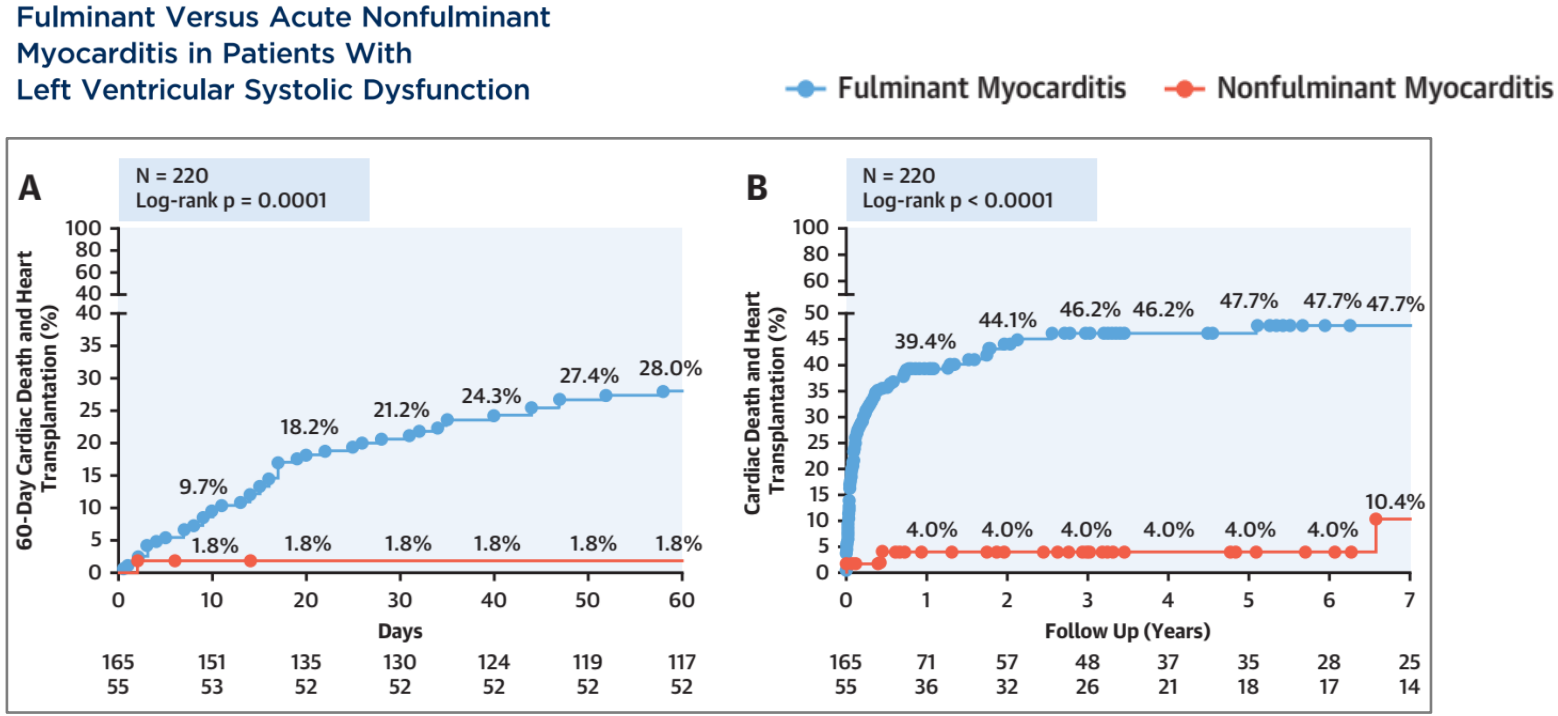
Diagnosis and management of patients with fulminant myocarditis

Nicoletta D'Ettore [1]*, Kaveh Eghbalzadeh[2], Mehmet Oezkur [3], Letizia F. Bertoldi[4], Matthias Bossard[5], and Federico Pappalardo [6]



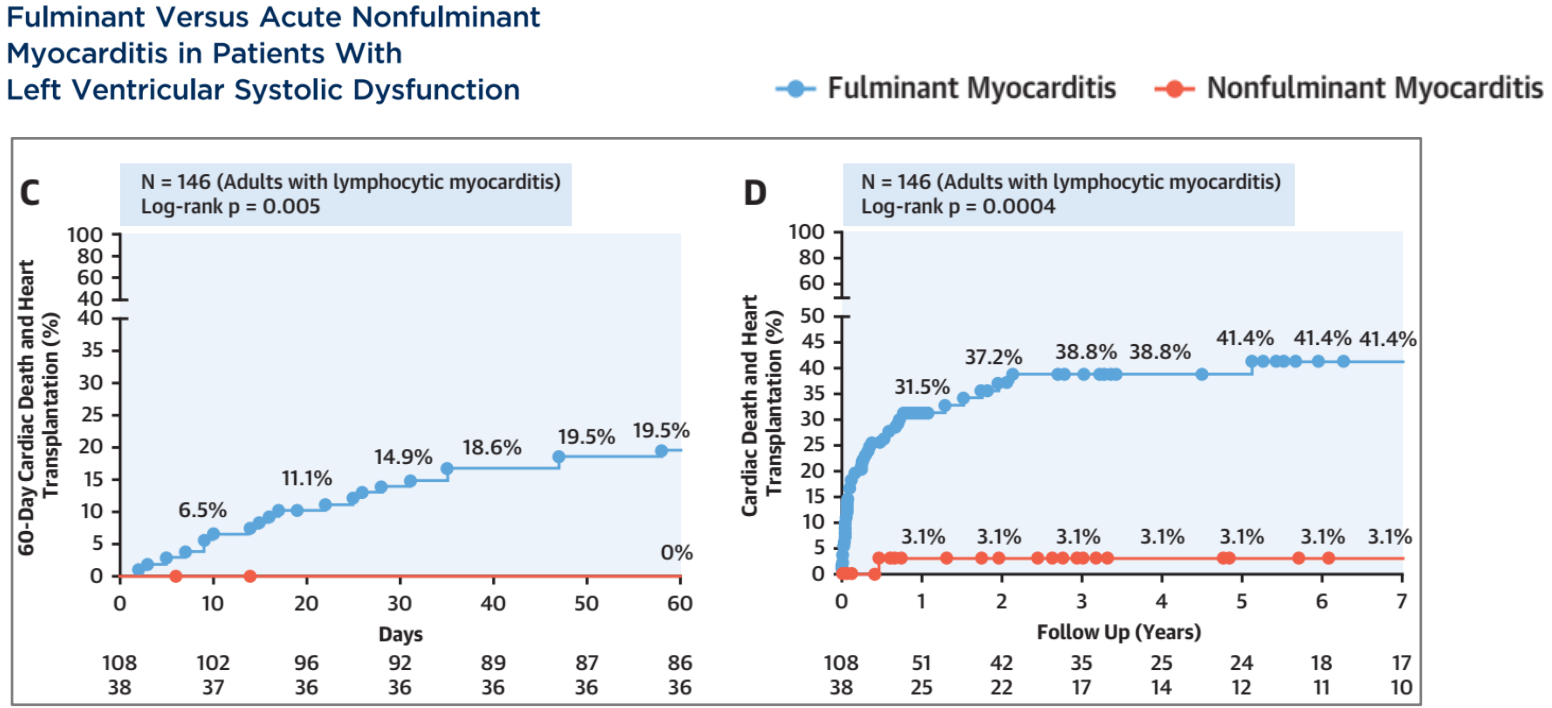
experience. The most frequently used short-term MCS in FM patients is VA-ECMO. However, during VA-ECMO support, LV distention and increased afterload may cause pulmonary oedema and hinder myocardial recovery. An early and effective unloading strategy should be associated. The combined ECMELLA (VA-ECMO + Impella) provides potent haemodynamic support, oxygenation, and ventricular unloading and is associated with lower mortality compared to VA-ECMO alone, despite higher complication rates. The combination in ECMELLA or BIPELLA should be considered when the right ventricular function is compromised.[31,32]

Prognóza fulminantní vs nefulminantní myokarditidy



Ammirati, E. et al. J Am Coll Cardiol. 2019;74(3):299-311.

Prognóza fulminantní vs nefulminantní lymfocytární myokarditidy

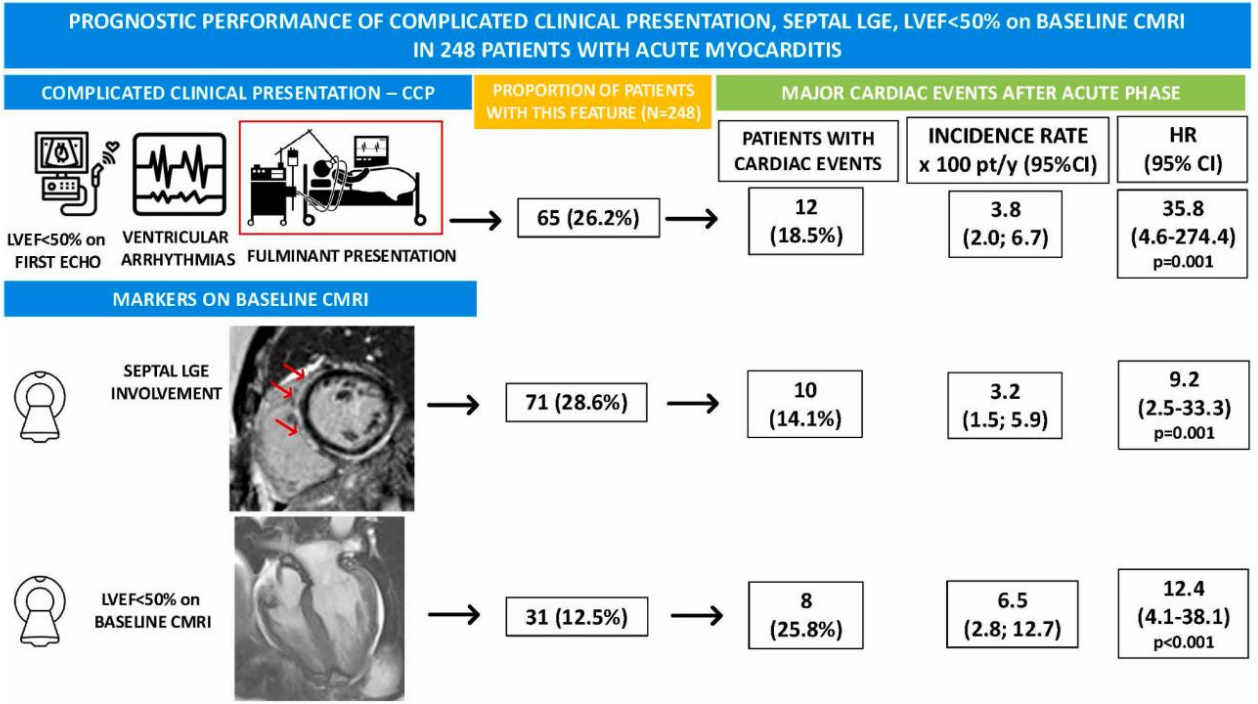


Ammirati, E. et al. J Am Coll Cardiol. 2019;74(3):299-311.

Riziková stratifikace myokarditidid – CMR markery vs klinický stav

Long-term prognostic performance of cardiac magnetic resonance imaging markers versus complicated clinical presentation after an acute myocarditis

Ammirati et al. Int J Cardiol 2024



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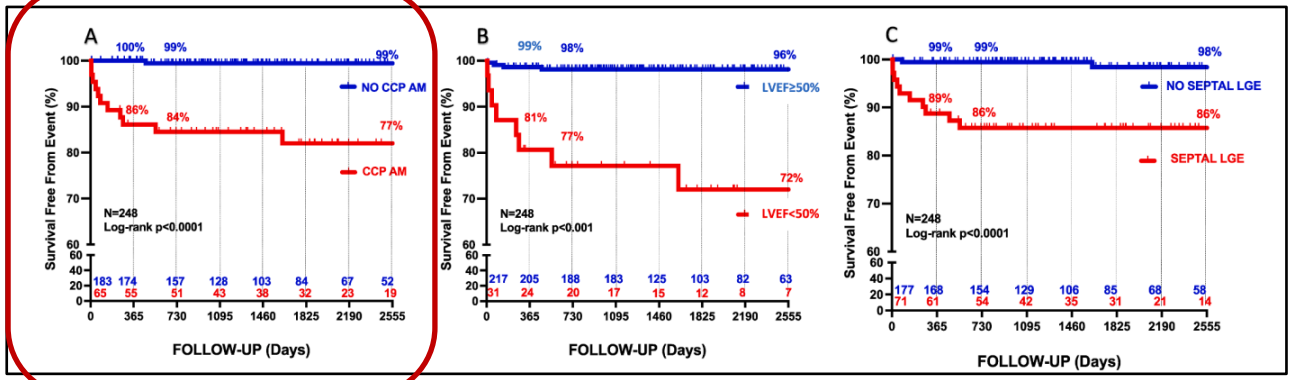
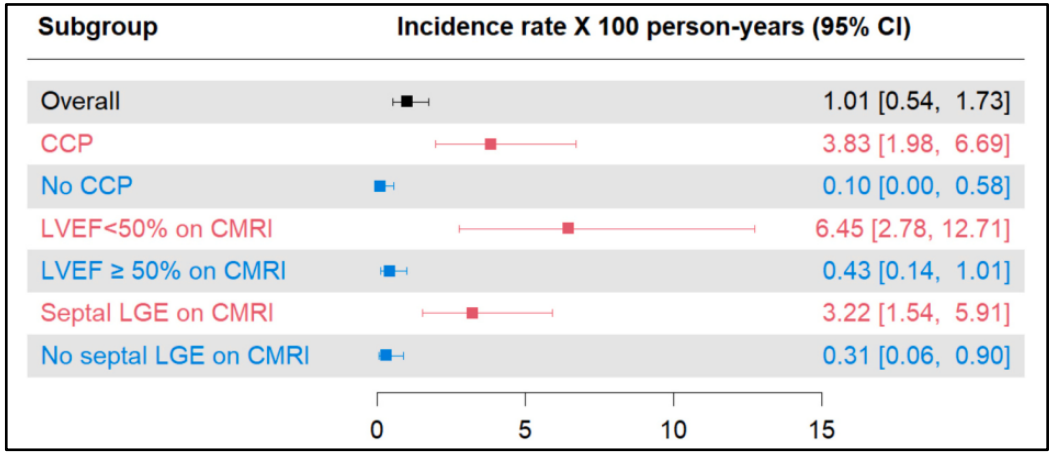
Riziková stratifikace myokarditidid – CMR markery vs klinický stav



Ammirati et al. Int J Cardiol 2024



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Závěry

- **Fulminantní myokarditida je onemocnění s vysokou krátko- i dlouhodobou mortalitou a morbiditou.**
- **Invazivní diagnostický přístup a komplexní farmakologická i nefarmakologická léčba může pomoci překlenout akutní fázi onemocnění.**
- **V post-akutní fázi je třeba kardiologický follow-up zaměřený na stratifikaci rizika SCD a včasné detekce progrese onemocnění vyžadující LVAD / HTx.**
- **Nezbytná je koncentrace závažných forem MC do terciálních center s dostupností komplexní diagnostiky a přístrojové léčby, ale také se zkušeností s IS / IM léčbou.**

Děkuji za pozornost!