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NOVINE U ESC VODIČU ZA MIOKARDITIS I PERIKARDITIS IZ 2025. GODINE: INTEGRATIVNI PRISTUP INFLAMATORNIM MIOPERIKARDNIM SINDROMIMA I IMPLIKACIJE ZA KLINIČKU PRAKSU

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Sažetak: UVOD: Miokarditis predstavlja inflamatorno oboljenje miokarda koje može imati veoma heterogenu kliničku prezentaciju, od asimptomatskih oblika do fulminantne srčane insuficijencije i iznenadne srčane smrti. **Cilj** ovog preglednog rada je prikaz savremenih dijagnostičkih i terapijskih pristupa prema najnovijim ESC preporukama, uz integraciju kliničkih iskustava i naglašavanje potrebe za daljim istraživanjima. **PREGLED LITERATURE**: Evropsko kardiološko udruženje (ESC) objavilo je 2025. godine prve integrisane smernice koje objedinjeno obrađuju dijagnostiku i terapiju miokarditisa i perikarditisa, uvodeći novi koncept inflamatornog mioperikardnog sindroma (IMPS). Ovaj krovni termin prepoznaje čestu kliničku ispreplетanost ova dva entiteta i njihov zajednički patofiziološki mehanizam. U radu se analiziraju ključne novine u klasifikaciji, dijagnostici, genetskoj obradi i terapijskom pristupu, uz poseban osvrt na revidirane kriterijume kardiomagnetne rezonance-CMR (Lake Louise kriterijumi), proširene indikacije za endomiokardnu biopsiju (EMB) i inovacije u terapiji perikarditisa, uključujući interleukin-1 inhibitore. Promenjena je paradigma za dijagnozu miokarditisa Diskusija obuhvata poređenje ESC preporuka sa američkim ACC/AHA smernicama, kao i doprinose domaće literature, posebno radove iz oblasti dijastolnog stres testa i inflamatornih kardiomiopatija. Pandemija COVID-19 dodatno je skrenula pažnju na miokarditis kao potencijalnu komplikaciju virusnih infekcija. **ZAKLJUČAK:** Savremeni pristup miokarditisu menja paradigmu uvodeći koncept Inflamatornog mioperikardnog sindroma i podrazumeva integrisanu dijagnostiku i terapiju u skladu sa najnovijim ESC smernicama, uz prepoznavanje inflamatornog mioperikardnog sindroma kao klinički značajnog entiteta. Unapređenja u primeni kardiomagnetne rezonance, šire indikacije za endomiokardnu biopsiju i uvođenje ciljane terapije, uključujući interleukin-1 inhibitore, omogućavaju precizniju dijagnozu i individualizovan terapijski pristup. Uprkos napretku, heterogenost kliničke slike i dalje predstavlja izazov u svakodnevnoj praksi. Neophodna su dodatna istraživanja radi boljeg razumevanja patofiziologije i optimizacije lečenja ovih bolesnika.

Ključne reči: miokarditis, perikarditis, inflamatorni mioperikardni sindrom, ESC smernice, magnetna rezonanca srca, COVID-19, endomiokardna biopsija.

UVOD

ESC smernice iz 2025. godine predstavljaju prekretnicu u pristupu inflamatornim oboljenjima srca, ujedinjujući miokarditis i perikarditis u jedan vodič [1]. Ova odluka proističe iz sve jasnijeg razumevanja da su ova dva entiteta funkcionalno, anatomski i patofiziološki usko povezana, te da njihov odvojen pristup često vodi fragmentisanju dijagnostike i terapije. Novi koncept inflamatornog mioperikardnog sindroma (IMPS) predstavlja krovni terminobuhvata klinički kontinuum od i obuhvata klinički kontinuum od izolovanog miokarditisa, preko kombinovanog mioperikarditisa i perimiokarditisa, do izolovanog perikarditisa, uključujući i složene mešovite oblike do hronične inflamatorne kardiomiopatije i konstriktivnog perikarditisa [2-5,6-8,]. Takav integrativni pristup ima za cilj unapređenje saradnje između stručnjaka i usmeravanje budućih istraživanja. Uveden je i termin inflamatorna kardiomiopatija, koji se odnosi na hronični miokarditis povezan sa srčanom disfunkcijom i remodelovanjem komora sa hipokinetičkim fenotipom, sa ili bez dilatacije. Uloga kardio-magnetne rezonance (CMR) sada je centralna u dijagnostici [9- 11]. U domaćoj literaturi, između ostali radovi autora ovog preglednog rada sa saradnicima su doprineli razumevanju aspekta dijastolne disfunkcije i ehokardiografskih parametara kod inflamatornih kardiomiopatija [12–14], dok se

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UPDATES IN THE 2025 ESC GUIDELINES FOR MYOCARDITIS AND PERICARDITIS: AN INTEGRATIVE APPROACH TO INFLAMMATORY MYOPERICARDIAL SYNDROMES AND IMPLICATIONS FOR CLINICAL PRACTICE

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Apstrakt: Introduction: Myocarditis is an inflammatory disease of the myocardium that can present with highly heterogeneous clinical manifestations, ranging from asymptomatic forms to fulminant heart failure and sudden cardiac death. The aim of this review paper is to present contemporary diagnostic and therapeutic approaches according to the latest ESC recommendations, integrating clinical experience and emphasizing the need for further research. LITERATURE REVIEW: In 2025, the European Society of Cardiology (ESC) published the first integrated guidelines addressing the diagnosis and treatment of myocarditis and pericarditis, introducing the new concept of inflammatory myopericardial syndrome (IMPS). This umbrella term recognizes the frequent clinical overlap between these two entities and their shared pathophysiological mechanisms. The paper analyzes key updates in classification, diagnostics, genetic evaluation, and therapeutic approaches, with particular emphasis on revised cardiac magnetic resonance (CMR) criteria (Lake Louise criteria), expanded indications for endomyocardial biopsy (EMB), and innovations in the treatment of pericarditis, including interleukin-1 inhibitors. The diagnostic paradigm for myocarditis has been changed. The discussion includes a comparison of ESC recommendations with American ACC/AHA guidelines, as well as contributions from domestic literature, particularly studies in the field of diastolic stress testing and inflammatory cardiomyopathies. The COVID-19 pandemic has further highlighted myocarditis as a potential complication of viral infections. CONCLUSION: The contemporary approach to myocarditis is shifting the paradigm by introducing the concept of inflammatory myopericardial syndrome and involves integrated diagnostics and therapy in accordance with the latest ESC guidelines, recognizing this syndrome as a clinically significant entity. Advances in the use of cardiac magnetic resonance imaging, broader indications for endomyocardial biopsy, and the introduction of targeted therapies, including interleukin-1 inhibitors, enable more precise diagnosis and individualized treatment strategies. Despite these advances, the heterogeneity of clinical presentation remains a challenge in everyday practice. Further research is necessary to improve understanding of the pathophysiology and to optimize the treatment of these patients..

Key words: Myocarditis, pericarditis, inflammatory myopericardial syndrome, ESC guidelines, cardiac magnetic resonance imaging, COVID-19, endomyocardial biopsy.

INTRODUCTION

The 2025 ESC guidelines represent a turning point in the approach to inflammatory heart diseases, unifying myocarditis and pericarditis within a single framework [1]. This decision stems from an increasingly clear understanding that these two entities are functionally, anatomically, and pathophysiologically closely related, and that treating them separately often leads to fragmentation in diagnosis and therapy. The new concept of inflammatory myopericardial syndrome (IMPS) serves as an umbrella term encompassing a clinical continuum ranging from isolated myocarditis, through combined myopericarditis and perimyocarditis, to isolated pericarditis, including complex mixed forms, up to chronic inflammatory cardiomyopathy and constrictive pericarditis [2–5, 6–8]. Such an integrative approach aims to improve collaboration among specialists and guide future research.

The term inflammatory cardiomyopathy has also been introduced, referring to chronic myocarditis associated with cardiac dysfunction and ventricular remodeling with a hypokinetic phenotype, with or without dilation. The role of cardiac magnetic resonance (CMR) is now central in diagnostics [9–11]. In the domestic literature, among others, contributions by the

endomiokardna biopsija preporučuje u visoko rizičnim slučajevima [1,15-21].

EPIDEMIOLOGIJA I KLASIFIKACIJA

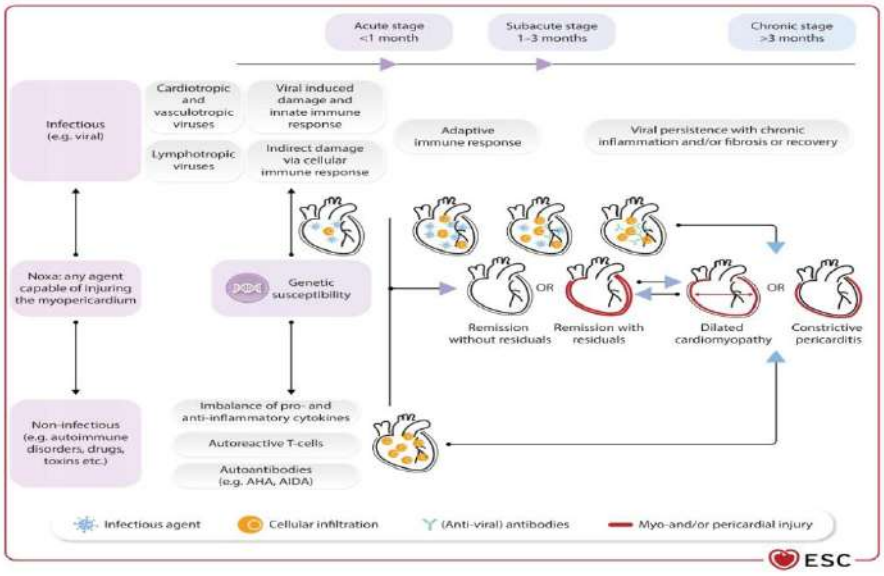
Smernice navode incidenciju perikarditisa od 3 do 32 slučaja na 100.000 stanovnika godišnje, dok je incidencija miokarditisa između 6 i 8 slučajeva na 100.000 stanovnika [1,15]. Veće stope su zabeležene kod muškaraca i mlađih odraslih osoba. Poseban izazov predstavlja činjenica da veliki broj subkliničkih i blagih slučajeva, uključujući one dijagnostikovane u sklopu MINOCA-e (infarkt miokarda sa neobstruktivnim koronarnim arterijama), ostaje nedijagnostikovan [6,9], što može dovesti do potcenjivanja stvarne incidence i prevalence hroničnih oblika bolesti. IMPS se klasifikuje na sledeće kliničke entitete: Izolovani perikarditis, Izolovani miokarditis, Mioperikarditis (dominantan perikarditis sa blagim miokardnim oštećenjem), Perimiokarditis (dominantan miokarditis sa perikardnim znakovima) i Hronična inflamatorna kardiomiopatija (hronični miokarditis sa strukturnim remodelovanjem, disfunkcijom i aritmogenim supstratom) [1].

ETIOLOGIJA I PATOFIZIOLOGIJA

Etiologija miokarditisa i perikarditisa je heterogena. U razvijenim zemljama dominiraju virusne infekcije (enterovirusi, adenovirusi, parvovirus B19, humani herpes virus 6, virus influence, hepatitisa C) [5,16,17] dok u endemskim područjima tuberkuloza ostaje značajan uzrok perikarditisa, posebno kod predisponiranih osoba sa HIV infekcijom. Bakterijski uzroci (difterija, borelioza, stafilokokne infekcije) su ređi. Autoimuni mehanizmi mogu dovesti do inflamacije u okviru sistemskih bolesti (lupus, sarkoidoza, vaskulitisi), dok toksični agensi (antraciklini, alkohol, kokain) i lekovi (inhibitori kontrolnih tačaka-point check inhibitors) takođe mogu biti uzrok miokarditisa. Genetska osnova je jako važna za prijemčvost virusne infekcije i težinu kliničke slike, pri čemu su varijante mutacija u sarkomernim i dezmozomskim genima povezane sa miokarditisom, a autoinflamatorne bolesti sa rekurentnim perikarditisom [6,8,15].

Patofiziologija miokarditisa je kompleksna Patofiziološki tok obuhvata akutnu, imunološku i hroničnu fazu inflamacije [5,6,17] i odvija se kroz nekoliko faza**:** (Slika 1) **1**. **Akutna faza:** Direktno oštećenje miokarda ulaskom patogena (npr. virusa) u kardiomiocite, što dovodi do njihove nekroze. **2. Imunološka faza:** Aktivacija urođenog i adaptivnog imunskog odgovora (makrofagi, T-limfociti) sa oslobađanjem citokina i inflamatornih medijatora, što dodatno oštećuje miokard. Genetske varijante u sarkomernim i dezmozomskim genima sve se češće identifikuju [1,18-20]. **3. Hronična faza:** Kod nekih pacijenata inflamatorni odgovor perzistira, što dovodi do progresivne fibroze miokarda, remodelovanja komora i razvoja dilatativne kardiomiopatije.

Slika 1. Stadijumi inflamatornog mioperikardijalnog sindroma. AHA – anti-srčana antitela; AIDA – antitela na interkalarni disk. *preuzeto sa Eur Heart J*, Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192



authors of this review and their collaborators have advanced the understanding of diastolic dysfunction and echocardiographic parameters in inflammatory cardiomyopathies [12–14], while endomyocardial biopsy is recommended in high-risk cases [1, 15–21]..

EPIDEMIOLOGY AND CLASSIFICATION

The guidelines report an incidence of pericarditis ranging from 3 to 32 cases per 100,000 inhabitants per year, while the incidence of myocarditis is between 6 and 8 cases per 100,000 inhabitants [1,15]. Higher rates have been observed in men and younger adults. A particular challenge is the fact that a large number of subclinical and mild cases, including those diagnosed within the context of MINOCA (myocardial infarction with non-obstructive coronary arteries), remain undiagnosed [6,9], which may lead to underestimation of the true incidence and prevalence of chronic forms of the disease.

IMPS is classified into the following clinical entities: isolated pericarditis, isolated myocarditis, myopericarditis (predominant pericarditis with mild myocardial involvement), perimyocarditis (predominant myocarditis with pericardial features), and chronic inflammatory cardiomyopathy (chronic myocarditis with structural remodeling, dysfunction, and an arrhythmogenic substr [1].

ETIOLOGY AND PATHOPHYSIOLOGY

The etiology of myocarditis and pericarditis is heterogeneous. In developed countries, viral infections predominate (enteroviruses, adenoviruses, parvovirus B19, human herpesvirus 6, influenza virus, hepatitis C virus) [5,16,17], whereas in endemic regions tuberculosis remains an important cause of pericarditis, particularly in predisposed individuals with HIV infection. Bacterial causes (diphtheria, borreliosis, staphylococcal infections) are less common. Autoimmune mechanisms may lead to inflammation in the context of systemic diseases (lupus, sarcoidosis, vasculitis), while toxic agents (anthracyclines, alcohol, cocaine) and drugs (checkpoint inhibitors) can also induce myocarditis. A genetic basis plays an important role in susceptibility to viral infections and in determining the severity of the clinical presentation, with variants in sarcomeric and desmosomal genes being associated with myocarditis, and autoinflammatory diseases with recurrent pericarditis [6,8,15].

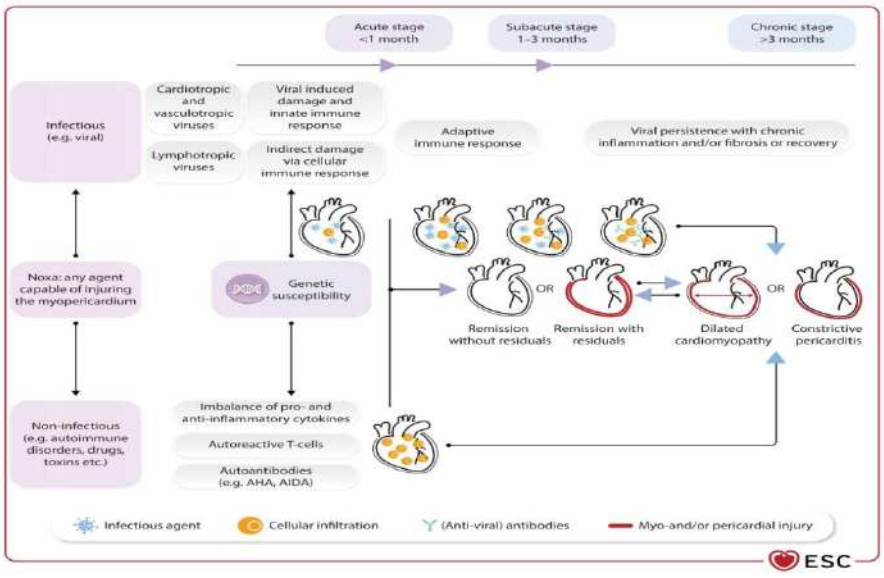
The pathophysiology of myocarditis is complex and involves acute, immune-mediated, and chronic phases of inflammation [5,6,17], progressing through several stages (Figure 1):

Acute phase: Direct myocardial injury caused by pathogen entry (e.g., viruses) into cardiomyocytes, leading to cell necrosis.

Immunological phase: Activation of the innate and adaptive immune response (macrophages, T-lymphocytes) with the release of cytokines and inflammatory mediators, resulting in further myocardial damage. Genetic variants in sarcomeric and desmosomal genes are increasingly being identified [1,18–20].

Chronic phase: In some patients, the inflammatory response persists, leading to progressive myocardial fibrosis, ventricular remodeling, and the development of dilated cardiomyopathy..

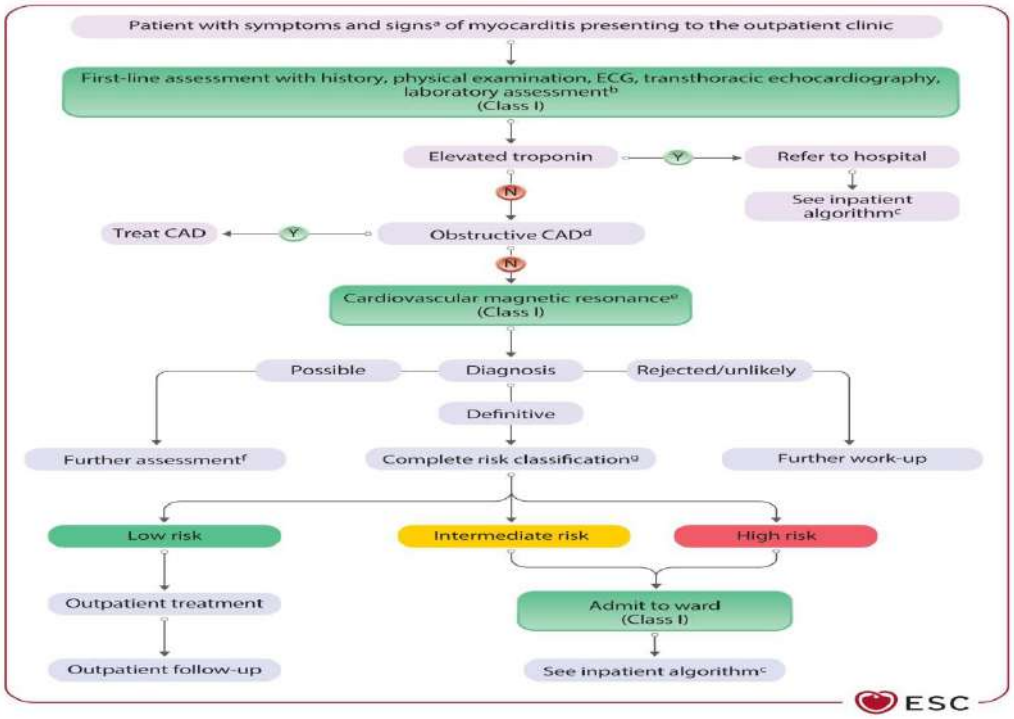
Figure 1. Stages of inflammatory myopericardial syndrome. AHA – anti-cardiac antibodies; AIDA – antibodies against the intercalated disc. Adapted from: *Eur Heart J*, Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192



KLINIČKA PREZENTACIJA

Klinička prezentacija IMPS je veoma varijabilna. Prema vremenskom toku, miokarditis se deli na: Akutni (≤4 nedelje); Subakutni (4-12 nedelja) i Hronični (>3 meseca, perzistentna inflamacija i remodelovanje). Miokarditis se klinički manifestuje od blagih simptoma u heterogenim formama: asimtomatski blagi miokarditis, bol u grudima, perimiokarditis, srčana insuficijencija, aritmijski tip, iznenadna smrt i fulminantni miokarditis sa fulminantnom srčanom insuficijencijom kardiogenim šokom [6,18-20]. Miokarditis se smatra komplikovanim kada postoji LVEF <50%, akutna srčana insuficijencija, ventrikularne aritmije ili visokostepeni AV blok. Komplikovani oblici mogu pratiti ventrikularne aritmije, AV blokove i značajno sniženje EF [7–9, 18-20] (Slika 2).

Slika 2. Dijagnostički algoritam i trijaža za ambulantne pacijente sa miokarditisom. *preuzeto sa Eur Heart J,* Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192



CAD (coronary artery disease) – koronarna bolest srca (KBS); CRP – C-reaktivni protein; ECG (electrocardiogram) – elektrokardiogram (EKG); N (no) – ne; NT-proBNP – N-terminalni pro-natriuretički peptid tipa B; Y (yes) – da; B-Laboratorijsko testiranje uključuje troponin, NT-proBNP, C-reaktivni protein, diferencijalnu krvnu sliku; d-Invazivna koronarna angiografija ili kompjuterizovana tomografska angiografija (CT) u zavisnosti od kliničke verovatnoće; E-U zavisnosti od kliničke situacije (srčana insuficijencija, aritmije) primiti pacijenta na bolničko odeljenje.

Termin **fulminantni miokarditis** [21] rezervisan je za bolesnike sa kardiogenim šokom i najtežim oblikom bolesti, koji često zahteva intenzivno lečenje i **mehaničku cirkulatornu podršku**. Perikarditis se klinički manifestuje kao suvi, eksudaztiv, kao preteća i akutna tamponada srca i ili revrezibilna parcijalna kosntrikcija te hronični konstriktivni oblik [2,4]. Pravovremena diferencijacija između inflamatornih i neinflamatornih fenotipova je ključna.

DIJAGNOSTIČKI PRISTUP

ESC 2025 preporuke SADA MENJAJU suštinu DIJAGNOSTIKE I STADIJUME U DIJAGNOSTIČKOM PROCESU - dolazi do procene patradigme za dijagnozu, zahvaljujući ogromnoj ulozi kardio-magnetne rezonance (CMR) koja postaje zlatni standard za dijagnozu miokarditisa, dok je sada smanjena uloga endomiokardne biopsije za teže i nejasne, visokorizične slučajeve i zbog odredjivanja adekvatne terapije po patodistološkom tipu sa imunohistohemijom i PCR dijagnozom prisustva virusa u miokardu. RANIJE su bili: suspektan, potvrđen i dokazan a SADA: malo verovatan/odbačen, moguć i definitivan (Slika 3 i Tabela 1 i 2).

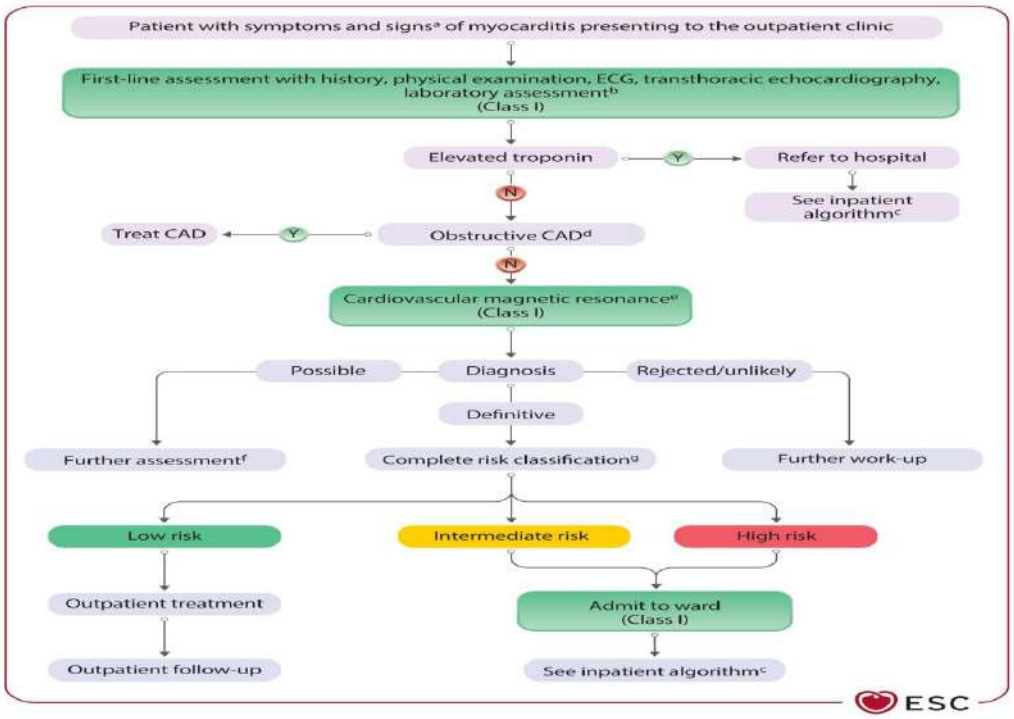
CLINICAL PRESENTATION

The clinical presentation of IMPS is highly variable. According to the time course, myocarditis is classified into: acute (≤4 weeks), subacute (4–12 weeks), and chronic (>3 months, with persistent inflammation and remodeling).

Myocarditis may present with a wide spectrum of clinical manifestations, ranging from mild or asymptomatic forms to heterogeneous clinical phenotypes, including asymptomatic mild myocarditis, chest pain, perimyocarditis, heart failure, arrhythmic presentation, sudden cardiac death, and fulminant myocarditis with fulminant heart failure and cardiogenic shock [6,18–20].

Myocarditis is considered complicated when there is LVEF <50%, acute heart failure, ventricular arrhythmias, or high-degree atrioventricular (AV) block. Complicated forms may be associated with ventricular arrhythmias, AV blocks, and significantly reduced ejection fraction [7–9,18–20] (Figure 2).

Figure 2. Diagnostic algorithm and triage for outpatients with myocarditis. Adapted from: *Eur Heart J*, Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192



The term fulminant myocarditis [21] is reserved for patients presenting with cardiogenic shock and the most severe form of the disease, which often requires intensive treatment and mechanical circulatory support.

Pericarditis clinically manifests as dry (fibrinous), effusive, as an impending or acute cardiac tamponade, reversible partial constriction, or a chronic constrictive form [2,4]. Timely differentiation between inflammatory and non-inflammatory phenotypes is crucial.

DIAGNOSTIC APPROACH

The 2025 ESC recommendations significantly reshape the essence of the diagnostic pathway and disease staging, reflecting a paradigm shift in the diagnostic process. This is largely driven by the major role of cardiac magnetic resonance imaging (CMR), which has become the gold standard for diagnosing myocarditis. At the same time, the role of endomyocardial biopsy has been refined and is now mainly reserved for severe, unclear, or high-risk cases, as well as for guiding appropriate therapy based on pathological and histological characterization with immunohistochemistry and PCR detection of viral genomes in the myocardium.

Previously, diagnostic categories included: suspected, confirmed, and proven myocarditis. In the new framework, classification has been updated to: unlikely/excluded, possible, and definite myocarditis (Figure 3 and Tables 1 and 2)..

Tabela 1. **Dijagnostički kriterijumi i klasifikacija za inflamatorni mioperikardni sindrom (IMPS)**

Ako su ispunjeni dijagnostički kriterijumi za miokarditis i/ili perikarditis

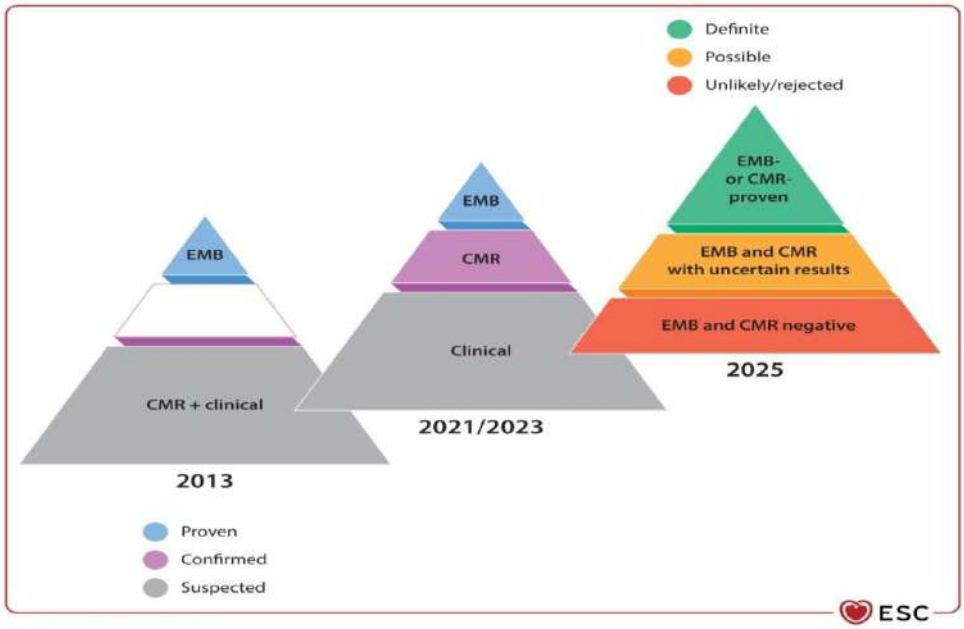
Kategorija	Miokarditis	Perikarditis
Definitivan	Klinička slika + potvrda putem **CMR**-a ili **EMB**-a	Klinička slika sa **>1 dodatnim** kriterijumom
Moguć	Klinička slika sa najmanje **1 dodatnim** kriterijumom; CMR ili EMB nesigurni ili nedostupni	Klinička slika sa **1 dodatnim** kriterijumom
Malo verovatan / Odbačen	Samo klinička slika bez dodatnih kriterijuma	Samo klinička slika bez dodatnih kriterijuma

Tabela 2. Dodatni kriterijumi (pored kliničke slike)

Kriterijum	Miokarditis	Perikarditis
Klinički	Nespecifični nalazi	**Perikardno trenje**
EKG	ST-T promene	**PR depresija**, difuzna elevacija ST-segmenta
Biomarkeri	Povišen **troponin**	Povišen **CRP**
Imidžing (Snimanje)	Poremećaj strain-a, pokretljivosti zida, smanjena ejekciona frakcija (EF)	Nov ili pogoršan **perikardni izliv**
CMR nalazi	Edem miokarda i/ili **LGE** (kasno nakupljanje gadolinijuma)	

CMR – Magnetna rezonanca srca; EMB – Endomiokardna biopsija; LGE – Kasno nakupljanje gadolinijuma (ukazuje na fibrozu ili upalu)

Slika 3. Promena paradigme u kliničkoj dijagnozi miokarditisa



CMR, kardiovaskularna magnetna rezonanca; EMB, endomiokardijalna biopsija. I EMB i CMR mogu pružiti konačnu kliničku dijagnozu, ali sa različitim indikacijama.

Osnovni dijagnostički elementi:

Inicijalna procena: putem biomarkeri: Obavezno određivanje troponina (marker lezije-nekroze miokarda), visoko senzitivnog C reaktivnog proteina (hsCRP-a, markera inflamacije) i natriuretskih peptida BNP/NT-proBNP (markeri srčane insuficijencije). Rutinske virusne serologije se ne preporučuju [1, 3,5,19-20];

Elektrokardiografija (EKG): Može pokazati nespecifične promene ST-segmenta [5]: ST-elevacija/depresija, promene T talasa, AV blok, aritmije). nema tipičnog EKG obrasca za miokarditis, ali se smatra da ipak EKG nije nikad normalan -heterogeni nalaz kod raznih oblika IMPS. Difuzna ST-elevacije konkavnog tipa naviše su tipične za perikarditis

Ehokardiografija je bazična slikovna metoda za procenu funkcije komora (LVEF), prisustva perikardnog izliva, tamponade i regionalnih poremećaja kontraktilnosti, ali često ne može sa sigurnošću potvrditi inflamaciju [12–14];

Ako je troponin uredan i LVEF očuvana - to znači povoljnu prognozu.

Neinvazivna dijagnostika – Kardio-MR (CMR) Kardio magnetna rezonanca (CMR):

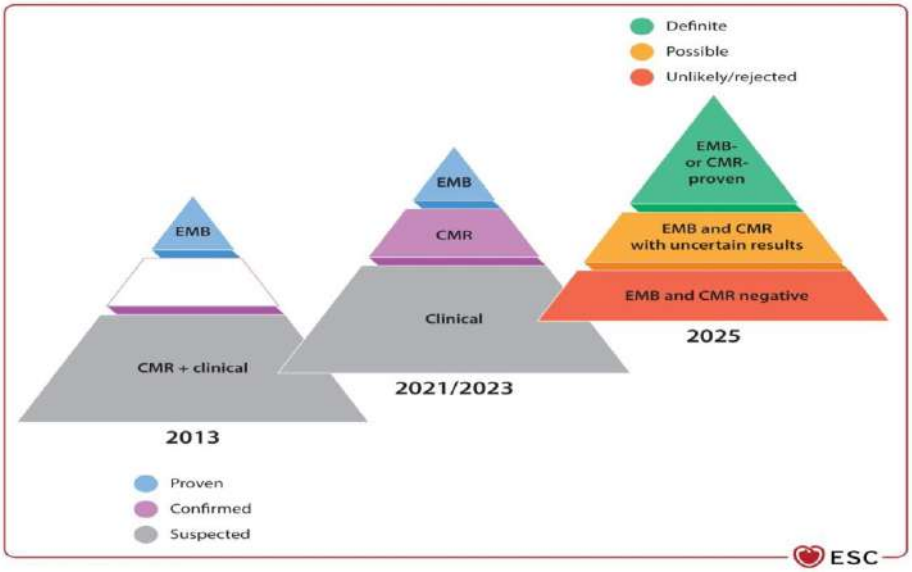
Table 1. Diagnostic criteria and classification for inflammatory myopericardial syndrome (IMPS)
If diagnostic criteria for myocarditis and/or pericarditis are fulfilled

Category	Myocarditis	Pericarditis
Definite	Clinical presentation + confirmation by CMR or EMB	Clinical presentation with >1 additional criterion
Possible	Clinical presentation with at least 1 additional criterion; CMR or EMB inconclusive or unavailable	Clinical presentation with 1 additional criterion
Unlikely / Excluded	Clinical presentation only, without additional criteria	Clinical presentation only, without additional criteria

Table 2. Additional criteria (in addition to clinical presentation)

Criterion	Myocarditis	Pericarditis
Clinical	Nonspecific findings	Pericardial friction rub
ECG	ST–T changes	PR depression, diffuse ST-segment elevation
Biomarkers	Elevated troponin	Elevated CRP
Imaging	Abnormal strain, wall motion abnormalities, reduced ejection fraction (EF)	New or worsening pericardial effusion
CMR findings	Myocardial edema and/or LGE (late gadolinium enhancement)	—

Figure 3. Paradigm shift in the clinical diagnosis of myocarditis



Basic diagnostic elements

Initial evaluation – biomarkers: Mandatory measurement of troponin (marker of myocardial injury/necrosis), high-sensitivity C-reactive protein (hsCRP, marker of inflammation), and natriuretic peptides BNP/NT-proBNP (markers of heart failure). Routine viral serologies are not recommended [1,3,5,19–20].

Electrocardiography (ECG): May show nonspecific ST-segment changes [5] (ST elevation/depression, T-wave changes, AV block, arrhythmias). There is no typical ECG pattern for myocarditis; however, ECG is rarely completely normal and is considered heterogeneous across different IMPS forms. Diffuse, concave upward ST-segment elevation is typical of pericarditis.

Echocardiography: A basic imaging modality for assessment of ventricular function (LVEF), presence of pericardial effusion, tamponade, and regional wall motion abnormalities. However, it often cannot definitively confirm inflammation [12–14].

If troponin is normal and LVEF is preserved, this indicates a favorable prognosis.

Non-invasive imaging – Cardiac Magnetic Resonance (CMR)

ključna metoda prema revidiranim Lake Louise kriterijumima [1,10,11];.CMR je postao centralna dijagnostička metoda za potvrdu IMPS. Dijagnoza se postavlja prema **revidiranim Lake Louise kriterijumima**, koji zahtevaju prisustvo najmanje jedne abnormalnosti zasnovane na sekvenci **T1 mapa-mapiranja** (koje ukazuje na intersticijalnu fibrozu ili edem) i najmanje jedne abnormalnosti zasnovane na sekvenci **T2 mapa-mapiranja** (koje ukazuje na edem miokarda) [11];

CMR omogućava detekciju edema, nekroze i fibroze putem kasnog nakupljanja gadolinijuma epikardno ili mezomiokardno (LGE – late gadolinium enhancement), što pravi difernecijalnu dijagnozu od ishemije miokarda i koronarne bolesti

ESC 2025 preporuke ističu individualizovan pristup zasnovan na kliničkoj prezentaciji i proceni rizika (Tabela 3)[1].

Tabela 3. Algoritam za procenu rizika (risk stratification) i trijažu pacijenata sa sumnjom na miokarditis i perikarditis u ambulantnim uslovima. Hospitalizacija se preporučuje za sve pacijente sa miokarditisom i visokorizičnim perikarditisom.

Rizik	Visok	Srednji	Nizak
Miokarditis	Akutna srčana slabost / kardiogeni šok Dispneja NYHA III–IV refraktorna na terapiju Srčani zastoj / sinkopa Ventrikularna fibrilacija / održana VT Visokostepeni AV blok	Nova/progresivna dispneja Nesustavne ventrikularne aritmije Perzistentno/relapsno povišen troponin	Stabilni ili blagi simptomi
	Kriterijumi snimanja	**Kriterijumi snimanja**	**Kriterijumi snimanja**
	LVEF <40% Opsežno LGE na CMR	LVEF 41–49% i/ili WMA LVEF ≥50% + LGE ≥2 segmenta	LVEF ≥50% bez LGE ili LGE <2 segmenta
Perikarditis	Znaci tamponade Temperatura >38°C Efuzivno-konstriktivni perikarditis Neuspeh NSAIL terapije Incesantni perikarditis	Znaci desnostrane srčane slabosti	Odgovor na terapiju za 1–2 nedelje
	Kriterijumi snimanja	**Kriterijumi snimanja**	**Kriterijumi snimanja**
	Izliv >20 mm Tamponada Opsežno perikardijalno LGE	Izliv 10–20 mm Konstriktivna fiziologija	Bez ili mali izliv Bez perikardijalnog LGE

Invazivna dijagnostika – Endomiokardijalna biopsija (EMB): Endomiokardijalna biopsija (EMB): zlatni standard kod teških formi [17,21,22] i definitivnu dijagnozu i etiološku klasifikaciju. Indikacije su proširene u odnosu na ranije smernice i rezervisane su za visokorizične slučajeve (Tabela 4). Obavezna je molekularno-biološka (PCR) analiza na viruse pre započinjanja imunosupresivne terapije [21-23].

TABELA 4. Indikacije za endomiokardijalnu biopsiju (EMB) prema ESC 2025 [21]

Klinička situacija	Nivo preporuke
Fulminantni miokarditis sa kardiogenim šokom	**Jaka indikacija**
Sumnja na giant-cell miokarditis	**Jaka indikacija**
Sumnja na eozinofilni miokarditis	**Jaka indikacija**
Akutna srčana insuficijencija nepoznate etiologije (<2 nedelje trajanja)	Preporučuje se
Srčana insuficijencija (2 nedelje – 3 meseca) uz dilataciju leve komore (LV) i nove ventrikularne aritmije	Preporučuje se
Sumnja na sarkoidozu srca ili autoimuni miokarditis	Preporučuje se
Refraktarne ventrikularne aritmije nepoznate etiologije	Razmotriti
Perzistentna disfunkcija leve komore bez jasnog uzroka (LVEF <40%, opsežan LGE na CMR)	Razmotriti

Cardiac magnetic resonance imaging is a key modality according to the revised Lake Louise criteria [1,10,11] and has become central in the diagnostic work-up of IMPS.

Diagnosis is established based on the revised Lake Louise criteria, which require at least one abnormality based on T1 mapping (indicating interstitial fibrosis or edema) and at least one abnormality based on T2 mapping (indicating myocardial edema) [11].

CMR enables detection of edema, necrosis, and fibrosis through late gadolinium enhancement (LGE), typically in an epicardial or mid-myocardial distribution, which helps differentiate inflammatory disease from myocardial ischemia and coronary artery disease.

The 2025 ESC recommendations emphasize an individualized approach based on clinical presentation and risk assessment (Table 3).1].

Table 3. Risk stratification algorithm and triage of patients with suspected myocarditis and pericarditis in outpatient settings. Hospitalization is recommended for all patients with myocarditis and high-risk pericarditis.

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
Pericarditis	• Signs and symptoms of cardiac tamponade • Fever (temperature >38°C) • Effusive–constrictive pericarditis • Failure of NSAID therapy • Incessant pericarditis	• Signs and symptoms of right HF	• Response to adequate therapy within 1–2 weeks
	Imaging criteria:	**Imaging criteria:**	**Imaging criteria:**
	• Large PEff (>20 mm end-diastole) • Cardiac tamponade • Extensive pericardial LGE on CMR	• Moderate–large PEff (10–20 mm end-diastole) • Constrictive physiology regardless of the size of the effusion	• Absence or mild PEff • Absence of pericardial LGE on CMR

Invasive diagnostics – Endomyocardial biopsy (EMB)

Endomyocardial biopsy (EMB) is considered the gold standard in severe forms of disease [17,21,22], providing definitive diagnosis and etiological classification. Indications have been expanded compared with previous guidelines and are now reserved for high-risk cases (Table 4). Molecular biological (PCR) analysis for viral genomes is mandatory prior to initiation of immunosuppressive therapy [21–23]].

TABLE 4. Indications for endomyocardial biopsy (EMB) according to ESC 2025 [21]

Clinical situation	Level of recommendation
Fulminant myocarditis with cardiogenic shock	Strong indication
Suspected giant-cell myocarditis	Strong indication
Suspected eosinophilic myocarditis	Strong indication
Acute heart failure of unknown etiology (<2 weeks duration)	Recommended
Heart failure (2 weeks–3 months) with left ventricular (LV) dilation and new ventricular arrhythmias	Recommended
Suspicion of cardiac sarcoidosis or autoimmune myocarditis	Recommended
Refractory ventricular arrhythmias of unknown etiology	Consider
Persistent left ventricular dysfunction without clear cause (LVEF <40%, extensive LGE on CMR)	

GENETSKO TESTIRANJE

Sve je više dokaza o povezanosti miokarditisa sa naslednim kardiomiopatijama. ESC 2025 preporučuje genetsko testiranje kod selektovanih pacijenata sa familijarnim oblicima i rekurentnim perikarditisom [1]. Studije ističu genetske mutacije u dezmozomskim genima kod nasledne predispozicije [1] kod selektovanih pacijenata sa visokim dijagnostičkim prinosom, kao što su: Porodična anamneza kardiomiopatija ili iznenadne srčane smrti, a ritmijska prezentacija bolesti , prisustvo septalnog ili "ring-like" LGE na CMR, trajna sistolna disfunkcija bez oporavka i slučajevi rekurentni miokarditisa ili perikarditis (genetski uzrok se nalazi kod oko 15% bolesnika sa rekurentnim perikarditisom) [1].

TERAPIJA MIOKARDITISA

Terapijski pristup je individualizovan i zavisi od etiologije, kliničke prezentacije i hemodinamskog statusa. Lečenje je individualizovano prema etiologiji i hemodinamskom statusu [1,6] (Tabela 5). Kod stabilnih pacijenata primenjuju se analgetici i NSAID uz kolhicin [1,31]; kod srčane insuficijencije važe standardne HF smernice (ACEi, ARNI, BB, MRA, SGLT2i) [6,29]. Imunosupresija je rezervisana za virus negativne oblike [21] ili specifične entitete poput giant cell i eozinofilnog miokarditisa [22-24]. Kod fulminantnog miokarditisa preporučuje se mehanička cirkulatorna podrška (VA ECMO) [1,20]. Sistematizovano je lečenje miokardita prikazano od 1 do 5 :

1. Opšte mere i simptomatska terapija: Ograničenje fizičke aktivnosti u trajanju od 3 do 6 meseci. U akutnoj fazi, kod hemodinamski stabilnih pacijenata, primenjuju se analgetici, nesteroidni antiinflamatorni lekovi (NSAIL) uz dodatak kolhicina ako postoje perikardni simptomi.

2. Terapija srčane insuficijencije: Kod bolesnika sa srčanom insuficijencijom primenjuje se standardna terapija prema važećim smernicama za srčanu insuficijenciju (HF): ACE inhibitori ili ARNI, beta-blokatori, antagonisti mineralokortikoidnih receptora (MRA), inhibitori natrijum-glukoznog kotransportera 2 (SGLT2-I) i diuretici kod kongestije.

3. Imunosupresivna terapija: Primenjuje se samo kod neinfektivnih etiologija I nakon što je PCR analizom EMB uzorka isključena aktivna virusna infekcija u miokardu. Indikovana je kod: Virus-negativnog inflamatornog (autoimunog) miokarditisa, Giant-cell miokarditisa (jaka preporuka) (24) Eozinofilnog miokarditisa (jaka preporuka), miokarditisa povezanog sa sistemskim autoimunim bolestima (npr. sarkoidoza). Najčešće korišćeni lekovi su kortikosteroidi (prednizon), azatioprin, mikofenolat mofetil i ciklosporin [1].

4. Antiaritmijska terapija i uređaji: Kod simptomatskih aritmija primenjuju se antiaritmici. Implantabilni kardioverter-defibrilator (ICD) se razmatra kod pacijenata sa perzistentnom disfunkcijom leve komore nakon najmanje 3 meseca optimalne terapije. Nosivi defibrilator (wearable defibrillator koji se oblače kao prsluk) može biti opcija tokom 3-6 meseci [1].

5. Mehanička cirkulatorna podrška (MCS): Kod fulminantnog miokarditisa sa kardiogenim šokom, MCS služi kao "most do oporavka" ili "most do transplantacije". Preporučene metode uključuju intraaortnu balon pumpu (IABP) i venoarterijski ECMO (VA-ECMO) kao najefikasniju podršku [20-21].

Tabela 5. Terapijske preporuke za miokarditis prema ESC 2025

Terapijski pristup	Preporuka
Ograničenje fizičke aktivnosti 3–6 meseci	Preporučuje se **klasa II**
Standardna terapija srčane insuficijencije	Preporučuje se **klasa II**
Imunosupresivna terapija kod virus-negativnog autoimunog miokarditisa	Preporučuje se **klasa II**
Kortikosteroidi kod giant-cell ili eozinofilnog miokarditisa	**Jaka preporuka-klasa I**
Antivirusna terapija kod potvrđene virusne etiologije	Selektivno
Mehanička cirkulatorna podrška kod kardiogenog šoka	Preporučuje se

TERAPIJA PERIKARDITISA

Prva linija terapije: Aspirin ili NSAID u kombinaciji s akolhicinom tokom najmanje 3 do 6 meseci (preporuka IA) [1-4];

Druga linija terapije: kortikosteroidi su druga linija kod refraktarnih oblika [2]. Kortikosteroidi se koriste samo ako prva linija terapije zakaže ili je kontraindikovana.

GENETIC TESTING

There is increasing evidence of an association between myocarditis and inherited cardiomyopathies. The ESC 2025 guidelines recommend genetic testing in selected patients with familial forms and recurrent pericarditis [1]. Studies highlight mutations in desmosomal genes as part of an inherited predisposition [1], particularly in patients with high diagnostic yield, such as those with:

Family history of cardiomyopathy or sudden cardiac death

Arrhythmic presentation of disease

Presence of septal or "ring-like" LGE on CMR

Persistent systolic dysfunction without recovery

Recurrent myocarditis or pericarditis (a genetic cause is identified in approximately 15% of patients with recurrent pericarditis) [1]

THERAPY OF MYOCARDITIS

Therapeutic management is individualized and depends on etiology, clinical presentation, and hemodynamic status [1,6] (Table 5). In stable patients, analgesics and NSAIDs are used, with the addition of colchicine when pericardial symptoms are present [1,31]. In heart failure, standard HF guideline-directed medical therapy is applied (ACE inhibitors/ARNI, beta-blockers, mineralocorticoid receptor antagonists, SGLT2 inhibitors) [6,29].

Immunosuppressive therapy is reserved for virus-negative forms [21] or specific entities such as giant-cell and eosinophilic myocarditis [22–24]. In fulminant myocarditis, mechanical circulatory support (VA-ECMO) is recommended [1,20].

The treatment of myocarditis is systematized into five key domains:

1. General measures and symptomatic therapy

Restriction of physical activity for 3–6 months. In the acute phase, in hemodynamically stable patients, analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), and colchicine are used if pericardial symptoms are present.

2. Heart failure therapy

In patients with heart failure, standard guideline-directed therapy is used: ACE inhibitors or ARNI, beta-blockers, mineralocorticoid receptor antagonists (MRA), sodium-glucose cotransporter-2 inhibitors (SGLT2i), and diuretics in cases of congestion.

3. Immunosuppressive therapy

Used only in non-infectious etiologies and after exclusion of active viral infection in the myocardium by PCR analysis of EMB samples. Indications include:

Virus-negative inflammatory (autoimmune) myocarditis

Giant-cell myocarditis (strong recommendation)

Eosinophilic myocarditis (strong recommendation)

Myocarditis associated with systemic autoimmune diseases (e.g., sarcoidosis)

Commonly used agents include corticosteroids (prednisone), azathioprine, mycophenolate mofetil, and cyclosporine [1].

4. Antiarrhythmic therapy and devices

Antiarrhythmic drugs are used for symptomatic arrhythmias. Implantable cardioverter-defibrillator (ICD) implantation is considered in patients with persistent LV dysfunction after at least 3 months of optimal therapy. A wearable defibrillator (vest-type device) may be used as a temporary option for 3–6 months [1].

5. Mechanical circulatory support (MCS)

In fulminant myocarditis with cardiogenic shock, MCS serves as a "bridge to recovery" or "bridge to transplantation." Recommended modalities include intra-aortic balloon pump (IABP) and veno-arterial ECMO (VA-ECMO) as the most effective support strategies [20–21].].

Table 5. Therapeutic recommendations for myocarditis according to ESC 2025

Therapeutic approach	Recommendation
Restriction of physical activity for 3–6 months	Recommended (Class II)
Standard heart failure therapy	Recommended (Class II)
Immunosuppressive therapy in virus-negative autoimmune myocarditis	Recommended (Class II)
Corticosteroids in giant-cell or eosinophilic myocarditis	Strong recommendation (Class I)
Antiviral therapy in confirmed viral etiology	Selective
Mechanical circulatory support in cardiogenic shock	Recommended

TREATMENT OF PERICARDITIS

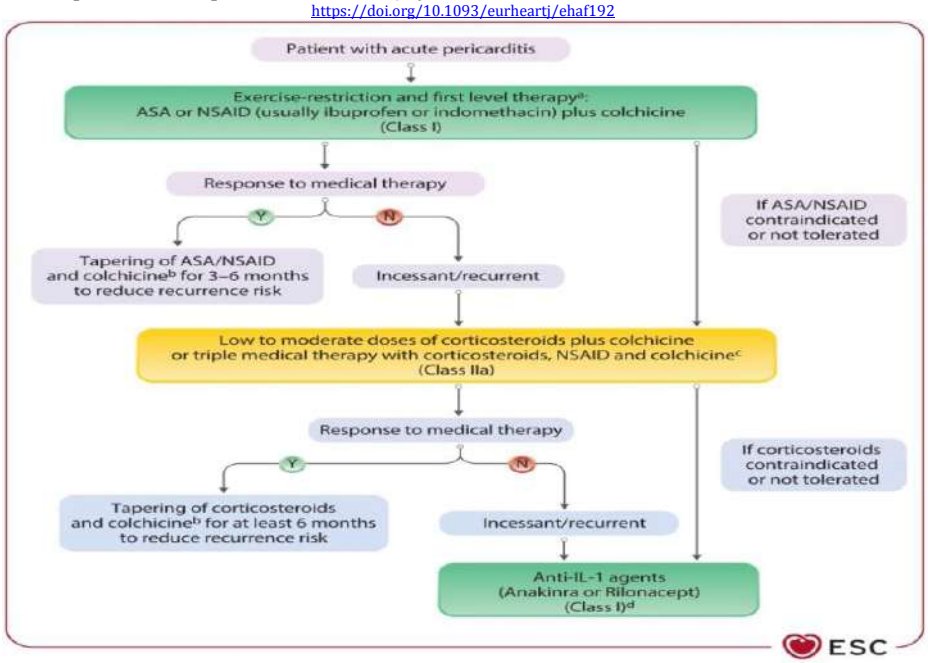
First-line therapy: Aspirin or NSAIDs in combination with colchicine for at least 3 to 6 months (Class I A recommendation) [1–4].

Second-line therapy:

Corticosteroids are considered second-line treatment for refractory forms [2]. They are

Refraktarni perikarditis: Inhibitori interleukina-1 (IL-1) predstavljaju novu terapijsku opciju kod refraktornog na lečenje i/ili rekurentnog perikarditisa, posebno kod jako povišenog hsCRP-a (preporuka IA kod izrazito inflamatornog fenotipa) (Slika 4 i Tabela 6).

SLIKA 4. Predloženi algoritam medikamentne terapije za perikarditis kod odraslih (ne uključujući interventne procedure i perikardiektomiju). *preuzeto sa Eur Heart J*, Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192



ASA – acetilsalicilna kiselina (aspirin); IL-1 – interleukin-1; CRP – C-reaktivni protein; CMR – magnetna rezonanca srca; LOE (level of evidence) – nivo dokaza; N (no) – ne; NSAID – nesteroidni antiinflamatorni lekovi (NSAIL); Y (yes) – da; A-ASA (aspirin) je prva opcija ako su pacijenti već na antiagregacionoj terapiji aspirinom. Ibuprofen se obično preferira kao prvi NSAIL. Isprobati više od jednog sredstva kako bi se procenio odgovor. Uz primenu aspirina/NSAIL uvek se preporučuje gastroprotekcija inhibitorom protonske pumpe; B-Kolhicin se preporučuje radi sprečavanja recidiva (ponovnog javljanja). Razmotriti primenu od najmanje 3 meseca za prvu epizodu perikarditisa i najmanje 6 meseci za neprekidne/recidivirajuće slučajeve. Kolhicin se isključuje kao poslednji lek tek nakon stabilne remisije; Postepeno smanjivanje doze (tapering) se preporučuje radi smanjenja perzistencije ili recidiva simptoma. Smanjivanje doze je sporije kod kortikosteroida. Postepeno smanjivanje doze kolhicina se obično ne sprovodi zbog trajanja terapije od preko 3–6 meseci. Pod odgovorom na terapiju podrazumevamo kliničku remisiju; C-Niska doza do umerena doza kortikosteroida (npr. prednizon 0,2–0,5 mg/kg dnevno ili ekvivalentne doze alternativnog kortikosteroida); D-Klasa I, nivo dokaza A; Klasa IIa, nivo dokaza C bez obzira na nivoe C-reaktivnog proteina, ukoliko postoji CMR dokaz inflamacije perikarda.

TABELA 6. terapijski protokol za lečenje perikarditisa. *preuzeto sa Eur Heart J*, Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192

Terapija	Doziranje	Trajanje	Smanjivanje doze (tapering)
Aspirin	750–1000 mg 3× dnevno	1–2 nedelje	Smanjivati za 250 mg na 1–2 nedelje
Ibuprofen	600–800 mg 3× dnevno	1–2 nedelje	Smanjivati za 200 mg na 1–2 nedelje
Indometacin	25–50 mg 3× dnevno	1–2 nedelje	Smanjivati za 25 mg na 1–2 nedelje
Kolhicin	0,5 mg 1× dnevno (<70 kg ili teška bubrežna insuficijencija) ili 0,5 mg 2× dnevno	3–6 meseci	Nije potrebno
Prednizon	0,2–0,5 mg/kg/dan	2–4 nedelje	Nekoliko meseci
Terapija samo kod recidiva			
Azatioprin	Početno 1 mg/kg/dan, zatim postepeno povećati na 2–3 mg/kg/dan	Nekoliko meseci	Nekoliko meseci
IVIG (intravenozni imunoglobulini)	400–500 mg/kg i.v. dnevno tokom 5 dana	5 dana	Nije potrebno
Anakinra	1–2 mg/kg/dan (do 100 mg/dan kod odraslih)	Najmanje 6 meseci / >12 meseci	Potrebno (najmanje 3–6 meseci) / nepoznato
Rilonacept	320 mg početno, zatim 160 mg nedeljno	>12 meseci	Nije navedeno

used only when first-line therapy fails or is contraindicated.

Refractory pericarditis:

Interleukin-1 (IL-1) inhibitors represent a novel therapeutic option for treatment-refractory and/or recurrent pericarditis, particularly in patients with markedly elevated hsCRP levels (Class I A recommendation in highly inflammatory phenotypes) (Figure 4 and Table 6)..

Figure 4. Proposed algorithm for pharmacological treatment of pericarditis in adults (excluding interventional procedures and pericardiectomy). Adapted from: *Eur Heart J*, Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192

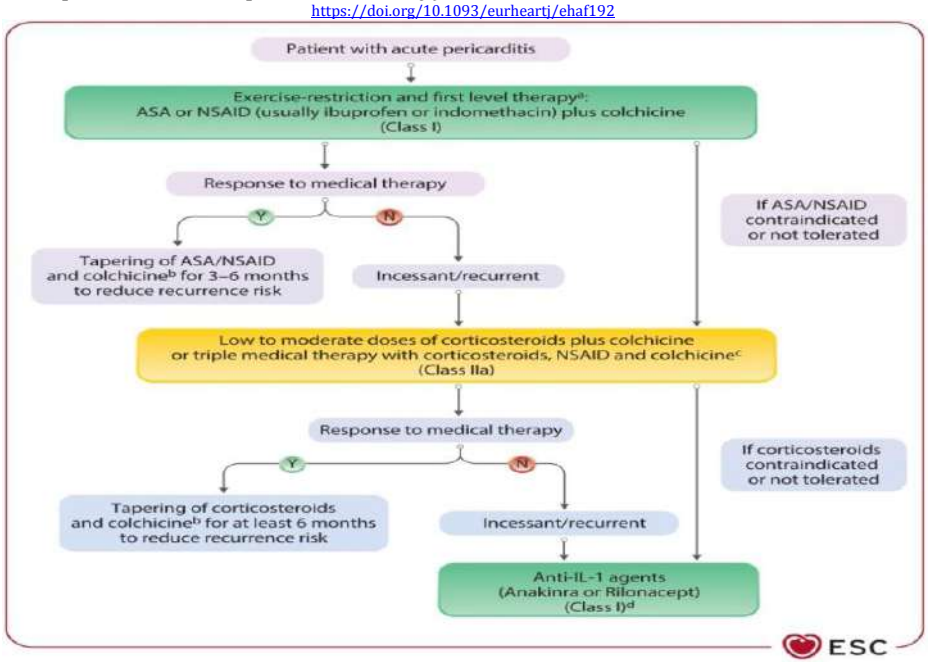


TABLE 6. Therapeutic protocol for the treatment of pericarditis. Adapted from: *Eur Heart J*, Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192

Therapy	Dosing	Duration[a]	Tapering[a]
Aspirin[b]	750–1000 mg 3 times daily	1–2 weeks	Decrease by 250 mg every 1–2 weeks
Ibuprofen[b]	600–800 mg 3 times daily	1–2 weeks	Decrease by 200 mg every 1–2 weeks
Indomethacin	25–50 mg 3 times daily	1–2 weeks	Decrease by 25 mg every 1–2 weeks
Colchicine[b]	0.5 mg once daily (<70 kg or severe renal impairment) or 0.5 mg twice daily	3–6 months	Not required
Prednisone	0.2–0.5 mg/kg/day	2–4 weeks	Several months
Treatment for recurrences only:			
Azathioprine	Starting with 1 mg/kg/day then gradually increased to 2–3 mg/kg/day	Several months	Several months
IVIG	400–500 mg/kg i.v. daily for 5 days	5 days	Not required
Anakinra	1–2 mg/kg/day up to 100 mg/day in adults	At least 6 months/ >12 months	Needed (at least 3–6 months)/ unknown
Rilonacept[c]	320 mg once daily followed by 160 mg weekly		

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TABELA 7. ZBIRNE PREPORUKE ESCESC ZA TERAPIJU MIOPERIKARDNOG INFLAMATORNOG SINDROMA

Preporuke	Klasa	Nivo
Lečenje simptoma		
NSAIL (uz inhibitor protonske pumpe) treba razmotriti kod pacijenata sa simptomima perikarditisa radi smanjenja tegoba	IIa	C
Kolhicin treba razmotriti kod pacijenata sa mioperikarditisom radi smanjenja recidiva	IIa	B
Lečenje srčane slabosti		
Pridržavanje ESC smernica za srčanu slabost preporučuje se kod miokarditisa sa sistolnom disfunkcijom leve komore i/ili srčanom slabošću radi smanjenja simptoma i poboljšanja funkcije leve komore	I	C
Terapiju srčane slabosti treba razmotriti kod pacijenata sa miokarditisom i sistolnom disfunkcijom leve komore najmanje 6 meseci nakon potpunog oporavka funkcije leve komore radi stabilizacije	IIa	C
Lečenje aritmija		
Beta-blokatori, uz nastavak najmanje 6 meseci, treba razmotriti kod akutnog miokarditisa (posebno uz povišen troponin) radi kontrole simptoma i prevencije aritmija	IIa	C
Antiaritmijska terapija treba razmotriti kod pacijenata nakon miokarditisa sa rekurentnom, simptomatskom ventrikularnom tahikardijom radi smanjenja opterećenja aritmijama	IIa	C
Imunosupresivna terapija		
Kortikosteroide treba razmotriti kod fulminantnih, neinfektivnih oblika miokarditisa radi stabilizacije pacijenta	IIa	C
Kortikosteroidi se mogu razmotriti kod akutnog miokarditisa sa smanjenim LVEF ako je refraktoran na standardnu terapiju srčane slabosti	IIb	C
Rutinska primena imunosupresivne terapije se ne preporučuje kod akutnog miokarditisa sa očuvanom funkcijom leve komore (nije pokazana korist)	III	C

ESC – Evropsko kardiološko društvo; HF – srčana slabost; LV – leva komora; LVEF – ejekciona frakcija leve komore; NSAIL – nesteroidni antiinflamatorni lekovi; VT – ventrikularna tahikardija

POSEBNE POPULACIJE

Post-COVID miokarditis: Može nastati kao posledica direktne virusne infekcije, sistemskog inflamatornog odgovora ili imunološke disfunkcije(25-26). Dijagnoza se često postavlja CMR-om, a terapija je uglavnom suportivna. Post COVID miokarditis i postvakcinalni oblici analizirani su u više studija [23–28]. Retki slučajevi postvakcinalnog miokarditisa nakon mRNA vakcina, najčešće kod mlađih muškaraca nekoliko dana nakon druge doze. Klinička slika je obično blaga, a prognoza povoljna. Korist od vakcinacije daleko je veća od rizika [27-30].

Deca: Primenjuju se slični dijagnostički kriterijumi, ali je neophodan oprez sa kortikosteroidima zbog uticaja na rast.

Trudnoća: Kolhicin se može koristiti za prevenciju recidiva perikarditisa (preporuka IIb C).

Stariji pacijenti: Potrebno je prilagoditi dozu kolhicina i pratiti bubrežnu funkciju.

PROGNOZA I PRAĆENJE

Prognoza zavisi od početne kliničke prezentacije i etiologije. Najvažniji prediktor nepovoljnog ishoda je biventrikularna disfunkcija. Većina pacijenata sa blagim oblikom bolesti ima dobar oporavak. Kod manjeg broja pacijenata može doći do razvoja dilatativne kardiomiopatije i hronične srčane insuficijencije. [14, 15]. Praćenje pacijenata nakon akutnog miokarditisa je sistematsko tokom prvih 6 do 24 meseca i uključuje: kliničke kontrole, EKG, Holter monitoring, biomarkere (troponin, CRP)i ehokardiografiju, test opterećenja i CMR u

TABLE 7. SUMMARY OF ESC RECOMMENDATIONS FOR THE TREATMENT OF INFLAMMATORY MYOPERICARDIAL SYNDROME (IMPS)

Recommendations	Class[a]	Level[b]
Management of symptoms		
NSAIDs (together with proton pump inhibition) should be considered in patients with associated symptoms of pericarditis to reduce symptoms.	IIa	C
Colchicine should be considered in patients with myopericarditis to reduce recurrences.[263]	IIa	B
Management of heart failure		
Adherence to the ESC HF guidelines is recommended in cases of myocarditis with LV systolic dysfunction and/or HF to reduce symptoms and to improve LV function.[12]	I	C
HF therapy should be considered in patients with myocarditis and LV systolic dysfunction for at least 6 months upon complete LV functional recovery to stabilize LV function.	IIa	C
Management of arrhythmias		
β-Blockers, with a continuation for at least 6 months, should be considered in patients with acute myocarditis, especially those with troponin elevation, to control symptoms and prevent arrhythmias.	IIa	C
Anti-arrhythmic treatment should be considered in post-myocarditis patients with recurrent, symptomatic VT to reduce arrhythmic burden.[58]	IIa	C
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

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ESC, European Society of Cardiology; HF, heart failure; LV, left ventricle; LVEF, left ventricular ejection fraction; NSAID, non-steroidal anti-inflammatory drug; VT, ventricular tachycardia.
[a]Class of recommendation.
[b]Level of evidence

SPECIAL POPULATIONS

Post-COVID myocarditis: May occur as a result of direct viral infection, systemic inflammatory response, or immune dysregulation (25–26). Diagnosis is often established by CMR, and therapy is mainly supportive. Post-COVID myocarditis and post-vaccination forms have been analyzed in several studies [23–28]. Rare cases of post-vaccination myocarditis after mRNA vaccines have been reported, most commonly in young males within several days after the second dose. The clinical course is usually mild, and the prognosis is favorable. The benefits of vaccination far outweigh the risks [27–30].

Children: Similar diagnostic criteria are applied, but caution is required with corticosteroid use due to potential effects on growth.

odabranim slučajevima [1]. Prognoza zavisi od stepena disfunkcije leve komore i prisustva fibroze na CMR u [6, 10, 11]. Dijastolna disfunkcija može perzistirati i nakon kliničkog oporavka [12–14].

DISKUSIJA

ESC smernice iz 2025. godine donose značajan konceptualni napredak uvođenjem IMPS, ali i određene dileme. Najveće rasprave izazivaju:Centralna uloga CMR-a: Iako je CMR postao nezaobilazan, oslanjanje na njega kao "novi zlatni standard" nosi rizik od preterane dijagnostike i ograničene dostupnosti. Kontroverzna preporuka o beta-blokatorima[1,6]: Preporuka za primenu beta-blokatora kod *svih* pacijenata sa miokarditisom najmanje 6 meseci, bez obzira na EF, zasnovana je na ograničenim dokazima i predstavlja najdiskutovaniju tačku vodiča. Kontroverze se odnose i na pristup genetskom testiranju – ograničeno u ESC u, šire u ACC/AHA vodičima [3, 4].

Nedovoljna posvećenost u raščišćavanju etiopatogeneze kod MINOCA populacije: Smernice propuštaju priliku da preciziraju definiciju IMPS kod pacijenata sa MINOCA-om, gde je miokarditis jedan od najčešćih konačnih nalaza.

Razlike u odnosu na američke preporuke (ACC/AHA) [1,3]: Evropski pristup je konzervativniji po pitanju genetskog testiranja (samo selektovani pacijenti naspram svih), ranije primene IL-1 inhibitora kod perikarditisa (kasnije u odnosu na ACC) i ne uključuje mikroaksijalne pumpe (npr. Impella) u algoritme mehaničke potpore, za razliku od američkih smernica.

Tabela 8. Poređenje ESC 2025 i ACC/AHA smernica2024

Tema	ESC 2025	ACC/AHA konsenzus
Genetsko testiranje	Samo kod selektovanih pacijenata	Preporučeno kod svih pacijenata sa miokarditisom
Beta-blokatori	Preporučeni ≥6 meseci kod svih	Nema univerzalne preporuke
IL-1 inhibitori	Konzervativniji pristup (nakon kortikosteroida)	Ranija primena nakon neuspeha NSAID + kolhicina
Mehanička potpora	Naglašen VA-ECMO	Detaljnije uključuje mikroaksijalne pumpe (Impella)

ESC 2025 donosi koncept IMPS, naglašava ulogu CMR a i proširuje indikacije za EMB [1,10,17]. U kontekstu domaće prakse, radovi autora ovog prtegleda literature Dr Dušana Bastaća značajno dopunjuju praznine u praktičnoj primeni dijagnostičkih metoda u inflamatornom miperikardnom sindromu u Srbiji [12–14]. Njegova istraživanja o **dijastolnom stres testu** i ehokardiografskim markerima ukazuju da dijastolna disfunkcija i povišen pritisak punjenja leve komore (LV filling pressure)mogu perzistirati i nakon oporavka sistolne funkcije (LVEF), što se uklapa u koncept **inflamatorne kardiomiopatije** i fenotip HFpEF (srčana insuficijencija sa očuvanom ejekcionom frakcijom) kod ovih pacijenata. Ovo naglašava potrebu za pažljivim, multimodalnim praćenjem, čak i kod bolesnika sa normalizovanom EF.

Pregnancy: Colchicine may be used for recurrence prevention in pericarditis (Class IIb C recommendation).

Elderly patients:

Dose adjustment of colchicine is necessary, along with monitoring of renal function.

PROGNOSIS AND FOLLOW-UP

Prognosis depends on initial clinical presentation and etiology. The most important predictor of adverse outcome is biventricular dysfunction. Most patients with mild disease achieve full recovery. In a minority of cases, progression to dilated cardiomyopathy and chronic heart failure may occur [14,15].

Follow-up after acute myocarditis is systematic over the first 6–24 months and includes: clinical assessment, ECG, Holter monitoring, biomarkers (troponin, CRP), echocardiography, exercise testing, and CMR in selected cases [1].

Prognosis is influenced by the degree of left ventricular dysfunction and the presence of fibrosis on CMR [6,10,11]. Diastolic dysfunction may persist even after clinical recovery [12–14].

DISCUSSION

The ESC 2025 guidelines represent a significant conceptual advance with the introduction of IMPS, but also raise several controversies.

The most debated issues include: Central role of CMR: Although CMR has become indispensable, its position as a "new gold standard" carries the risk of overdiagnosis and limited accessibility.

Controversial beta-blocker recommendation [1,6]: The recommendation for beta-blocker use in all myocarditis patients for at least 6 months, regardless of EF, is based on limited evidence and is one of the most debated points in the guideline.

Genetic testing approach: Also controversial, being more limited in ESC guidelines compared with broader recommendations in ACC/AHA documents [3,4].

Nedovoljna posvećenost u raščišćavanju etiopatogeneze kod MINOCA populacije: Smernice propuštaju priliku da preciziraju definiciju IMPS kod pacijenata sa MINOCA-om, gde je miokarditis jedan od najčešćih konačnih nalaza.

Razlike u odnosu na američke preporuke (ACC/AHA) [1,3]: Evropski pristup je konzervativniji po pitanju genetskog testiranja (samo selektovani pacijenti naspram svih), ranije primene IL-1 inhibitora kod perikarditisa (kasnije u odnosu na ACC) i ne uključuje mikroaksijalne pumpe (npr. Impella) u algoritme mehaničke potpore, za razliku od američkih smernica.

Table 8. Comparison of ESC 2025 and ACC/AHA 2024 guidelines

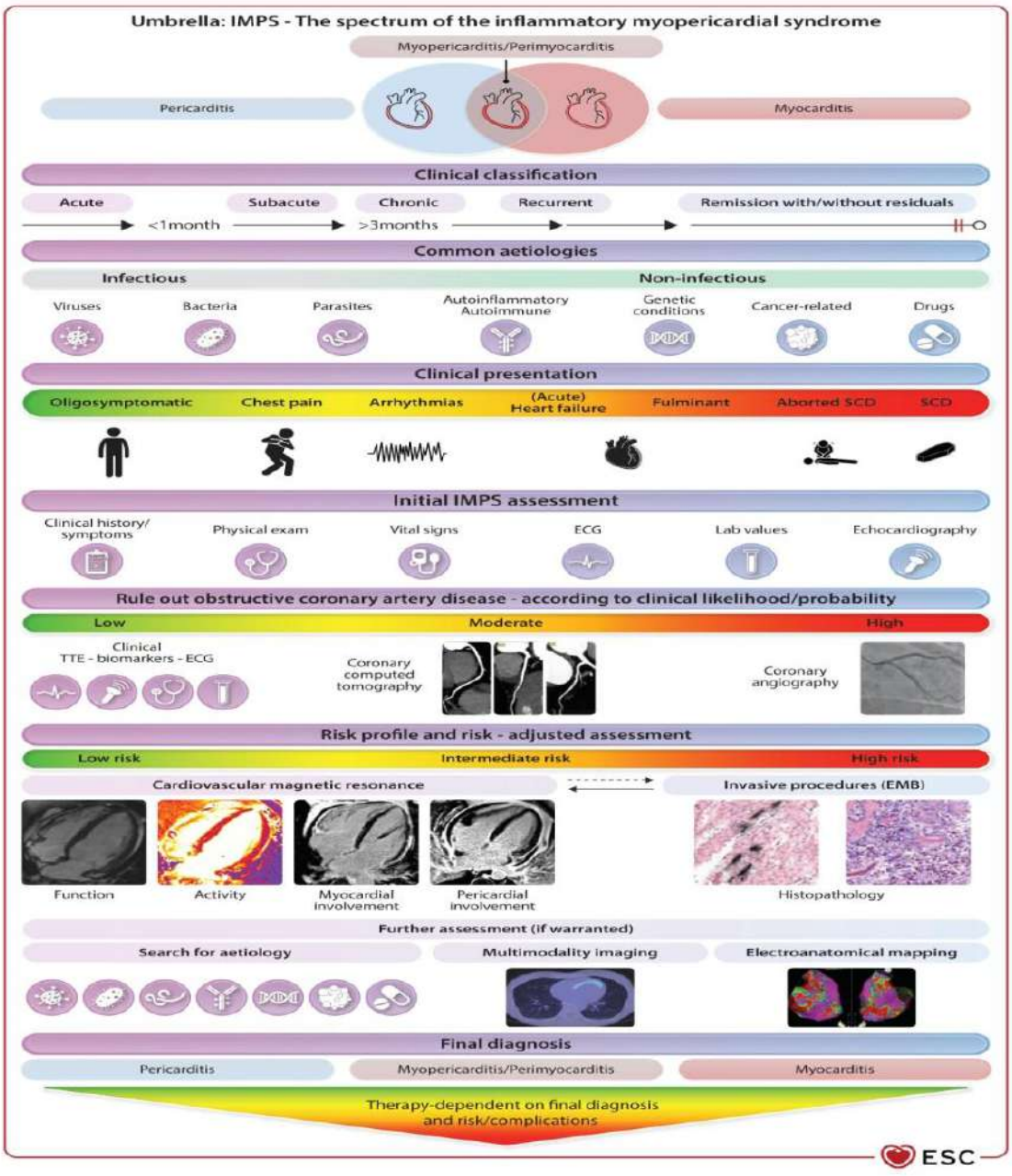
Topic	ESC 2025	ACC/AHA consensus
Genetic testing	Only in selected patients	Recommended in all patients with myocarditis
Beta-blockers	Recommended for ≥6 months in all patients	No universal recommendation
IL-1 inhibitors	More conservative approach (after corticosteroids)	Earlier use after failure of NSAIDs + colchicine
Mechanical support	Emphasis on VA-ECMO	More detailed inclusion of microaxial pumps (e.g., Impella)

The ESC 2025 guidelines introduce the IMPS concept, emphasize the role of CMR, and expand indications for EMB [1,10,17]. In the context of local clinical practice, the studies by the author of this literature review, Dr Dušan Bastać, significantly help bridge gaps in the practical application of diagnostic methods for inflammatory myopericardial syndrome in Serbia [12–14].

His research on diastolic stress testing and echocardiographic markers indicates that diastolic dysfunction and elevated left ventricular filling pressures may persist even after recovery of systolic function (LVEF). This finding is consistent with the concept of inflammatory cardiomyopathy and the HFpEF phenotype (heart failure with preserved ejection fraction) in these patients.

These observations highlight the need for careful, multimodal follow-up even in patients with normalized ejection fraction..

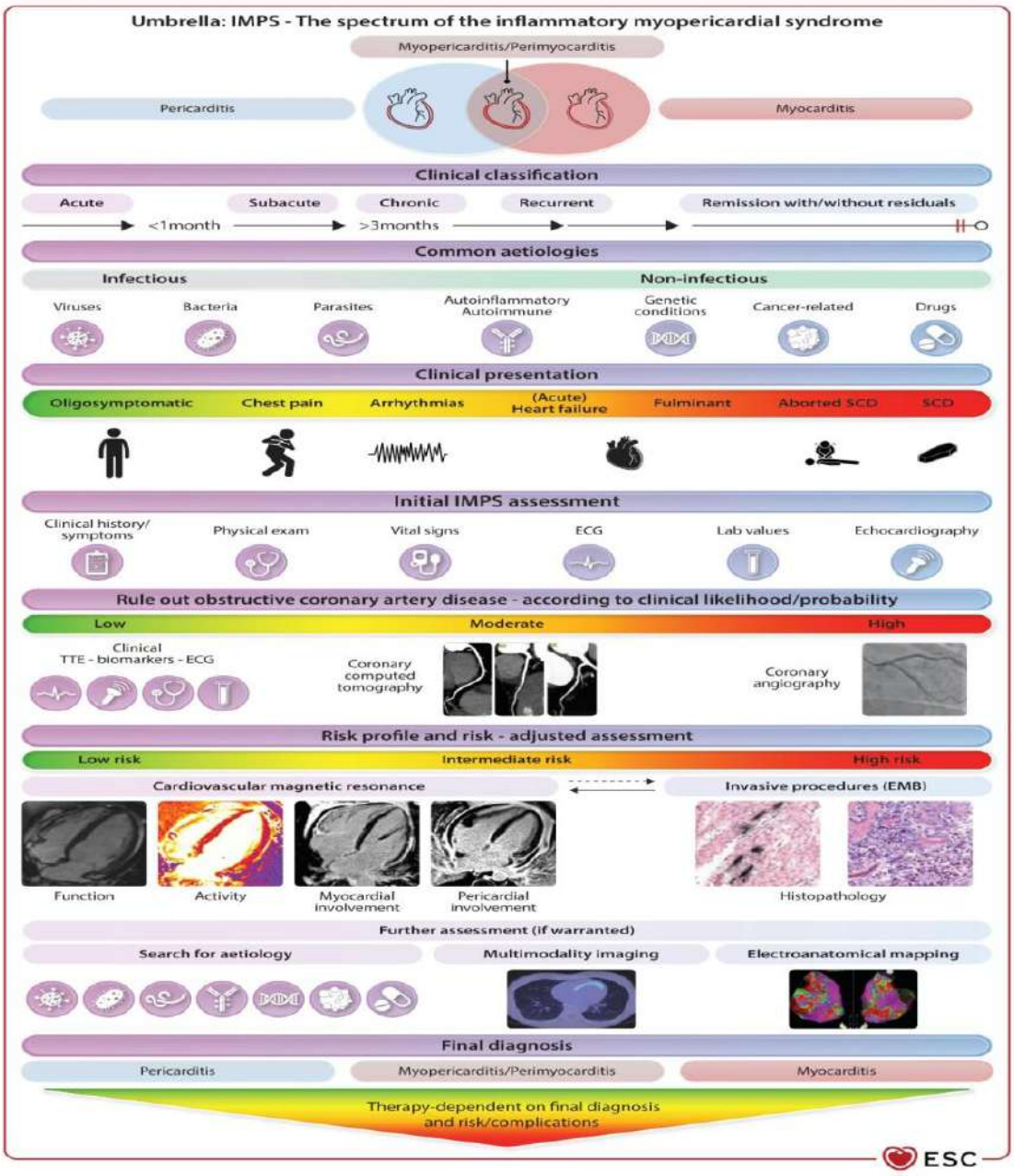
Slika 5. CENTRALNA ILUSTRACIJA ESC SMERNICA O MIOKARDITISU I PERIKARDITISU.
preuzeto sa Eur Heart J, Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192



ZAKLJUČAK

ESC preporuke i smernice iz 2025. godine predstavljaju najkompletniji do sada dokument koji spaja miokarditis i perikarditis u jedinstven koncept – inflamatorni mioperikardijalni sindrom (IMPS),što je prikazano na grafiku (Slika 5): Centralna ilustracija ESC smernica o miokarditisu i perikarditisu. Naglasak je na multimodalnom pristupu dijagnostici, sa centralnom ulogom kardiomagnetne rezonance CMR-a, racionalnoj primeni endomiokardne biopsije (EMB), selektivnoj upotrebi imunosupresije i personalizaciji terapije. Uprkos značajnom napretku, veliki broj preporuka i dalje se zasniva na ekspertskom konsenzusu, što naglašava potrebu za daljim visokokvalitetnim istraživanjima, naročito u oblastima kao što su

Figure 5. Central illustration of the ESC guidelines on myocarditis and pericarditis. Adapted from: *Eur Heart J*, Volume 46, Issue 40, 21 October 2025, Pages 3952–4041, https://doi.org/10.1093/eurheartj/ehaf192



CONCLUSION

The ESC 2025 recommendations and guidelines represent the most comprehensive document to date, unifying myocarditis and pericarditis into a single concept—inflammatory myopericardial syndrome (IMPS), as illustrated in the figure (Figure 5: Central illustration of ESC guidelines on myocarditis and pericarditis).

The emphasis is on a multimodal diagnostic approach, with a central role of cardiac magnetic resonance imaging (CMR), rational use of endomyocardial biopsy (EMB), selective application of immunosuppressive therapy, and overall personalization of treatment strategies.

Despite significant progress, many recommendations are still based on expert consensus, highlighting the need for further

optimalna upotreba beta-blokatora, novi antivirusni lekovi , genetsko testiranje i biološka terapija. Integracija domaćih kliničkih iskustava pokazuje da se smernice dobro uklapaju u postojeću praksu, ali i da otvaraju nova pitanja i mogućnosti za dalja istraživanja u cilju poboljšanja ishoda pacijenata sa inflamatornim bolestima srca

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high-quality research, particularly in areas such as optimal use of beta-blockers, novel antiviral therapies, genetic testing, and biological treatments.

The integration of domestic clinical experience shows that the guidelines are largely compatible with current practice, but also open new questions and research opportunities aimed at improving outcomes in patients with inflammatory heart diseases.

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