2025 ESC Guidelines for the management of myocarditis and pericarditis

Official slide set

2025 ESC Guidelines for the management of myocarditis and pericarditis
(European Heart Journal; 2025 – doi: 10.1093/eurheartj/ehaf192)

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The material was adapted from the *‘2025 ESC Guidelines for the management of myocarditis and pericarditis. Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC) and the European Association for Cardio-Thoracic Surgery (EACTS).’ (European Heart Journal*; 2025 - doi: 10.1093/eurheartj/ehaf192.

2025 ESC Guidelines for the management of myocarditis and pericarditis

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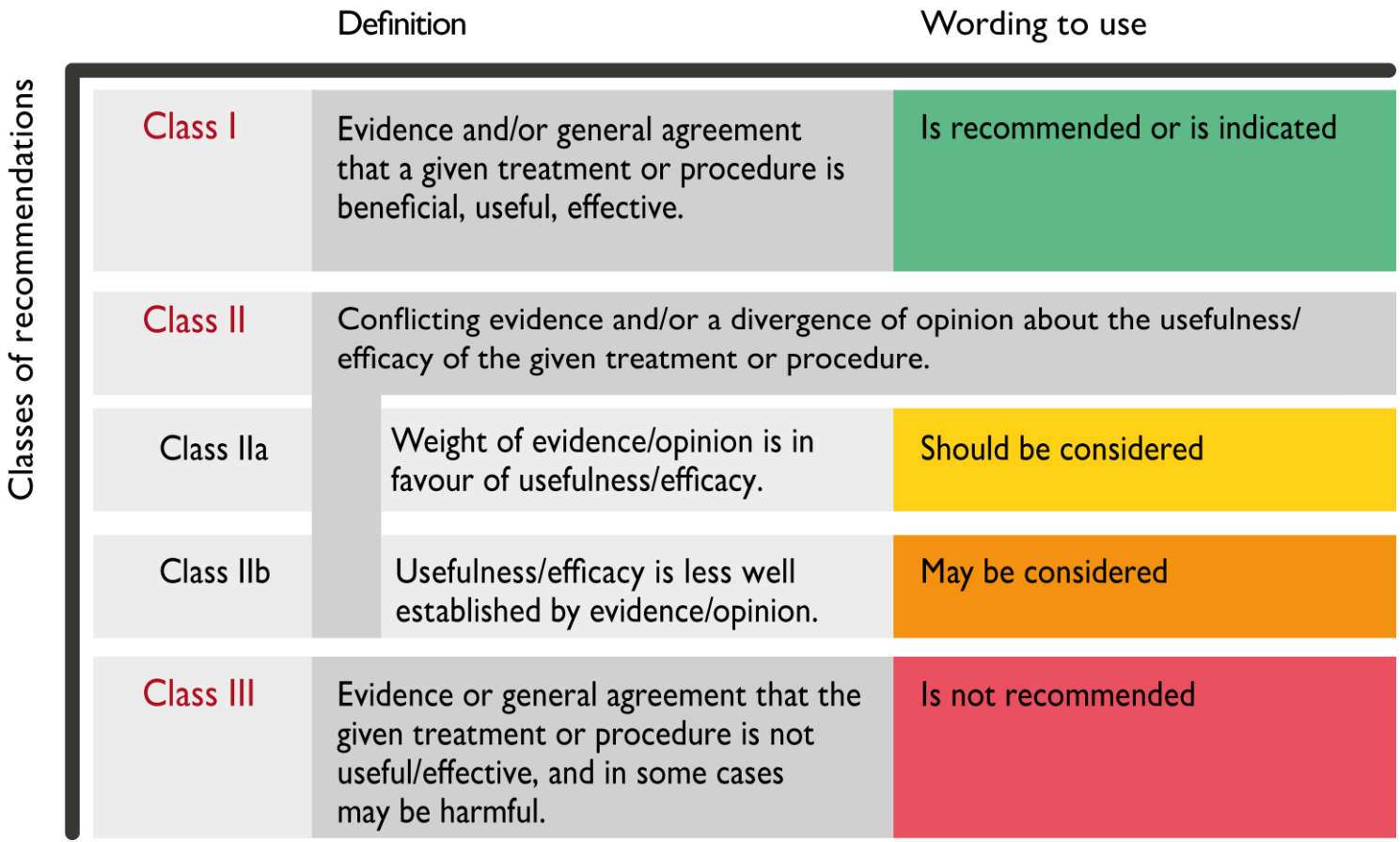
ESC Classes of recommendations



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ESC Levels of evidence

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

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Figure 1

Central illustration of the ESC guidelines on myocarditis and pericarditis

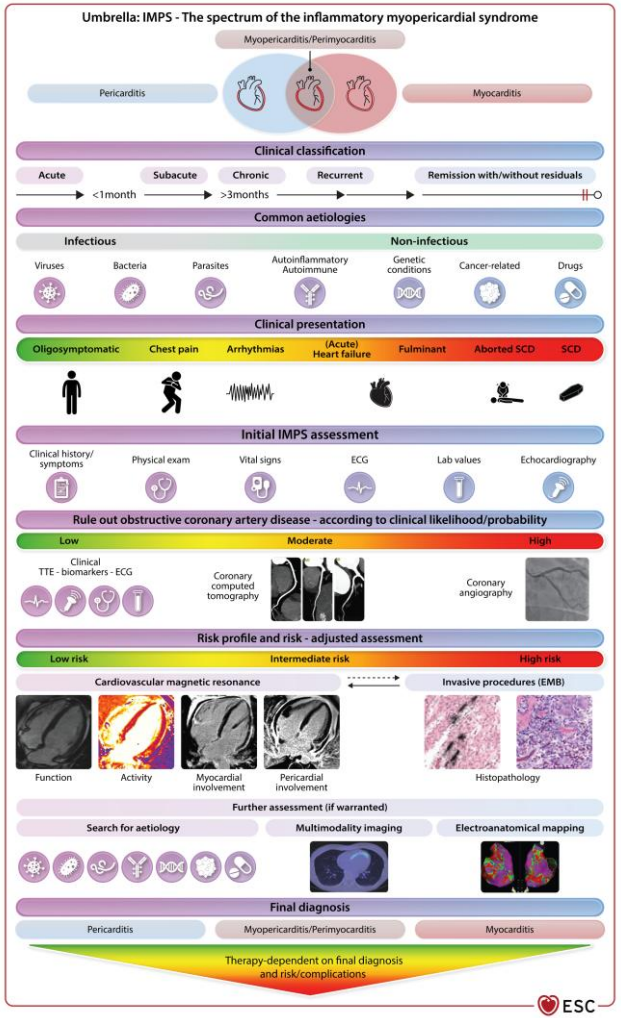

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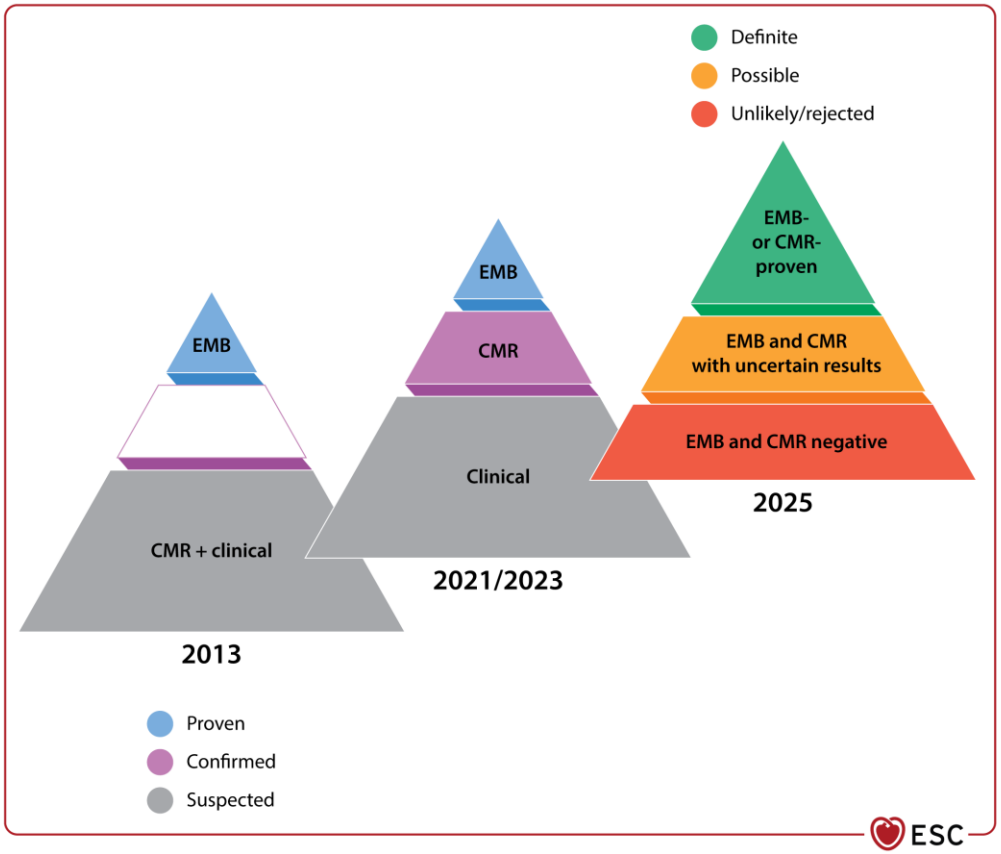
Figure 2

Paradigm change in the clinical diagnosis of myocarditis



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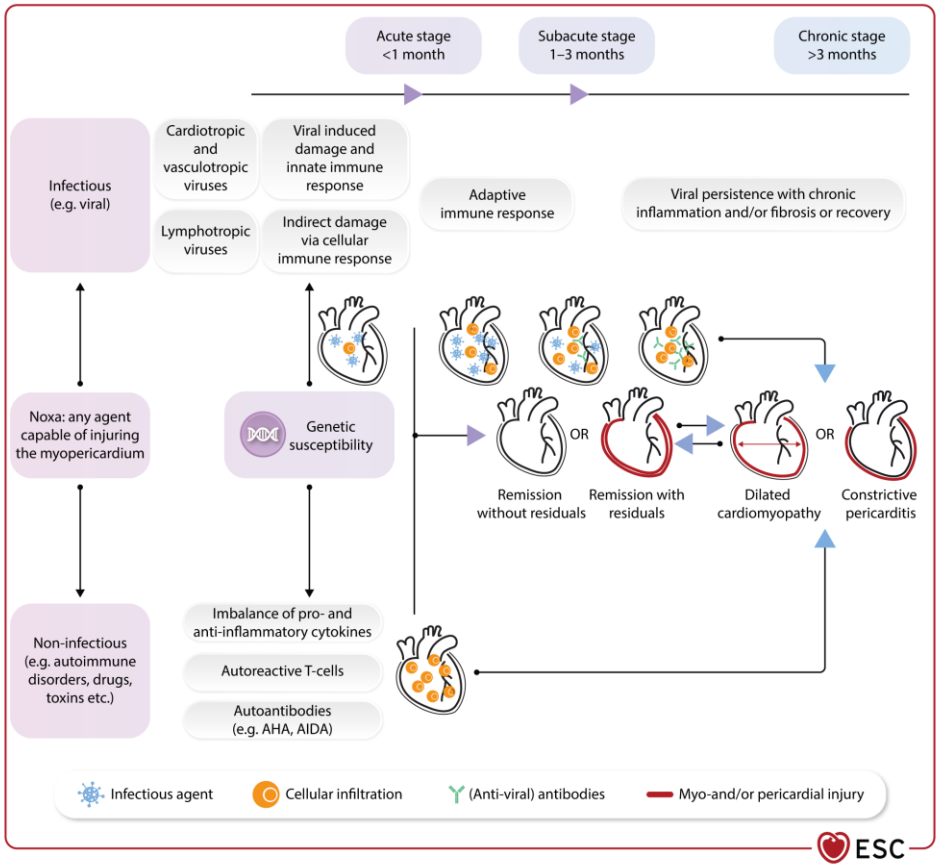
Terminology and stages

Terminology	Definition
IMPS	Umbrella term for inflammatory myocardial and pericardial syndromes
Myopericarditis	Predominant pericarditis
Perimyocarditis	Predominant myocarditis
Acute myocarditis	Duration of symptoms ≤4 weeks Fulminant if: - Acute onset and haemodynamic unstable patients requiring inotropes or mechanical circulatory support
Complicated myocarditis	AM and ≥1 of the following: - LVEF <50% on echocardiogram - Sustained ventricular arrhythmias - Advanced heart block - Heart failure - Cardiogenic shock
Acute pericarditis	Duration of symptoms ≤4 weeks
Subacute/ongoing myocarditis	Duration of symptoms >4 weeks to ≤3 months
Subacute/incessant pericarditis	Duration of symptoms >4 weeks to ≤3 months
Chronic myocarditis/pericarditis	Duration of symptoms >3 months
Inflammatory cardiomyopathy	Chronic myocarditis in association with cardiac dysfunction and ventricular remodelling with clinical phenotype of hypokinetic, either dilated or non-dilated cardiomyopathy with/without arrhythmogenic substrate
Recurrent myocarditis/pericarditis	New symptoms or disease activity after clinical remission
Remission without residuals	Regression/absence of symptoms, normalization of ECG, biomarkers, imaging abnormalities (echocardiography and CMR)
Remission with residuals	Regression/absence of symptoms, persistence of abnormalities on ECG, biomarkers and/or imaging (functional and/or structural abnormalities in echocardiography or CMR)

Figure 3

Stages of inflammatory myopericardial syndrome



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Diagnostic criteria and classification for inflammatory myopericardial syndrome

IMPS		
If diagnostic criteria for myocarditis and/or pericarditis are fulfilled		
	Myocarditis	**Pericarditis**
Definite	Clinical presentation and CMR- or EMB-proven	Clinical presentation with >1 additional criterion
Possible	Clinical presentation with at least 1 additional criterion CMR- or EMB-uncertain or not available	Clinical presentation with 1 additional criterion
Unlikely/ Rejected	Only clinical presentation without additional criteria	Only clinical presentation without additional criteria
Additional criteria beyond clinical presentations		
	Myocarditis	**Pericarditis**
Clinical	Non-specific findings	Pericardial rubs
ECG	ST-T changes	PR depression, widespread, ST-segment elevation
Biomarkers	Troponin elevation	CRP elevation
Imaging	Abnormal strain, wall motion, reduced EF Myocardial oedema and/or LGE (CMR findings)	New or worsening pericardial effusion Pericardial oedema and/or LGE (CMR findings)

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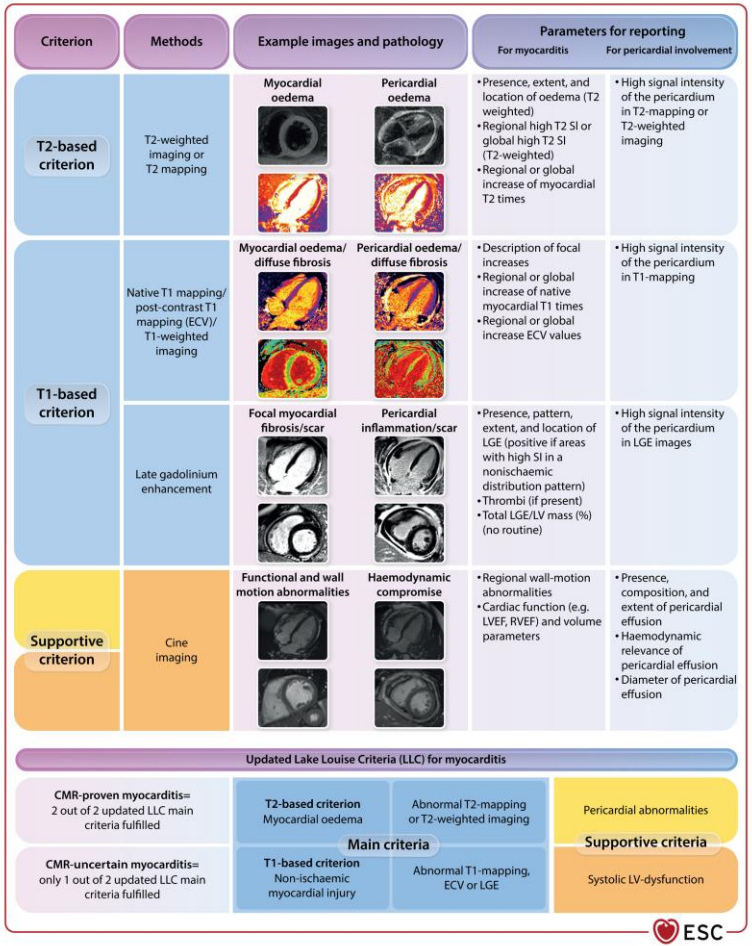
Figure 4

Diagnostic criteria by cardiovascular magnetic resonance based on the updated Lake Louise criteria



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Histopathological criteria for myocarditis

Term	Predominant inflammatory cells	Myocyte necrosis	Infections PCR positive (viruses, etc.)
Active lymphocytic myocarditis	$CD3^+$ T lymphocytes >7/mm^2, $CD68^+$ macrophages	yes	yes/no
Persistent lymphocytic myocarditis	$CD3^+$ T lymphocytes >7/mm^2, $CD68^+$ macrophages	yes	yes/no
Resolved lymphocytic myocarditis	-	no	yes/no
Eosinophilic myocarditis (acute stage)	Eosinophils, $CD3^+$ T lymphocytes, $CD68^+$ macrophages	yes	yes/no
Giant-cell myocarditis (acute stage)	Eosinophils, $CD68^+$ giant cells, $CD3^+$ T lymphocytes, $CD68^+$ macrophages	yes	no
Sarcoidosis	$CD68^+$ giant cells, granuloma, $CD3^+$ T lymphocytes, $CD68^+$ macrophages	yes/no	no

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Red flags for the clinical diagnosis of myocarditis and pericarditis

Myocarditis	Pericarditis
Recent or concomitant flu-like syndrome or gastroenteritis	Recent or concomitant flu-like syndrome or gastroenteritis
Infarct-like chest pain	Pleuritic/infarct-like chest pain
Palpitations	Right HF symptoms and signs of constriction
HF symptoms	Fever
ECG changes	Pericardial rubs
Ventricular arrhythmias (isolated, complex)	CRP elevation
Syncope	Pericardial effusion
Haemodynamic instability	Pleural effusion
Elevated markers of myocardial lesion (hs-Tn, CK-MB elevation)	Polyserositis
Elevated markers of HF (NT-proBNP)	CMR imaging with pericardial oedema and/or LGE
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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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 -Ventricular fibrillation/sustained ventricular tachycardia -High-level AV block **Imaging criteria:** -Newly reduced LVEF (<40%) -Extensive LGE on CMR	-New/progressive dyspnoea -Non-sustained ventricular arrhythmias -Persistent release or relapsing troponin **Imaging criteria:** -Newly mildly reduced LVEF (41%–49%) and/or WMA -Preserved LVEF (≥50%) and LGE ≥2 segments on CMR	-Stable symptoms or oligosymptomatic **Imaging criteria:** -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 **Imaging criteria:** -Large PEff (>20 mm end-diastole) -Cardiac tamponade -Extensive pericardial LGE on CMR	-Signs and symptoms of right heart failure **Imaging criteria:** -Moderate–large PEff (10–20 mm end-diastole) -Constrictive physiology regardless of the size of the effusion	-Response to adequate therapy within 1–2 weeks **Imaging criteria:** -Absence or mild PEff -Absence of pericardial LGE on CMR

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Figure 5

Diagnostic algorithm and triage for inpatient myocarditis

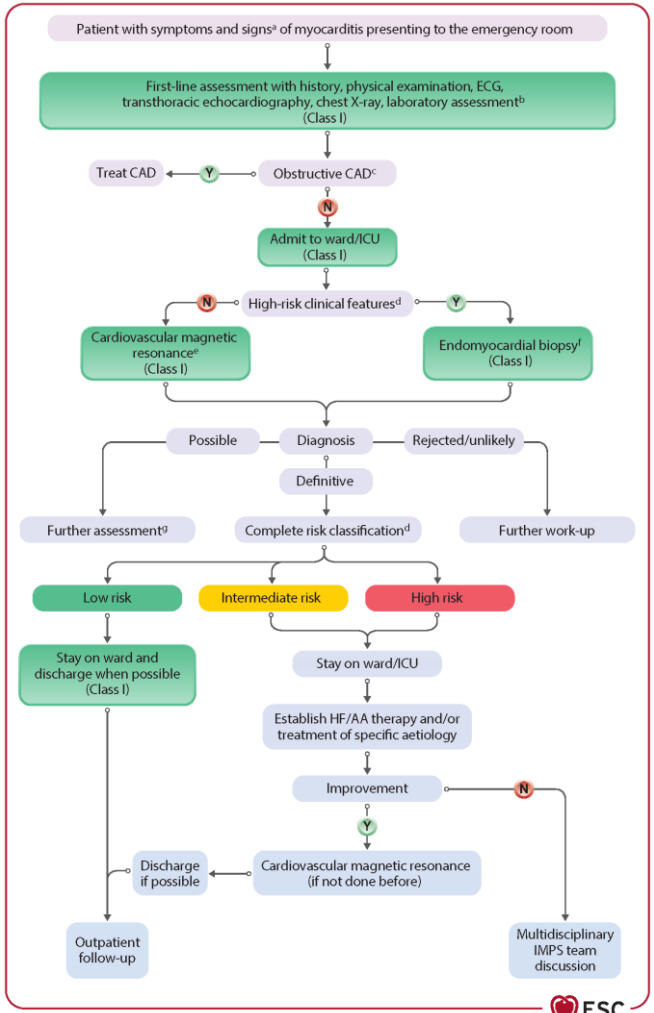

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Figure 6

Diagnostic algorithm and triage for outpatient myocarditis

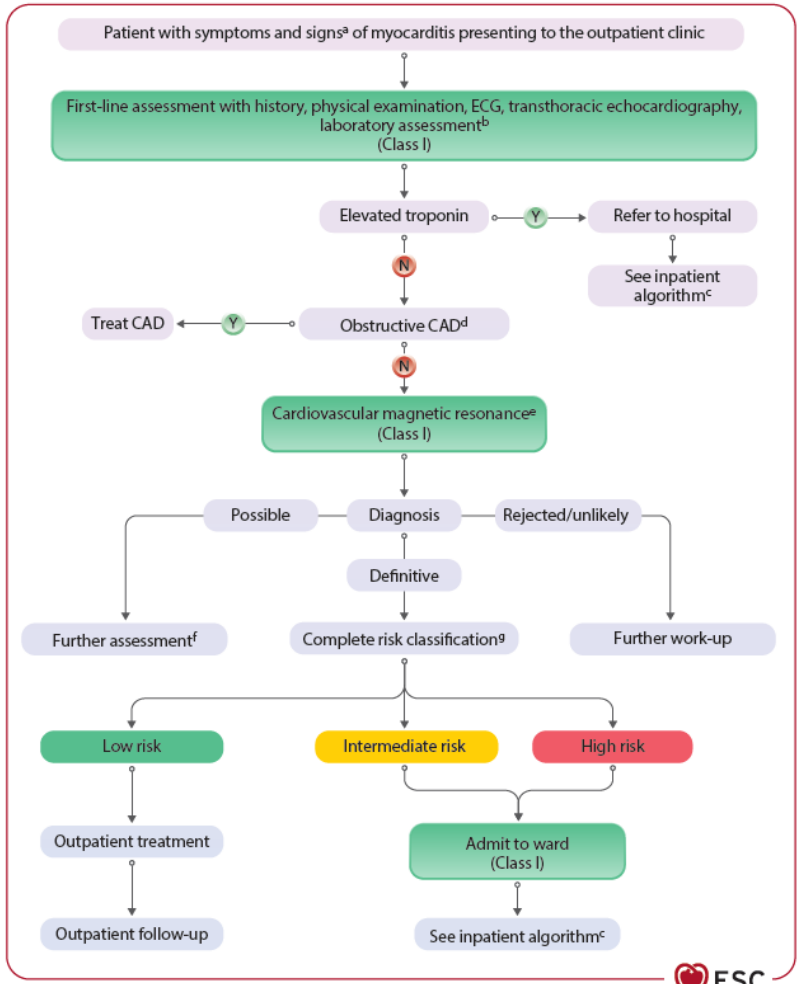

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Figure 7

Diagnostic algorithm and triage for pericarditis

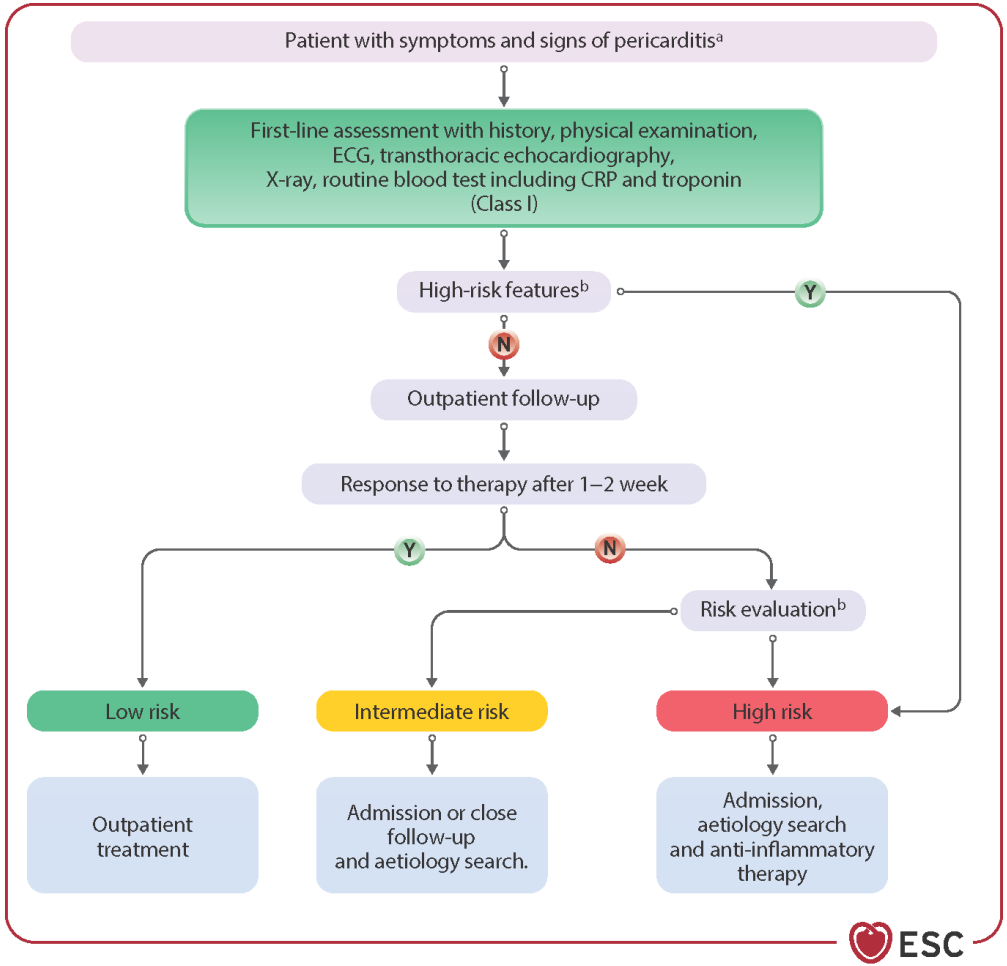

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Figure 8

Spectrum of myocarditis presentations and outcomes

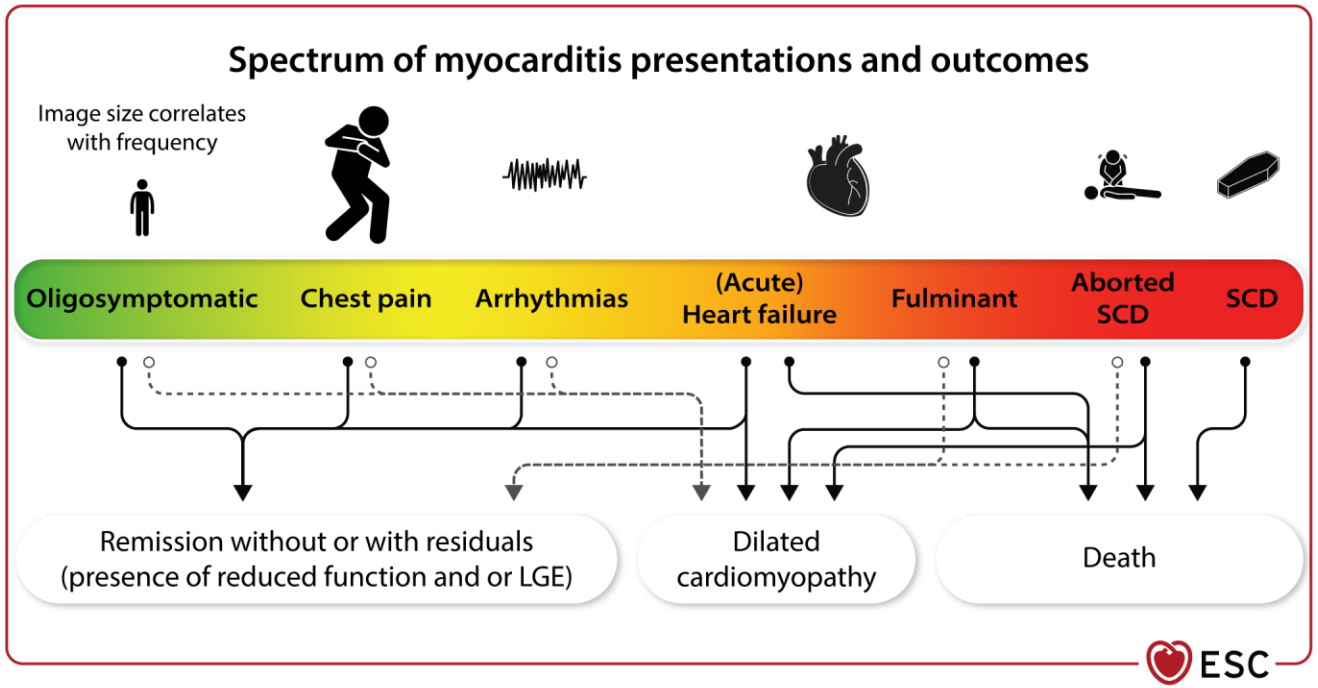

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Figure 9

Diagnostic algorithm for acute chest pain presentation

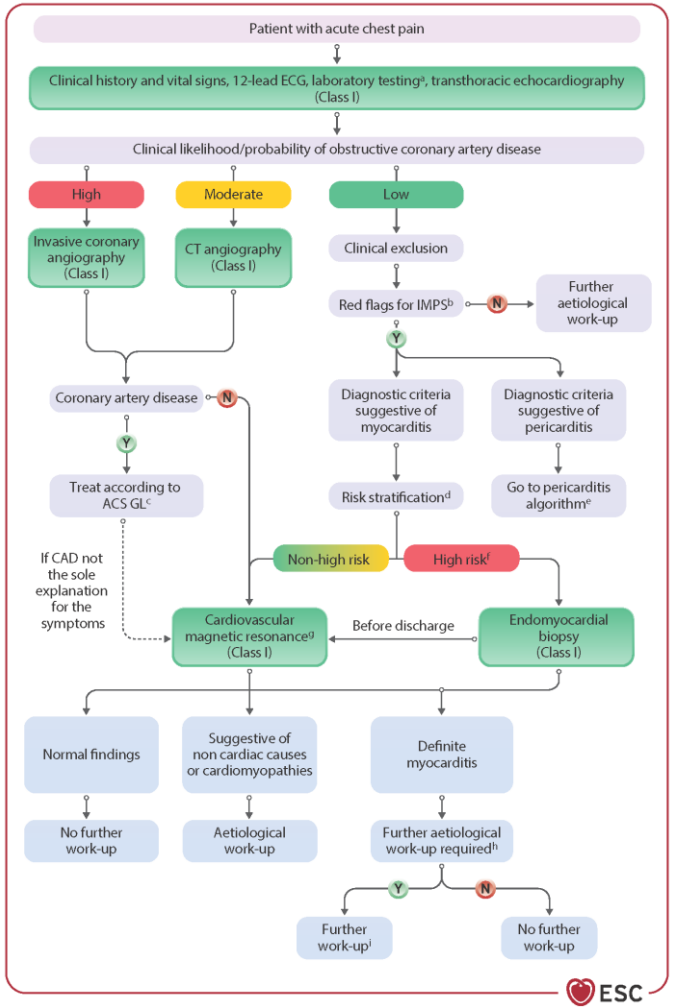

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Figure 10

Diagnostic algorithm for acute heart failure presentation

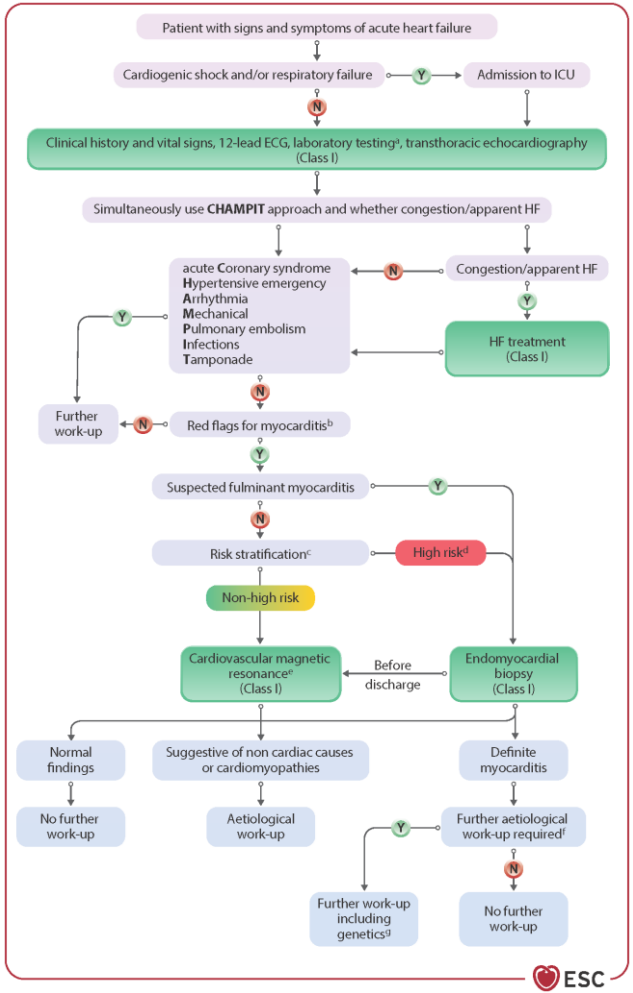

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Figure 11

Diagnostic algorithm for arrhythmia presentation

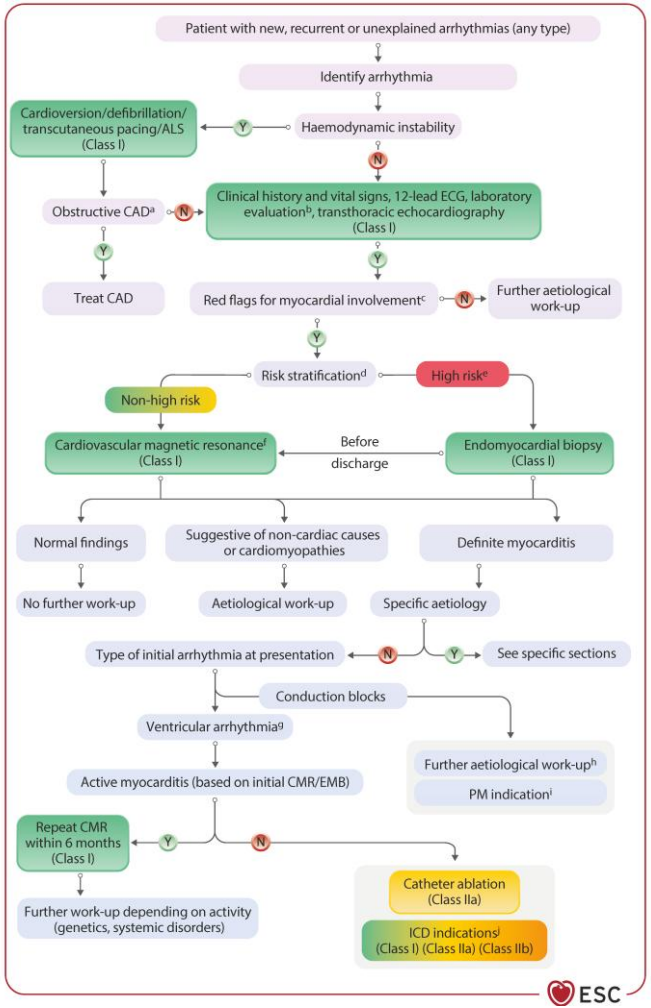

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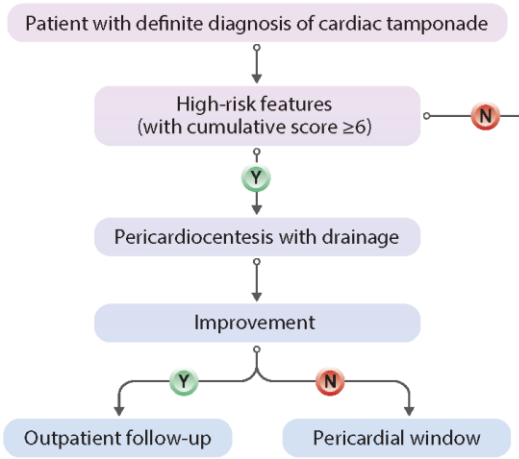
Figure 12

Management of cardiac tamponade



Criteria for triage for patients with pericardial effusion at risk for progression to cardiac tamponade

Aetiology		Clinical presentation		Imaging	
Malignant disease	2	Dyspnoea/tachypnoea	1	Cardiomegaly on chest x-ray	1
Tuberculosis	2	Orthopnoea	3	Electrical alternans on ECG	0.5
Recent radiotherapy	1	Hypotension (CBP <95 mmHg)	0.5	Microvoltage on ECG	1
Recent viral infection	1	Progressive sinus tachycardia	1	Circumferential large PEff	3
Recurrent PEff	1	Oliguria	1	Moderate PEff	1
Chronic terminal renal failure	1	Pulsus paradoxus (>10 mmHg)	2	Small PEff	-1
Immunosuppression	1	Pericardial chest pain	0.5	Right atrial collapse	1
Dysthyroidism	-1	Pericardial friction rub	0.5	IVC dilated not collapsible	1.5
Systemic autoimmune disease	-1	Rapid worsening of symptoms	2	Right ventricular collapse	1.5
		Slow disease evolution	-1	Left atrial collapse	2
				Mitral/tricuspid respiratory flow variations	1
				Swinging heart	1

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Causes of cardiac tamponade

Common causes (in order of relative frequency)
1. Neoplasm/malignancy
2. Iatrogenic/trauma
3. Pericarditis
4. Tuberculosis (most common in developing countries)
Less common causes (in order of relative frequency)
1. Collagen vascular diseases (systemic lupus erythematosus, rheumatoid arthritis, scleroderma)
2. Pericardial injury syndrome
3. Acute myocardial infarction
4. Aortic dissection
5. Uraemia
6. Bacterial infection
7. Pneumopericardium

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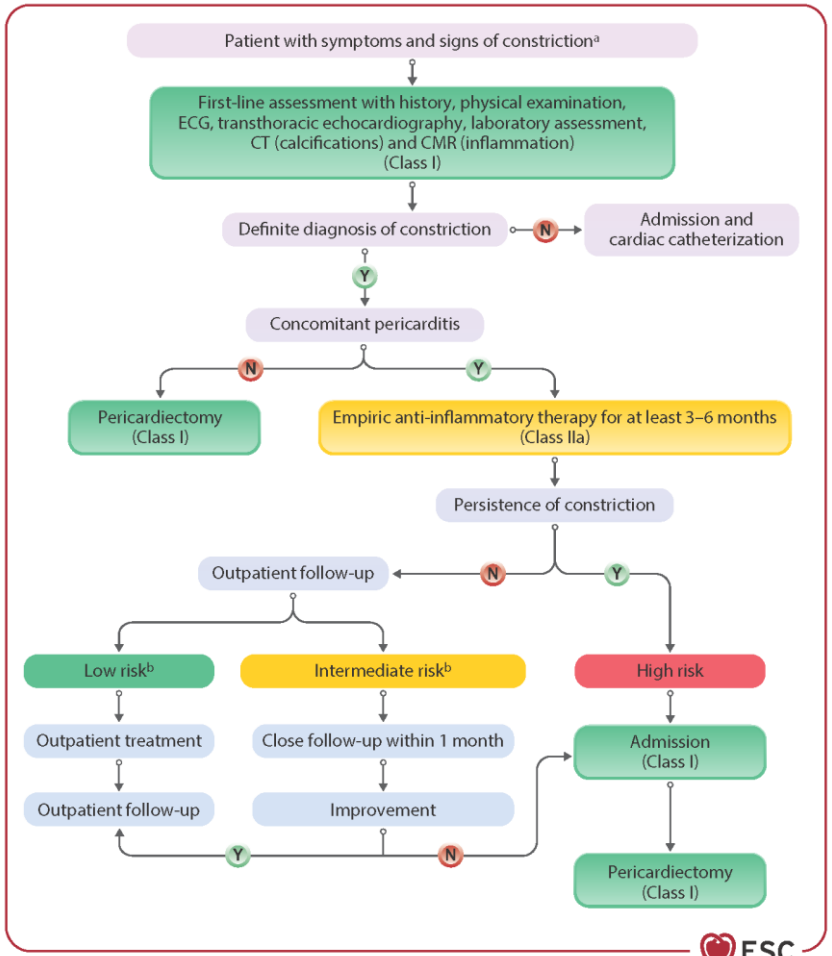
Figure 13

Management of constriction



Basic and advanced level assessment (1)

Basic assessment:
History: potential causes and triggers (viral infection of upper respiratory or gastrointestinal tract, toxins, drug use, medications), recurrent symptoms, family history of IMPS/cardiomyopathy/SCD, and systemic inflammatory/autoimmune diseases
Physical examination: assess clinical stability, symptoms (chest pain, HF symptoms, palpitations, syncope), malaise, general weakness and fatigue, pericardial friction rub, clinical symptoms/signs of CTP
ECG: PR-segment depression, ST/T-wave changes, AVB, and ventricular arrhythmias
Chest X-ray
Basic laboratory data: Markers of myocardial lesion (e.g. hs-TnT/TnI) Markers of systemic inflammation (e.g. CRP, ESR, WBC count) Markers of heart failure (e.g. NT-proBNP) Complete blood count (including eosinophilic count) Renal function and electrolytes (e.g. sodium, potassium, creatinine) Thyroid function (e.g. TSH) Hepatic function and additional testing (e.g. lactate dehydrogenase, aspartate aminotransferase, alanine aminotransferase)
Echocardiography including strain imaging

Basic and advanced level assessment (2)

Advanced assessment usually after admission:
Coronary anatomy evaluation (if needed for differential diagnosis by invasive coronary angiography or coronary CT depending on the clinical likelihood of ACS)
CMR to assess signs of myocardial and pericardial inflammation and/or fibrosis
Arrhythmia screening depending on risk stratification (e.g. Holter-ECG)
Additional laboratory parameters guided by clinical suspicion (e.g. if therapeutic consequences are expected)
Dedicated genetic testing if indicated
CT to assess concomitant pleuropulmonary diseases
Specific Myocarditis: EMB in high-risk cases and in intermediate-risk cases on a case-by-case decision to detect specific histology and some aetiologies if needed
Specific Pericarditis: diagnostic pericardiocentesis when indicated

Recommendations for clinical evaluation of myocarditis and pericarditis (1)

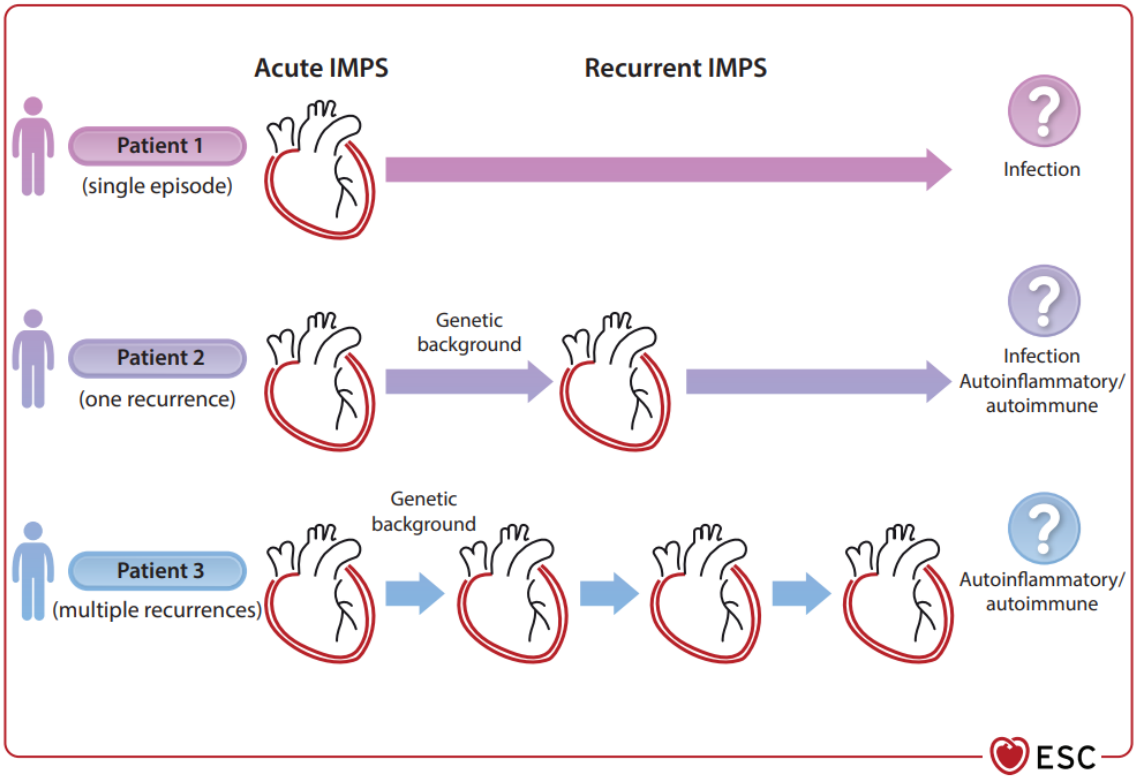
Recommendations	Class	Level
Complete clinical evaluation, including history, physical examination, chest X-ray, biomarkers, ECG, and echocardiography is recommended in all patients with a suspicion of myocarditis and/or pericarditis for the initial diagnostic assessment.	I	C
CMR is recommended in patients with the clinical suspicion of myocarditis (using updated LL criteria) and/or pericarditis for the non-invasive diagnosis of inflammatory reaction.	I	B
Hospital admission is recommended for patients with high-risk pericarditis for monitoring and treatment.	I	B
Hospital admission is recommended for patients with moderate- to high-risk myocarditis for monitoring and treatment.	I	C
EMB is recommended in patients with high-risk myocarditis 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.	I	C

Recommendations for clinical evaluation of myocarditis and pericarditis (2)

Recommendations	Class	Level
Invasive coronary angiography or coronary CT, depending on clinical likelihood, is recommended in patients with IMPS if an acute coronary syndrome is suspected to rule out obstructive coronary artery disease.	I	C
Hospital admission should be considered for patients with low-risk myocarditis for monitoring and treatment.	IIa	C
Pericardial or epicardial biopsy may be considered in relapsing pericardial effusion as part of the diagnostic work-up when the diagnosis cannot be reached with multimodality imaging and laboratory examinations.	IIb	C
Routine serology is not recommended in patients with myocarditis and/or pericarditis for the evaluation of viral aetiology except for hepatitis C, HIV, and Lyme disease.	III	C

Figure 14

The different courses of inflammatory myopericardial syndromes and the interplay between genetic background inflammation and autoimmunity beyond the initial infectious trigger



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Recommendations for genetic testing

Recommendations	Class	Level
It is recommended to obtain family history including pedigrees in cases of recurrent IMPS to provide clues to the underlying aetiology, determine inheritance pattern, and identify relatives at risk.	I	C
Genetic testing should be considered in patients with definite myocarditis/pericarditis in cases of: -family history of IMPS, inherited or suspected cardiomyopathy -severe ventricular arrhythmia -significant left/right LGE (e.g. ring-like pattern or septal LGE) or persistent LVEF systolic dysfunction -recurrent myocarditis or persistent troponin elevation -recurrent pericarditis with an inflammatory phenotype, refractory to conventional treatment, with the aim to detect an underlying genetic cause.	IIa	B

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Classification of pericardial effusion

Onset	Acute (≤4 weeks) Subacute (>4 weeks to ≤3 months) Chronic (>3 months)
Size	Mild <10 mm Moderate 10–20 mm Large >20 mm
Distribution	Circumferential/Loculated
Composition	Transudate/Exudate

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Recommendations for the use of cardiovascular magnetic resonance imaging

Recommendations	Class	Level
Myocarditis		
CMR is recommended in patients with suspected myocarditis to reach a clinical diagnosis and to determine the cause of acute myocardial injury, including assessment of oedema, ischaemia, and necrosis/fibrosis/scarring.	I	B
CMR is recommended for follow-up at least within the first 6 months in patients with myocarditis to identify a healed or ongoing process, for risk stratification and personalized therapy, and to enable a return to exercise.	I	C
Pericarditis		
CMR is recommended in patients with suspected pericarditis when a diagnosis cannot be made using clinical criteria to assess evidence of pericardial thickening, oedema, LGE, and to assess the persistence of disease during follow-up in selected cases.	I	B

Recommendations for computed tomography

Recommendations	Class	Level
CT is recommended to evaluate pericardial thickness, calcifications, masses, and loculated pericardial effusions, as well as concomitant pleuropulmonary diseases and chest abnormalities.	I	C

Recommendations for nuclear medicine

Recommendations	Class	Level
Carb-free ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT should be considered for the diagnostic work-up in patients with suspected myocarditis and/or pericarditis in whom echocardiography and CMR are inconclusive for the clinical diagnosis.	IIa	C

Parameters for reporting by endomyocardial biopsy

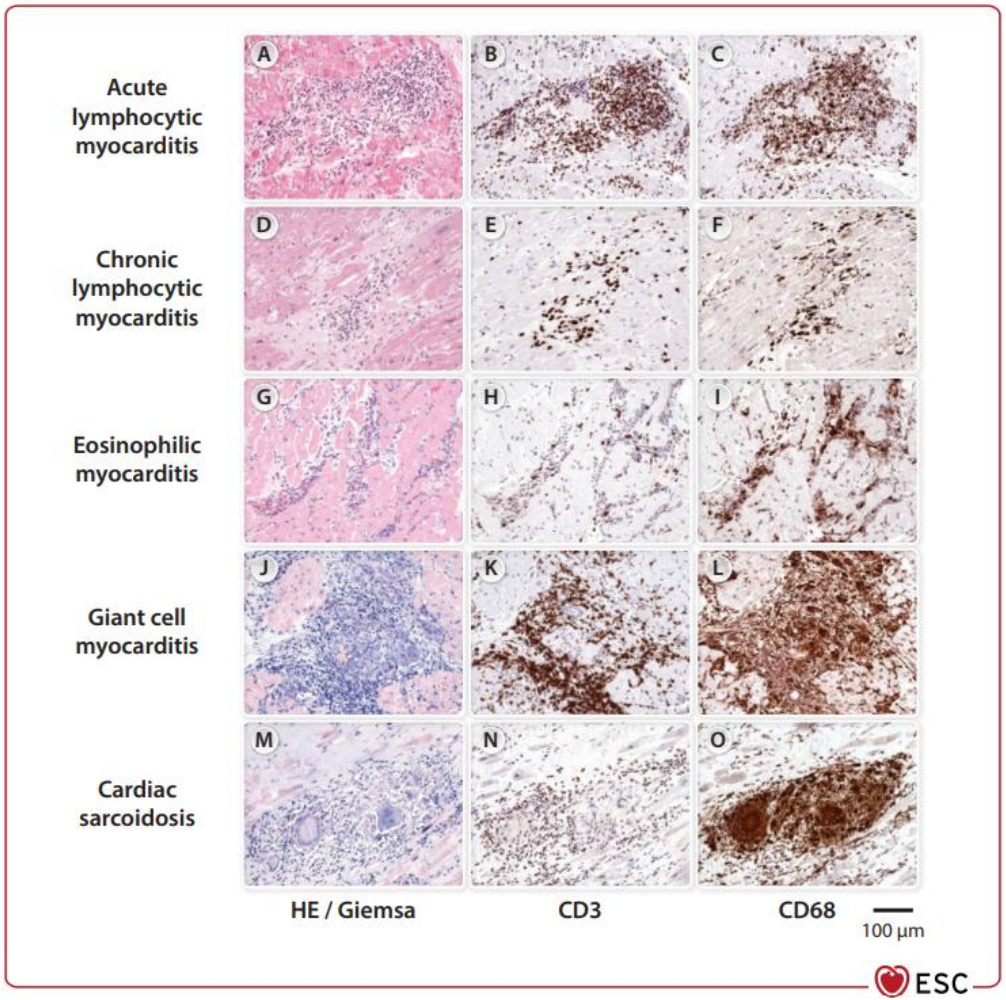
Criteria	Parameters for reporting
Histology (paraffin-embedded EMB, at least 3 EMB)	Presence and extent of cardiomyocyte necrosis, inflammation, fibrosis
Immunohistology (paraffin-embedded EMB, at least 3 myocardial samples)	Presence, extent, localization, and typing of immune cells in the myocardium: $CD3^+$ T lymphocytes, $CD68^+$ macrophages (≥14 leucocytes/mm^2 with T lymphocytes ≥7 cells/mm), HLA-DR expression in immune cells and endothelial cells
Molecular pathology [infections: RNAlater, snap frozen tissue (1–2 EMB), paraffin-embedded EMB]	Presence, typing, and quantification of DNA/RNA from infectious agents by q(RT)-PCR Viruses: mainly enteroviruses, parvovirus B19, human herpesvirus 6, Epstein–Barr virus; *Borrelia* spp, *Trypanosoma cruzi*
Blood	q(RT)-PCR for detection of systemic infections
Molecular pathology (genetics: RNAlater, frozen tissue, paraffin-embedded EMB, blood)	NGS for detection of pathogenic variants in cardiac genes, traditionally associated with cardiomyopathies (especially desmosomal and sarcomeric/cytoskeletal genes)

Recommendations for endomyocardial biopsy

Recommendations	Class	Level
EMB is recommended in patients with high-risk myocarditis, 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.	I	C

Figure 15

Histopathological findings in myocarditis



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Recommendations for autopsy

Recommendations	Class	Level
Comprehensive autopsy is recommended in all patients <50 years of age with SCD to evaluate the presence of acute myocarditis as a cause and to detect potential underlying inherited cardiac diseases.	I	B
Retaining samples suitable for DNA extraction and consulting a cardiac pathologist is recommended in cases of SCD, when an inherited cause is suspected, or the cause of death remains unexplained.	I	B

Recommendations for electro-anatomical mapping

Recommendations	Class	Level
Electro-anatomical mapping should be considered in cases of suspected myocarditis (especially cardiac sarcoidosis) to guide endomyocardial biopsy.	IIa	C

Therapy for specific forms of myocarditis (1)

Lymphocytic myocarditis (virus-negative)	
1st line therapy	Non-severe: prednisone 1 mg/kg/day p.o. then tapered Severe: i.v. methylprednisolone 7–14 mg/kg/day for 3 days, then 1 mg/kg/day p.o.
2nd line therapy	Oral corticosteroids + azathioprine[a] or mycophenolate mofetil[b], cyclosporine[c], methotrexate[d]
3rd line therapy	IVIG[e] or plasmapheresis[f]
Eosinophilic myocarditis	
1st line therapy	Same as lymphocytic myocarditis + Treat EM-associated condition if identified
2nd line therapy	Same as lymphocytic myocarditis + Treat EM-associated condition if identified
3rd line therapy	-

[a]Azathioprine (immunosuppressant purine analog): 1–2 mg/kg per day p.o. (typically 100–150 mg daily, in 1–2 divided doses, main target: lymphocytes).

[b]Mycophenolate mofetil (immunosuppressant that inhibits inosine monophosphate dehydrogenase, main target: lymphocytes): 500–1000 mg p.o. b.i.d. (total 1–2 g/day).

[c]Cyclosporine (calcineurin inhibitor that prevents IL-2 transcription in activated T-cells): ~3–5 mg/kg/day p.o. (divided b.i.d.) adjusted to target trough levels ~150–250 ng/mL

[d]Methotreaxate (antimetabolite that inhibits dihydrofolate reductase and other folate-dependent steps, reducing proliferation of active lymphocytes): 15–20 mg/week p.o. or s.c. (low-dose weekly, with folic acid supplementation).

[e]IVIG (immunomodulatory therapy providing pooled IgG antibodies) =standard dose off-label 2 g/kg total dose, typically administered over 1 to 2 days; alternative dosing: 0.4 g/kg/day for 5 consecutive days (less commonly used in myocarditis but sometimes used in autoimmune settings).

[f]Plasmapheresis (therapeutic plasma exchange that filters out and removes circulating autoantibodies, immune complexes, and inflammatory mediators) 3–5 sessions in 5–10 days.

Therapy for specific forms of myocarditis (2)

Giant-cell myocarditis	
1st line therapy	Non-severe: prednisone 1 mg/kg/day p.o. then tapered Severe: i.v. methylprednisolone 7–14 mg/kg/day for 3 days, then 1 mg/kg/day p.o. + immunosuppressive (azathioprine[a] or mycophenolate mofetil[b], cyclosporine[c])
2nd line therapy	Antithymocyte Globulin (ATG)[g] cyclophosphamide[h], rituximab[i]
3rd line therapy	-

[a]Azathioprine (immunosuppressant purine analog): 1–2 mg/kg per day p.o. (typically 100–150 mg daily, in 1–2 divided doses, main target: lymphocytes).
[b]Mycophenolate mofetil (immunosuppressant that inhibits inosine monophosphate dehydrogenase, main target: lymphocytes): 500–1000 mg p.o. b.i.d. (total 1–2 g/day).
[c]Cyclosporine (calcineurin inhibitor that prevents IL-2 transcription in activated T-cells): ~3–5 mg/kg/day p.o. (divided b.i.d.) adjusted to target trough levels ~150–250 ng/mL
[g]Antithymocyte Globulin (ATG; polyclonal anti-T-lymphocyte antibody that causes profound T-cell depletion): ~1 mg/kg i.v., often given daily for 3–5 days.
[h]Cyclophosphamide (cytotoxic alkylating agent that crosslinks DNA in rapidly dividing cells, main target: lymphocytes): 600 mg/m² i.v. bolus on days 1, 15, and 30 (pulse therapy).
[i]Rituximab (monoclonal antibody against CD20 on B cells): 375 mg/m² i.v. weekly ×4 doses (one month).

Therapy for specific forms of myocarditis (3)

Cardiac sarcoidosis	
1st line therapy	Non-severe: prednisone 1 mg/kg/day p.o., tapering from 40–60 mg daily Severe: i.v. methylprednisolone 7–14 mg/kg/day for 3 days, then 1 mg/kg/day p.o.
2nd line therapy	Methotrexate[d](1st choice), or azathioprine[a] mycophenolate mofetil[b], cyclophosphamide[h]
3rd line therapy	Infliximab[j] or adalimumab[k], rituximab[i]

[a]Azathioprine (immunosuppressant purine analog): 1–2 mg/kg per day p.o. (typically 100–150 mg daily, in 1–2 divided doses, main target: lymphocytes).

[b]Mycophenolate mofetil (immunosuppressant that inhibits inosine monophosphate dehydrogenase, main target: lymphocytes): 500–1000 mg p.o. b.i.d. (total 1–2 g/day).

[d]Methotreaxate (antimetabolite that inhibits dihydrofolate reductase and other folate-dependent steps, reducing proliferation of active lymphocytes): 15–20 mg/week p.o. or s.c. (low-dose weekly, with folic acid supplementation).

[h]Cyclophosphamide (cytotoxic alkylating agent that crosslinks DNA in rapidly dividing cells, main target: lymphocytes): 600 mg/m² i.v. bolus on days 1, 15, and 30 (pulse therapy).

[i]Rituximab (monoclonal antibody against CD20 on B cells): 375 mg/m² i.v. weekly ×4 doses (one month).

[j]Infliximab (monoclonal antibody against TNF-α): 5 mg/kg i.v. at weeks 0, 2, 6, then every ~8 weeks (maintenance).

[k]Adalimumab (anti-TNF-α fully human monoclonal antibody) 40 mg SC every week (or every 2 weeks, per clinical response).

Therapy for specific forms of myocarditis (4)

Lyme carditis	
1st line therapy	(a) Oral antibiotics (mild cases): - Doxycycline 100 mg b.i.d. (14–21 days) - Amoxicillin 500 mg t.i.d. (14–21 days) - Cefuroxime axetil 500 mg b.i.d. (14–21 days) (b) i.v. antibiotics (severe cases): - Ceftriaxone 2 g/day (14–21 days)
2nd line therapy	i.v. antibiotics: Cefotaxime (2 g q8h x 14–21 days) or Penicillin G (18–24 MU/day i.v. q4h x 14–21 days)
3rd line therapy	-
Chagas disease	
1st line therapy	Benznidazole 5–7 mg/kg/day in 2 doses for 60 days Nifurtimox 8–10 mg/kg/day in 3 doses for 60–90 days
2nd line therapy	-
3rd line therapy	-

Therapy for specific forms of myocarditis (5)

ICI-induced myocarditis	
1st line therapy	Withdraw ICI, reassess Non-severe: methylprednisolone 500–1000 mg/day x 3 days, then taper with oral prednisone Severe: i.v. methylprednisolone 7–14 mg/kg/day x 3 days, then 1 mg/kg/day
2nd line therapy	If no response in 24–48 h: mycophenolate mofetil[b], ATG[g] abatacept[l], alemtuzumab[m]
3rd line therapy	Infliximab[j] or adalimumab[k], rituximab[i]

[b]Mycophenolate mofetil (immunosuppressant that inhibits inosine monophosphate dehydrogenase, main target: lymphocytes): 500–1000 mg p.o. b.i.d. (total 1–2 g/day).

[g]Antithymocyte Globulin (ATG; polyclonal anti-T-lymphocyte antibody that causes profound T-cell depletion): ~1 mg/kg i.v., often given daily for 3–5 days.

[i]Rituximab (monoclonal antibody against CD20 on B cells): 375 mg/m² i.v. weekly ×4 doses (one month).

[j]Infliximab (monoclonal antibody against TNF-α): 5 mg/kg i.v. at weeks 0, 2, 6, then every ~8 weeks (maintenance).

[k]Adalimumab (anti-TNF-α fully human monoclonal antibody) 40 mg SC every week (or every 2 weeks, per clinical response).

[l]Abatacept (CTLA-4 Ig fusion protein that binds CD80/86 on antigen-presenting cells, blocking the CD28 co-stimulatory signal required for full T-cell activation): 500 mg i.v. every 2 weeks × 5 doses (approximately 10 weeks.

[m]Alemtuzumab (monoclonal antibody against CD52 on lymphocytes): 30 mg i.v. once (alternative: 15 mg i.v. daily for 2 days).

Therapy for specific forms of myocarditis (6)

Main mechanisms of action
- T-cell suppression (e.g., corticosteroids, cyclosporine, abatacept)
- B-cell depletion (rituximab)
- Cytokine inhibition (TNF-α blockers like infliximab, adalimumab)
- DNA synthesis inhibition (azathioprine, mycophenolate, methotrexate)
- Immunoglobulin replacement/modulation (IVIG)
- Plasma filtration (plasmapheresis)

Recommendations for medical therapy in myocarditis (1)

Recommendations	Class	Level
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	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.	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.	IIa	C

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Recommendations for medical therapy in myocarditis (2)

Recommendations	Class	Level
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

Specific initial dosing and duration of therapy for acute and recurrent pericarditis

Therapy	Dosing	Duration	Tapering
Aspirin	750–1000 mg 3 times daily	1–2 weeks	Decrease by 250 mg every 1–2 weeks
Ibuprofen	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	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	Needed (at least 3 to 6 months)
Rilonacept	320 mg once daily followed by 160 mg weekly	>12 months	Unknown

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Tapering of corticosteroids

Prednisone dose	Starting dose 0.20 to 0.50 mg/kg/day	Tapering
Prednisone daily dose	>50 mg	10 mg/day every 1 to 2 weeks
	50–25 mg	5–10 mg/day every 1 to 2 weeks
	25–15 mg	2.5 mg/day every 2 to 4 weeks
	<15 mg	1.25 to 2.5 mg/day every 2 to 6 weeks

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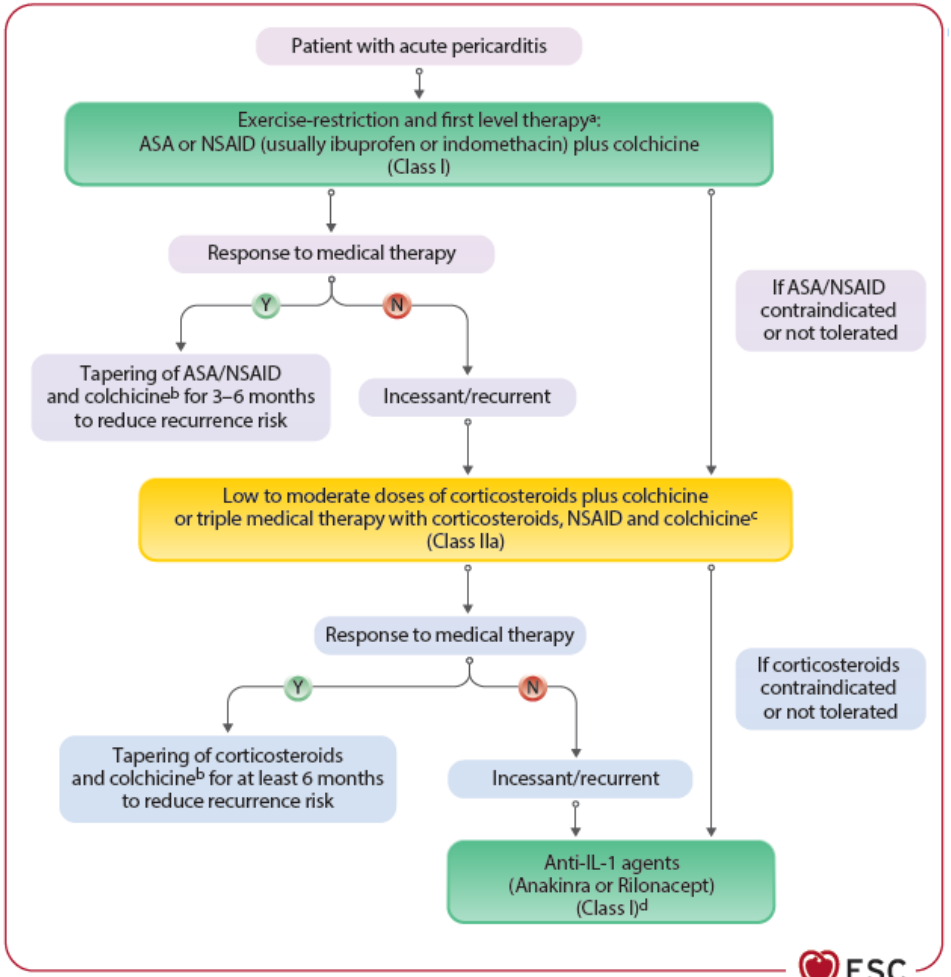
Figure 16

Proposed algorithm of medical therapy for pericarditis in adults (not including interventional therapies and pericardiectomy)



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Recommendations for medical therapy in pericarditis (1)

Recommendations	Class	Level
Colchicine is recommended as first-line therapy in patients with pericarditis as an adjunct to aspirin/NSAID or corticosteroid therapy to reduce subsequent recurrences	I	A
Anti-IL-1 agents (anakinra or rilonacept) are recommended for patients with recurrent pericarditis after failure of first-line therapies and corticosteroids and elevation of CRP levels to reduce recurrences and allow corticosteroid withdrawal.	I	A
High-dose aspirin or NSAIDs with proton pump inhibitors are recommended as first-line therapy in patients with pericarditis to control symptoms and reduce recurrences.	I	B
A β-blocker should be considered in symptomatic patients, despite full anti-inflammatory therapy, and heart rate at rest >75 bpm in order to improve symptoms control.	IIa	C
Anti-IL-1 agents (anakinra or rilonacept) should be considered in cases of incessant/recurrent pericarditis with evidence of pericardial inflammation on CMR after failure, contraindications, and intolerance to first-line therapies and corticosteroids regardless of CRP levels to reduce recurrences and allow corticosteroid withdrawal.	IIa	C

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Recommendations for medical therapy in pericarditis (2)

Recommendations (Continued)	Class	Level
Low- to medium-dose corticosteroids should be considered for patients with pericarditis only in cases of contraindication/failure of aspirin/NSAIDs and colchicine, or when there is a specific indication to control symptoms and reduce recurrences.	IIa	C
Hydroxychloroquine may be considered in patients with recurrent pericarditis refractory to standard therapy (including corticosteroids and anti-IL-1 agents) to prolong recurrence-free survival.	IIb	B
Corticosteroids are not recommended as the first option for patients with pericarditis therapy without a specific indication.	III	C

Recommendations for interventional techniques including circulatory support in myocarditis

Recommendations	Class	Level
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 should be considered in patients with myocarditis and cardiogenic shock or acute decompensation in chronic myocarditis to stabilize the patients.	IIa	C

Recommendations for interventional techniques in pericarditis

Recommendations	Class	Level
Pericardiocentesis (echocardiography-, CT-, or fluoroscopy-guided) is recommended for cardiac tamponade, or suspected bacterial or neoplastic pericarditis, or symptomatic moderate to large pericardial effusion despite medical therapy.	I	C
Surgical pericardial drainage is recommended in patients with pericardial effusion when percutaneous pericardiocentesis is not feasible or with purulent pericardial effusion to allow complete drainage and to prevent constriction.	I	C
Surgical pleuro-pericardial window is recommended in patients with relapsing pericardial effusion despite medical therapy.	I	C

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Recommendations for surgical therapy

Recommendations	Class	Level
Surgical pericardiectomy is recommended in patients with chronic pericardial constriction or persistent constrictive pericarditis despite medical therapy to improve symptoms and survival.	I	C
Tricuspid valve repair is recommended in patients with pericardial constriction and severe tricuspid valve regurgitation to improve symptoms and survival.	I	C

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Recommendations for management of arrhythmias and prevention of sudden cardiac death in myocarditis (1)

Recommendations	Class	Level
Pacing in myocarditis		
Temporary transvenous external pacing should be considered in patients with acute myocarditis and high-degree conduction disorders as a bridge to recovery.	IIa	C
WCD in myocarditis		
A WCD should be considered for 3–6 months in patients with sustained ventricular arrhythmia during the acute phase of myocarditis as a bridge to recovery.	IIa	C
Ablation in myocarditis		
Catheter ablation, performed in specialized centres, should be considered in post-myocarditis patients with recurrent symptomatic SMVT or ICD shocks in whom AAD are ineffective, not tolerated, or not desired.	IIa	C
ICD in myocarditis		
Secondary prevention		
ICD implantation is recommended in patients with non-active myocarditis and haemodynamically not-tolerated sustained VT to prevent SCD	I	C

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Recommendations for management of arrhythmias and prevention of sudden cardiac death in myocarditis (2)

Recommendations (Continued)	Class	Level
Secondary prevention (Continued)		
ICD implantation should be considered in patients with non-active myocarditis and haemodynamically tolerated sustained VT to prevent SCD.	IIa	C
ICD implantation may be considered in patients with acute myocarditis and sustained VA (VT/VF) in the acute phase to prevent SCD.	IIb	C
Primary prevention		
ICD implantation may be considered in patients with myocarditis after the acute phase (3–6 months) and persistent risk factors for VA to prevent SCD	IIb	C

Follow-up in inflammatory myopericardial syndromes after discharge

		Within 1 month	Within 3–6 months	12 months	>1 year and long-term FU
Clinical evaluation and ECG	Myocarditis	X	X	X	X
	Pericarditis	X	X	X	X
Biomarkers (TnI, CRP)	Myocarditis	X	X	(X)	(X)
	Pericarditis	X	X	(X)	(X)
Rhythm (stress and/or Holter-ECG)	Myocarditis	-	X	(X)	(X)
	Pericarditis	-	-	-	-
Imaging Myocarditis	TTE	X		X	X
	CMR	X		X	X
Imaging Pericarditis	TTE	X		X	X
	CMR	(X)		(X)	(X)

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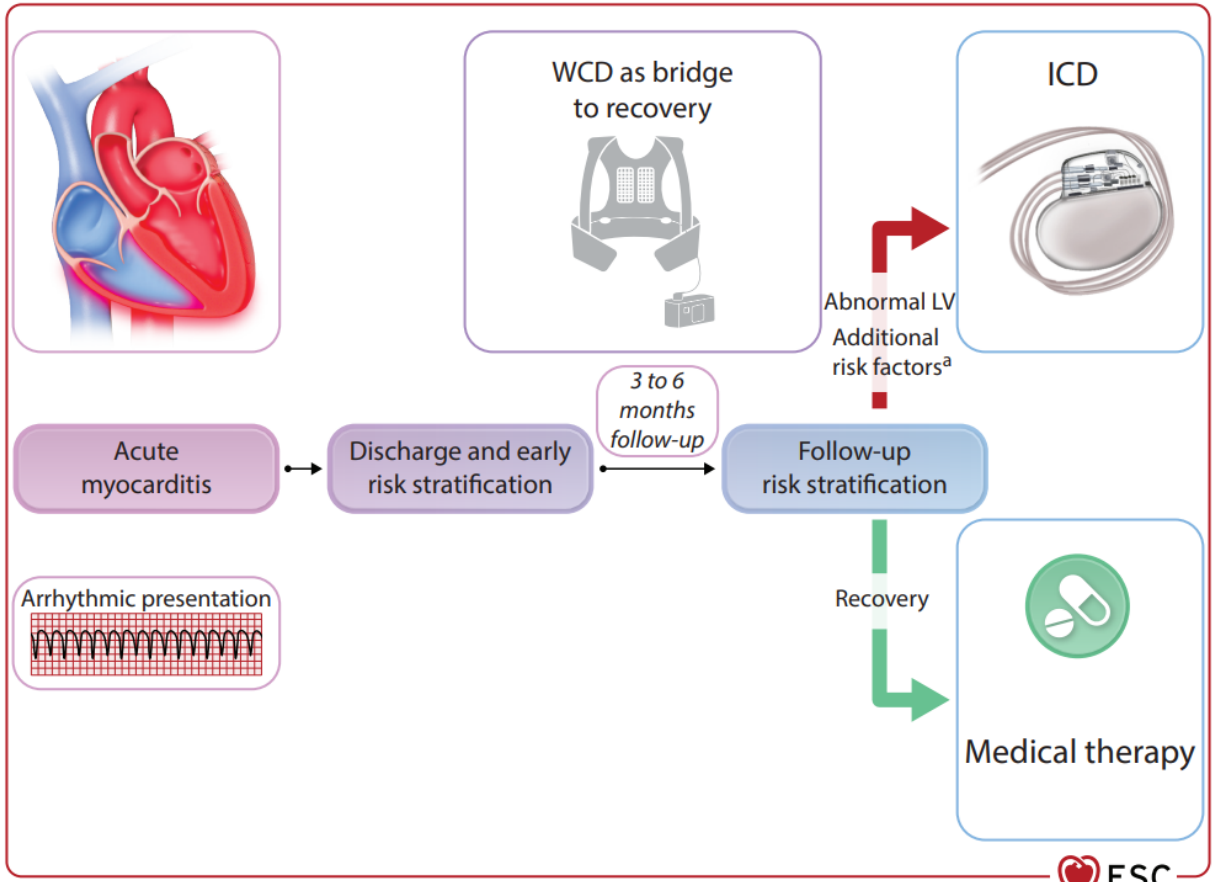
Figure 17

Follow-up and risk stratification after acute myocarditis with arrhythmic presentation.



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Recommendations for risk stratification, complications, and outcomes of inflammatory myopericardial syndromes

Recommendations	Class	Level
Follow-up with clinical assessment, biomarkers, ECG, exercise test, Holter-ECG monitoring, echocardiography, and CMR at least within 6 months after the index hospitalization is recommended in all patients with myocarditis to identify a potential progression or new risk factors.	I	C
Long-term follow-up is recommended for patients with complicated myocarditis to identify a potential progression or new complications.	I	C
Long-term follow-up is recommended for patients with incessant or recurrent pericarditis to identify a potential progression and new complications.	I	C

Indicators of non-viral aetiologies and complications (high-risk features or red flags in acute pericarditis)

Major
Fever >38°C (HR 3.56)
Subacute onset (HR 3.97)
Large pericardial effusion (>20 mm on echocardiography) (HR 2.15)
Cardiac tamponade (HR 2.15)
Lack of response to aspirin or NSAID after at least 1 week of therapy (HR 2.50)
Minor
Pericarditis associated with myocarditis
Immunodepression
Trauma
Oral anticoagulant therapy

Recommendations for giant-cell myocarditis

Recommendations	Class	Level
EMB is recommended in patients with suspected GCM due to unexplained new-onset HF of up to 2 weeks associated with a normal or dilated left ventricle and new ventricular arrhythmias, second- or third-degree AVB, or failure to respond to usual care within 1 to 2 weeks to initiate specific treatment.	I	C
Combined immunosuppressive therapy is recommended in patients with a diagnosed GCM.	I	C

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Recommendations for myocarditis in sarcoidosis

Recommendations	Class	Level
Diagnosis		
CMR, using tissue characterization techniques, is recommended in patients with suspected CS to assess cardiac inflammation and myocardial involvement.	I	B
^{18}F-FDG-PET is recommended for the diagnostic work-up, including detection of inflammation, as well as for follow-up and assessment of therapeutic response in patients with CS.	I	B
Therapy		
ICD implantation is recommended in patients with CS and sustained ventricular arrhythmia (VT/VF) or aborted CA to prevent SCD.	I	B
ICD implantation is recommended in patients with CS and LVEF ≤35% to prevent SCD.	I	C
ICD implantation should be considered in patients with CS and LVEF >35% after resolution of the active phase with significant LGE, a history of arrhythmias, unexplained syncope, inducible sustained VA at PVS, or with persistent high-degree AVB to prevent SCD.	IIa	C

Recommendations for immune checkpoint inhibitor-associated myocarditis

Recommendations	Class	Level
Diagnostic triage within 24 hours is recommended in patients with suspected myocarditis induced by ICI to initiate treatment rapidly.	I	C
Immediate disruption of ICI and administration of high-dosage corticosteroids are recommended in patients with ICI-associated myocarditis in order to stop the inflammatory reaction and stabilize the patient.	I	C
Second-line immunosuppression treatment should be considered in patients with steroid-refractory ICI-associated myocarditis.	IIa	C
Second-line immunosuppression treatment may be considered in patients with fulminant/severe ICI-associated myocarditis.	IIb	C

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Recommendations for inflammatory cardiomyopathy

Recommendations	Class	Level
Guideline-directed heart failure treatments are recommended in patients with inflammatory cardiomyopathy to improve and/or stabilize left ventricular function.	I	C
Specific medical therapy for the potentially underlying systemic disease is recommended in inflammatory cardiomyopathy.	I	C
Immunosuppressive therapy, guided by endomyocardial biopsy, should be considered in virus-negative inflammatory cardiomyopathies to suppress the autoimmune response.	IIa	B

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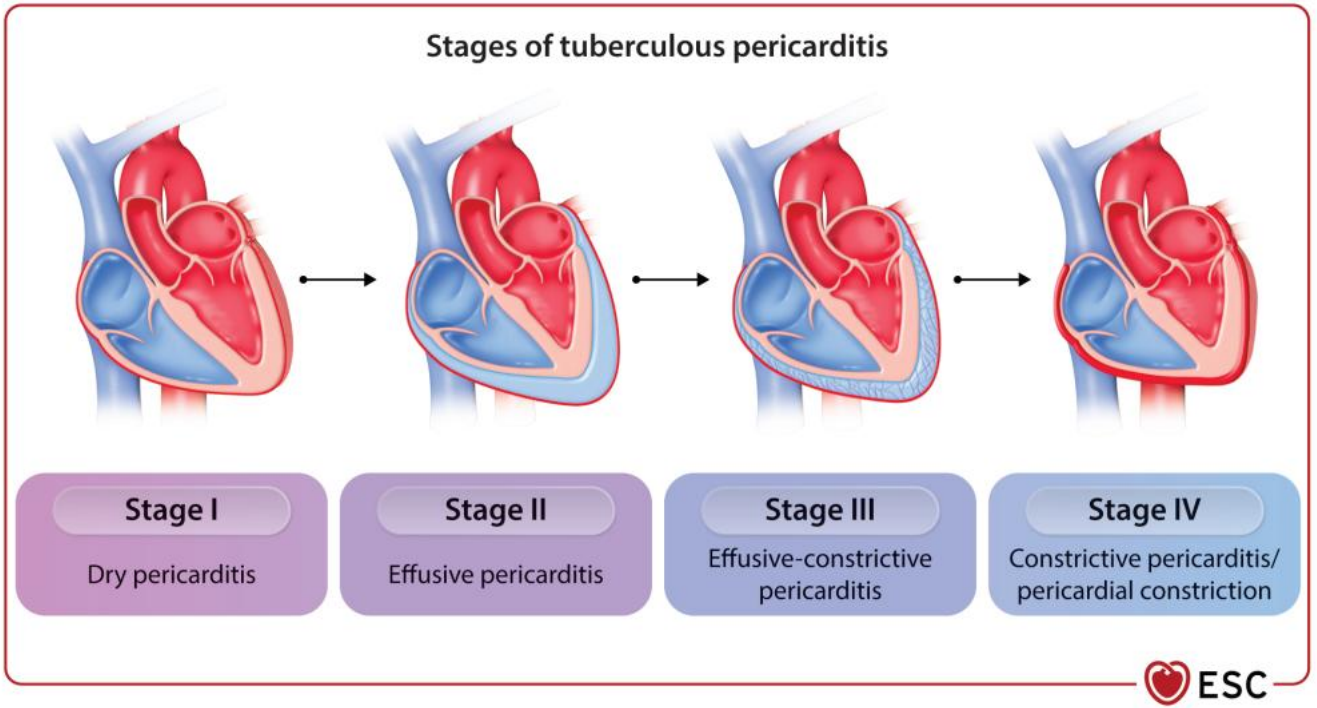
Figure 18

Stages of tuberculous pericarditis.



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Recommendations for tuberculous pericarditis (1)

Recommendations	Class	Level
Diagnosis and treatment of tuberculous pericarditis and effusion		
Diagnostic pericardiocentesis is recommended in all patients with suspected tuberculous pericarditis when diagnosis is not confirmed by non-invasive tests to identify the aetiological agent in pericardial fluid.	I	C
Empirical antituberculosis chemotherapy is recommended in patients living in endemic areas with exudative pericardial effusion after excluding other causes to treat the most likely cause.	I	C
Standard antituberculosis multidrug treatment for 6 months is recommended in patients with tuberculous pericarditis for the prevention of pericardial constriction.	I	C
Pericardiectomy is recommended in patients with tuberculous pericarditis if the condition is not improving or is deteriorating after 4–8 weeks of antituberculosis therapy to change the course of disease.	I	C
Adjunctive steroid therapy should be considered in HIV-negative cases to prevent the development of constrictive TB pericarditis.	IIa	C

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Recommendations for tuberculous pericarditis (2)

Recommendations (Continued)	Class	Level
Diagnosis and treatment of tuberculous pericarditis and effusion (Continued)		
In non-endemic areas a pericardial biopsy may be considered in patients with >3 weeks of illness without aetiologic diagnosis.	IIb	C
Empirical antituberculosis treatment is not recommended in patients living in non-endemic areas.	III	C

Recommendations for neoplastic pericardial involvement (1)

Recommendations	Class	Level
Pericardiocentesis is recommended for patients with cardiac tamponade to relieve symptoms and establish the diagnosis of malignant pericardial effusion.	I	C
Extended pericardial drainage (3–6 days) is recommended in patients with suspected or definite neoplastic pericardial effusion to prevent effusion recurrence.	I	B
Cytological analysis of pericardial fluid is recommended in patients with neoplastic pericarditis for the confirmation of malignant pericardial disease.	I	C
Systemic antineoplastic treatment is recommended in confirmed cases of neoplastic aetiology to treat the primary and secondary metastatic neoplastic involvement.	I	C
Pericardiocentesis should be considered in patients with moderate to large pericardial effusion to establish the diagnosis of malignant pericardial effusion when the diagnosis cannot be reached by multimodality imaging.	IIa	C

Recommendations for neoplastic pericardial involvement (2)

Recommendations (Continued)	Class	Level
Pericardial or epicardial biopsy may be considered in patients with suspected malignant pericardial disease when the diagnosis cannot be reached by multimodality imaging or cytological analysis, to confirm the diagnosis.	IIb	C
Intrapericardial therapy, in agreement with the oncologist, may be considered in cases refractory to systemic antineoplastic treatment.	IIb	C

Recommendations for post-cardiac injury syndrome

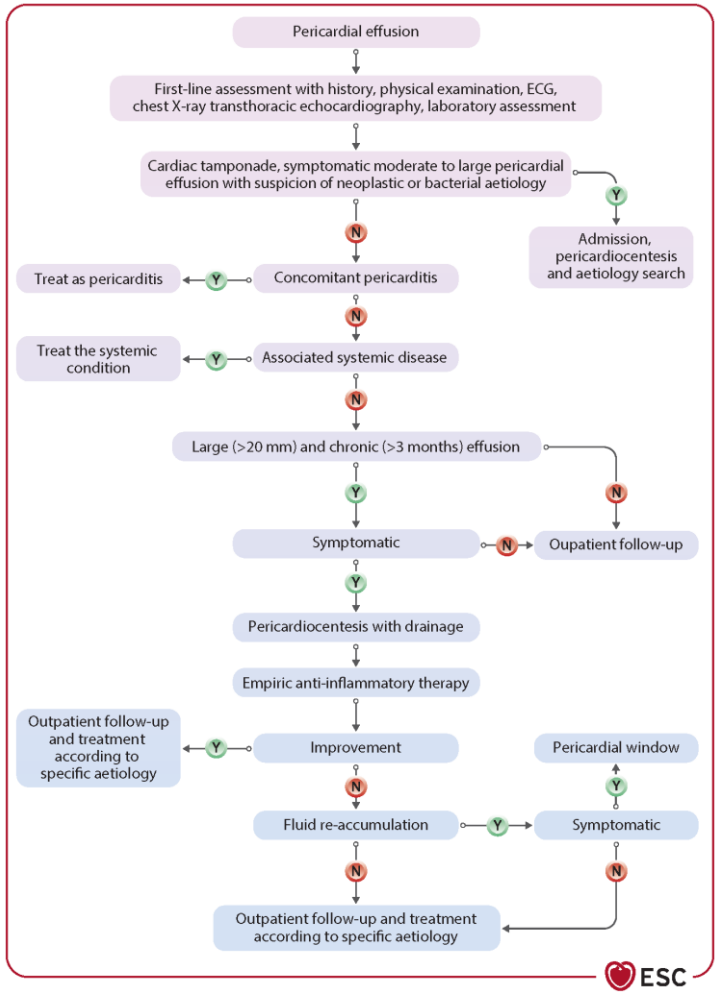
Recommendations	Class	Level
Anti-inflammatory therapy is recommended in patients with PCIS to hasten symptom remission and reduce recurrences.	I	B
IL-1 antagonists are recommended in patients with refractory PCIS to prevent recurrences and progression to constriction.	I	B
High-dose aspirin is recommended as the first-choice anti-inflammatory therapy for post-myocardial infarction pericarditis and in patients being already on antiplatelet therapy.	I	C
Colchicine, started 48 to 72 hours before cardiac surgery, should be considered for 1 month in patients after cardiac surgery for the prevention of PCIS if there are no contraindications and if it is tolerated.	IIa	A
Careful follow-up should be considered in patients with PCIS to exclude possible evolution towards constrictive pericarditis.	IIa	C

Recommendations for purulent pericarditis

Recommendations	Class	Level
Urgent pericardiocentesis and/or a surgical window is recommended in patients with suspicion of purulent pericarditis to establish a diagnosis.	I	C
Intrapericardial fibrinolysis should be considered in patients with purulent pericarditis to allow complete drainage of purulent fluid and to prevent constriction.	IIa	B

Figure 19

Triage and management of pericardial effusion.



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Echocardiographic signs of cardiac tamponade

Echocardiographic feature	Sensitivity	Specificity
Large pericardial effusion with swinging heart	n.a.	n.a
Diastolic collapse of the RA	50%–100%	33%–100%
Duration of diastolic collapse of the RA as a ratio of the cardiac cycle length >0.34	>90%	100%
Diastolic collapse of the RV	48%–100%	72%–100%
Respiratory changes of the mitral E velocity >25%–30%, tricuspid E velocity >40%–60%	n.a.	n.a.
Inferior vena cava plethora (dilatation >20 mm and <50% reduction of diameter with respiratory phases) as well as hepatic vein dilatation	97%	40%

Definitions and therapy of main constrictive pericardial syndromes

Syndrome	Definition	Therapy
Transient constriction (d.d. permanent constrictive pericarditis, restrictive CMP)	Reversible pattern of constriction following spontaneous recovery or anti-inflammatory therapy	A 3-6 months course of empiric anti-inflammatory medical therapy
Effusive–constrictive pericarditis (d.d. cardiac tamponade, constrictive pericarditis)	Failure of the right atrial pressure to fall by 50% or to a level <10 mmHg after pericardiocentesis May be diagnosed also by non-invasive imaging	Pericardiocentesis followed by medical therapy Surgery for persistent cases
Chronic constriction (d.d. transient constriction, restrictive CMP)	Persistent constriction after 3–6 months	Radical pericardiectomy, medical therapy for advanced cases or high risk of surgery or mixed forms with myocardial involvement

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Recommendations for constrictive pericarditis

Recommendations	Class	Level
Diagnosis		
Multimodality imaging is recommended in all patients with suspected constrictive pericarditis to make the diagnosis and assess pericardial thickening, calcifications, and active inflammation.	I	C
Cardiac catheterization for haemodynamic assessment should be considered in patients with suspected constrictive pericarditis when multimodality imaging is inconclusive.	IIa	C
Therapy		
Anti-inflammatory therapy is recommended in haemodynamically stable patients with a transient or new diagnosis of constriction with concomitant evidence of pericardial inflammation to prevent progression to constriction and avoid pericardiectomy.	I	C
Pericardiectomy is recommended in patients with permanent constriction if there is no active inflammation or anti-inflammatory treatment is not successful after 3–6 months.	I	C

Recommendations for pregnancy, lactation, and reproductive issues

Recommendations	Class	Level
Pre-conception counselling is recommended in women with recurrent pericarditis or myocarditis to assess disease activity and to review therapy.	I	C
NSAIDs should be considered in pregnant patients with pericarditis until the 20th week to treat an incessant/recurrent course.	IIa	C
Anti-inflammatory therapies should be considered in patients with pericarditis during lactation to treat and prevent pericarditis with timing adjusted to reduce drug exposure of the breastfed infant.	IIa	C
During pregnancy and breastfeeding, corticosteroids at the minimal effective dose (preferably up to 20 mg prednisone daily) should be considered in patients with active pericarditis, despite NSAID (if feasible), to prevent an incessant/recurrent course.	IIa	C
Colchicine may be considered in pregnant patients with pericarditis, especially in patients already receiving this drug to prevent recurrences.	IIb	C
Anakinra may be considered through pregnancy and lactation in pregnant patients with recurrent pericarditis who are not able to use alternative therapies to prevent an incessant/recurrent course.	IIb	C

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Recommendations for physical activity and myocarditis/pericarditis

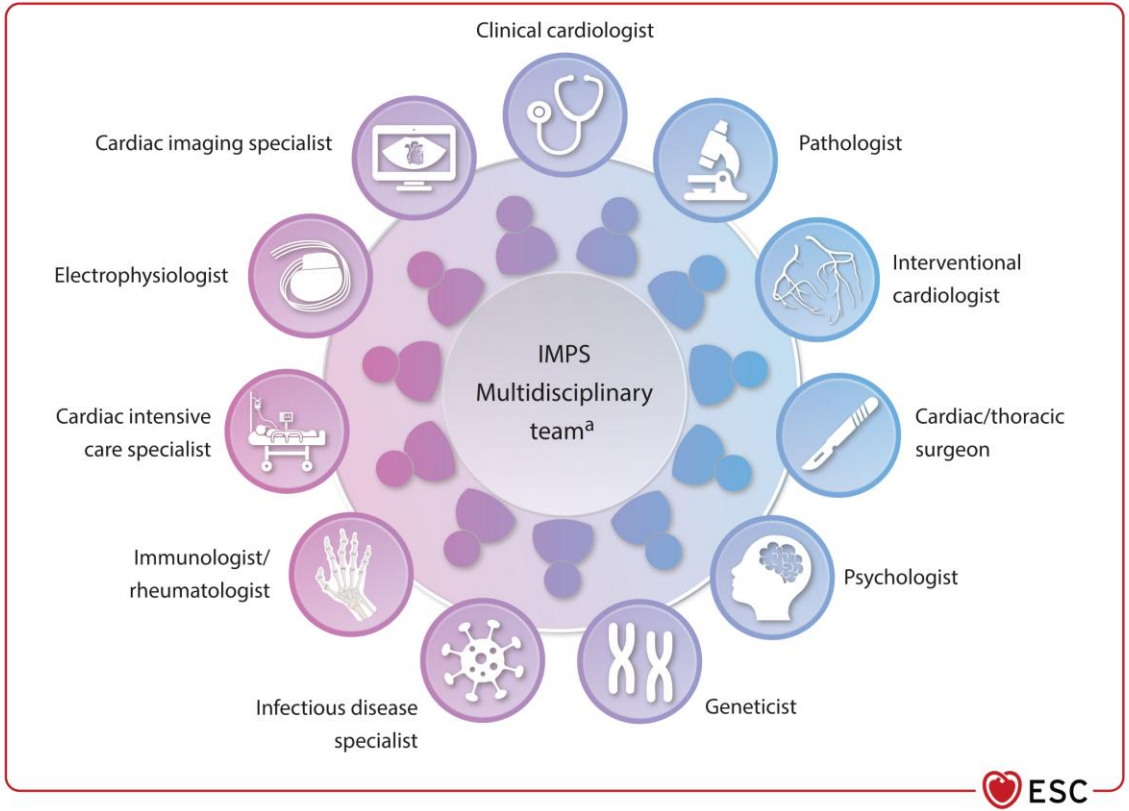
Recommendations	Class	Level
Restriction of physical exercise until remission, for at least 1 month, is recommended in athletes and non-athletes after IMPS using an individualized approach to accelerate recovery.	I	C

Recommendations for multidisciplinary teams in myopericardial syndromes

Recommendations	Class	Level
A multidisciplinary team discussion at a referral centre is recommended in patients with high-risk/complicated IMPS to provide a patient-tailored approach.	I	C

Figure 20

Multidisciplinary teams for inflammatory myopericardial syndrome.



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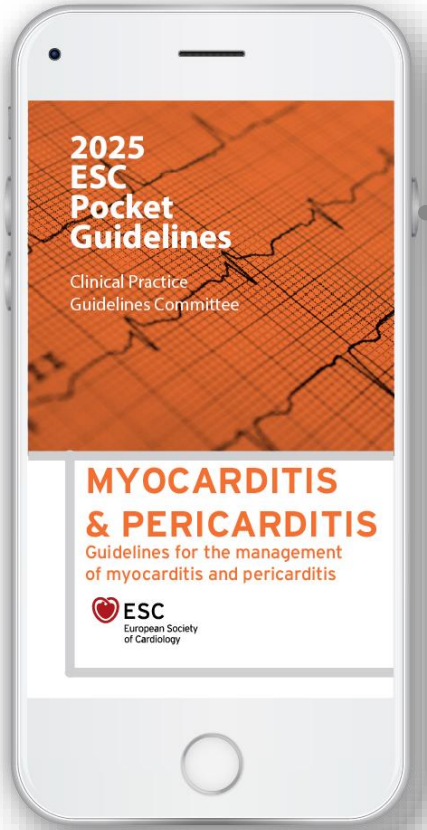

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