
5th iHEF CARD
The 5th Indonesian
Symposium on Heart Failure and
Cardiometabolic Disease
Indonesian Working Group
on Heart Failure
and Cardiometabolic Disease
WHFS
World Heart Failure Society
HEART FAILURE SOCIETY
(SINGAPORE)
Seen the Unseen
(in Myocarditis)
Notes from Cardiac Imager
June, 12-14 2025
Sheraton Grand Jakarta Gandaria City, Jakarta, Indonesia
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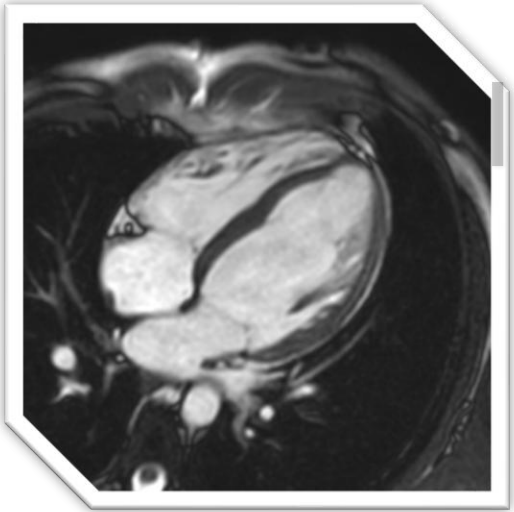
INTRODUCTION



- Myocarditis : a benign disease ?
- Symptoms: no or mild symptoms to chest pain, dyspnea, fatigue, palpitations, syncope, cardiogenic shock, and sudden cardiac death
- **Can present with symptoms and findings of acute heart failure or MI.**
  In MI and MINOCA: 33% myocarditis, the single most frequent underlying cause for MINOCA
- Neither the clinical presentation nor ECG or echo, are specific for non-ischaemic myocardial inflammation
- **CMR plays an important role in patients with suspected myocarditis**. In turn, myocarditis is one of the most frequent indications for CMR scans

INTRODUCTION

Infectious aetiologies (29%)		Non-infectious aetiologies (71%)	
Viral agents (28%)	Bacterial agents (< 1%)	Toxins (< 1%)	Autoreactive Myocarditis (53%)
Adenoviruses	Borrelia species	Anthracyclines	Immunological Syndromes (< 2%)
Enteroviruses (coxsackievirus)	Mycobacterium species	Cocaine	Churg-Strauss syndrome
Herpesviruses (Human Herpesviruses 6, Epstein-Barr virus)	Mycoplasma	Interleukin-2	Diabetes mellitus
Hepatitis C virus	Pneumoniae	Alcohol	Inflammatory bowel disease
HIV	Streptococcal species	Hypersensitivity (< 1%)	Giant cell myocarditis
Influenza A	Treponema pallidum	Cephalosporins	Granulomatosis with polyangiitis (Wegener granulomatosis)
Parovirus B19 (28%)	Fungal agents (< 1%)	Dogoxin	Sarcoidosis
Coronavirus (Sars-CoV2)	Aspergillus species	Diuretics	Systemic lupus erythematosus
Parasitic agents (< 1%)	Candida species	Dobutamine	Takayasu arteritis
Larva migrans	Coccidioides species	Sulfonamides	Thyrotoxicosis
Schistosomiasis	Cryptococcus species	Tricyclic antidepressant	
	Histoplasma species		
	Protozoal agents (< 1%)	Rejection (1%)	Other DCM patients (16%)
	Trypanosoma Cruzi (Chagas disease)	After heart transplantation (1%)	
		After stem cell transplantation	

Myocarditis: imaging up to date, Liguori et al, 2020

Pathophysiology Myocarditis

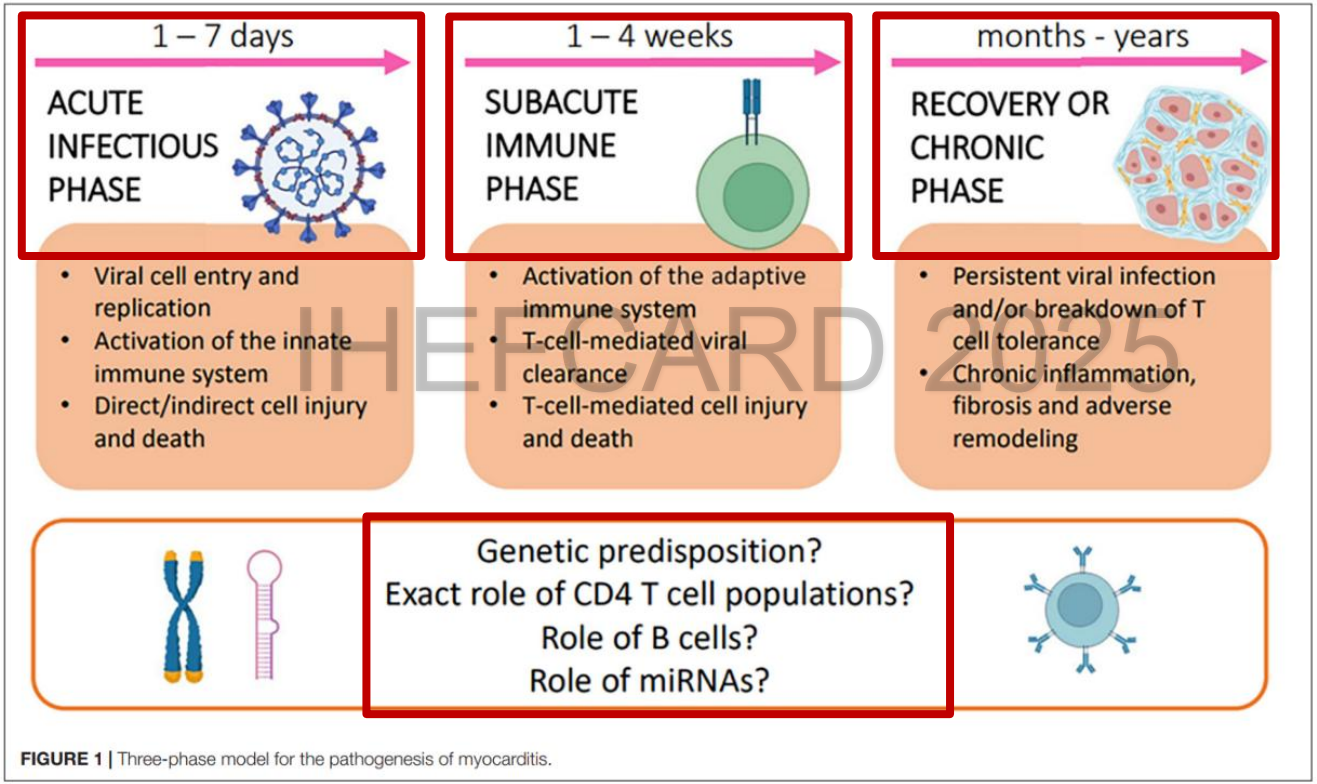


FIGURE 1 | Three-phase model for the pathogenesis of myocarditis.

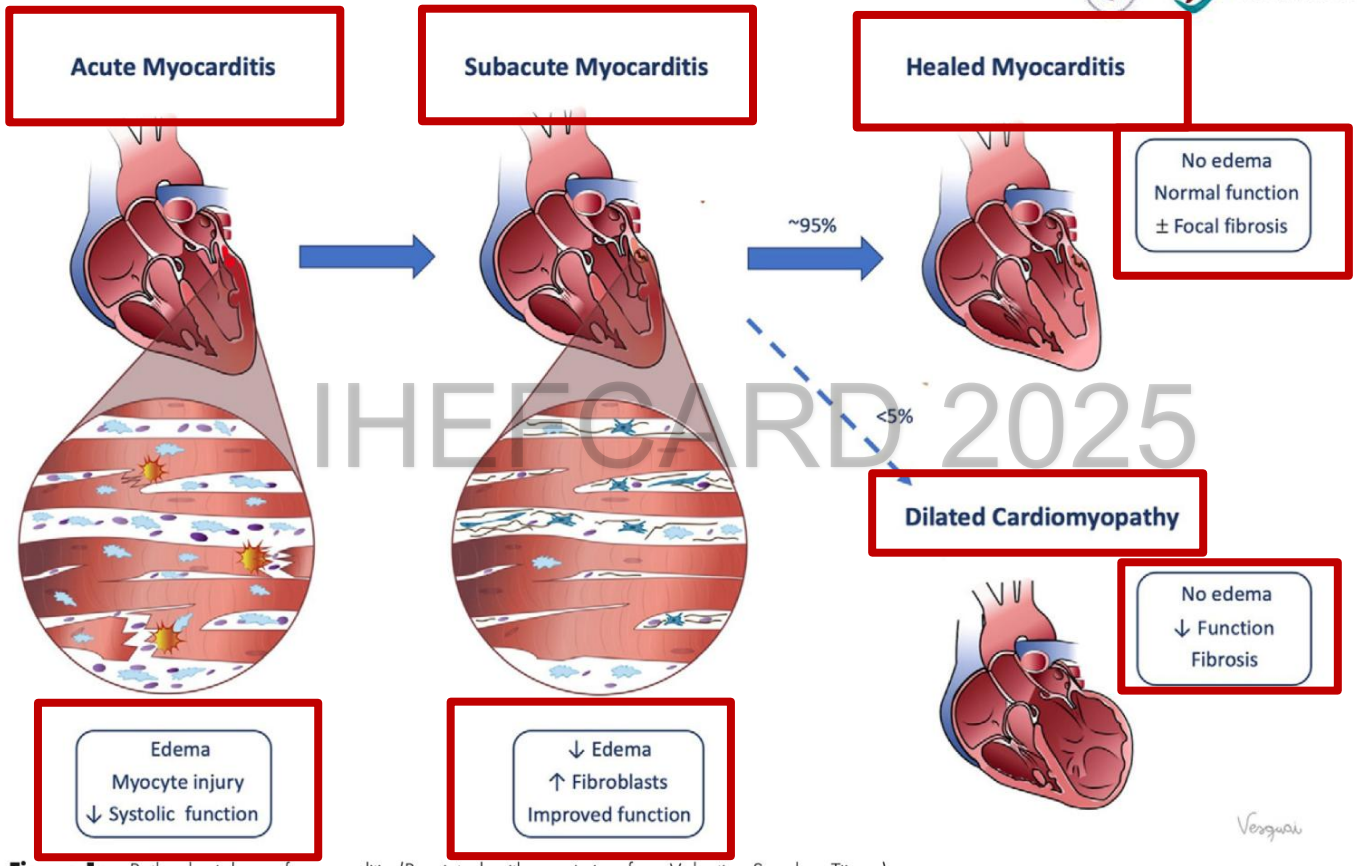
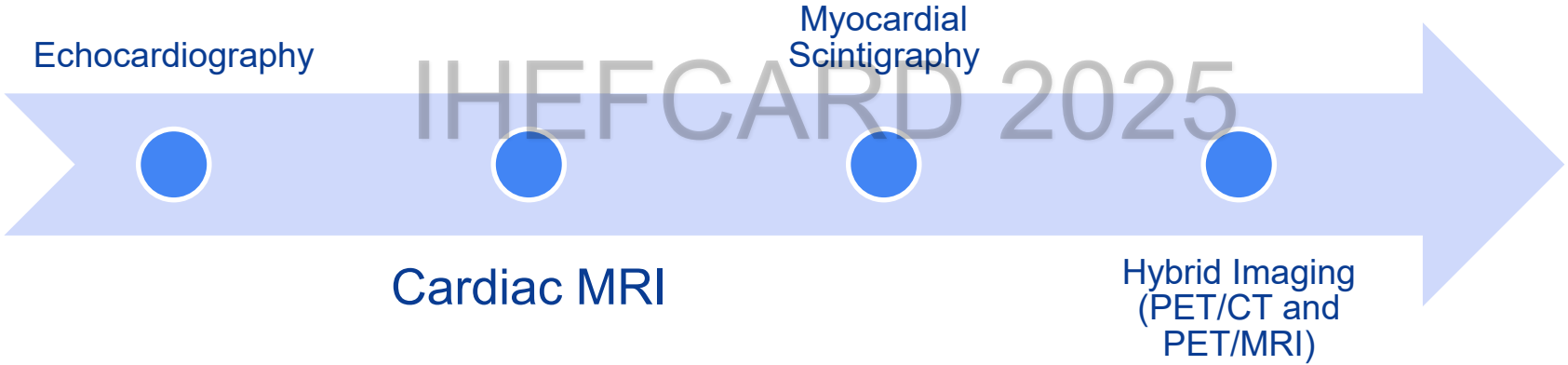
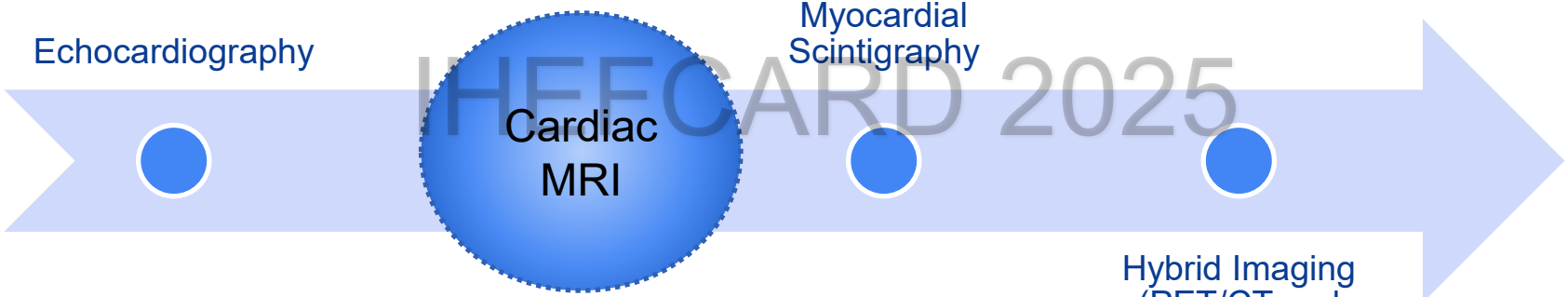


Figure 1: Pathophysiology of myocarditis. (Reprinted, with permission, from Valentina Sanchez Tijmes).

Modality



Modality



non-invasiveness, lack of radiation exposure, high image quality

Diagnostic Modalities and Correlation

Diagnostic Modality	Reference Standard	Benefits (Including Sensitivity and Specificity)	Limitations
EMB	Clinical correlate	Immunohistological: sensitivity 50.8%[73] Biventricular EMB sensitivities reported of up to 70.1% to 73.9%[8,74]	Low sensitivity, high false negative rate, high interobserver variability in interpretation, invasive procedure complications. Sufficient evidence of sensitivity of mRNA in EMB samples to be awaited
Troponin I	EMB	Sensitivity 34%, specificity 89%, PPV 82%, NPV 47%[75]	Raised in other cardiac and noncardiac insults as well as post endurance exercise
Troponin T	EMB Immunohistology	Sensitivity 100%, specificity 69%, PPV 18%, NPV 100%, effectiveness 71%[76] Sensitivity 53%, specificity 94%, PPV 93%, NPV 56%, effectiveness 69%[76]	As above
Creatine kinase-myocardial band	EMB	Sensitivity 6%, specificity 100%, PPV 100%, NPV 41%[75]	Very low sensitivity, troponin has been identified as the better marker of cardiac injury[4,5]; brief persistence in serum after myocardial injury
Viral serology	EMB + immunohistology	Sensitivity 9%, specificity 77%, PPV 25%, NPV 49%[7]	Expensive and time-consuming, often performed when acute viral phase has passed
Electrocardiogram	EMB[77] EMB + LGE on CMR[78]	Observed changes: ST-segment elevations, PQ depression, corrected QT-interval prolongation, or T-wave inversion Sensitivity 47%[77] to 77%,[78] specificity unknown	Unspecific changes, low sensitivity, unclear evidence in LGE-positive patients[3,78]
Echocardiography	—	Acute myocarditis: reduced LV systolic function, wall motion abnormalities, normal to increased LV thickness and LV dilatation Fulminant myocarditis: normal chamber size and severely impaired systolic LVEF[79]	Poor identification of tissue characteristics, user dependent, considered not to be equivalent to CMR
Speckle-tracking echocardiography	Clinical correlate	Sensitivity 85%, specificity 73% for prediction of delayed enhancement[80] GLS: sensitivity 95%, specificity 95%, AUC 0.99[23] Lateral wall circumferential strain: sensitivity 80%, specificity 63%, AUC 0.83[23]	Requires further studies but generally correlates with CMR calculated EF and strain values[40]
LLC—initial	EMB or clinical correlate	Diagnostic accuracy 83%,[81] sensitivity 67% to 80%, specificity 87% to 91%,[13,14,81] AUC 83%[14]	Surpassed by novel criteria
LLC—updated	EMB or clinical correlate	T1- and T2-based parameter approach: AUC 76% to 96%[12]	Growing importance of quantitative mapping has to be defined further, in particular which combinations of parameters are most relevant
CMR-FT	Clinical correlate	GLS: AUC 0.79, sensitivity 81%, specificity 71%, PPV 80%, NPV 74%[26] GCS: AUC 0.75, sensitivity 56%, 91%, PPV 90%, NPV 60%[26] Preserved EF: GLS: AUC 0.73[26] GCS: AUC 0.83[24] Combination of peak longitudinal strain with T1 or T2 mapping: AUC of 0.98, sensitivity 92% specificity 97%, PPV 98%, NPV 89%[26] LA peak early negative strain rate: AUC 0.72, sensitivity 69%, specificity 73%, PPV 0.85, NPV 0.52[32,33]	Interoperator and intraoperator variability, technical limitations, heterogeneity across studies
AI in CMR	EMB	Radiomics: Heart failure–like myocarditis: AUC 0.85 sensitivity 90%, specificity 72%[43] Infarct-like myocarditis: AUC 0.88, sensitivity 89%, specificity 92%[41]	Has yet to be applied to larger data sets with additional external validation and reproducibility studies

Table 5 **Diagnostic cardiac magnetic resonance criteria for myocarditis**

In the setting of clinically suspected myocarditis (*Tables 3–4*), CMR findings are consistent with myocardial inflammation, if at least two of the following criteria are present:

(1) Regional or global myocardial signal intensity increase in T2-weighted oedema images[a]
(2) Increased global myocardial early gadolinium enhancement ratio between myocardium and skeletal muscle in gadolinium-enhanced T1-weighted images[b]
(3) There is at least one focal lesion with non-ischaemic regional distribution in inversion recovery-prepared gadolinium-enhanced T1-weighted images (late gadolinium enhancement)[c]

A CMR study is consistent with myocyte injury and/or scar caused by myocardial inflammation if Criterion 3 is present

A repeat CMR study between 1 and 2 weeks after the initial CMR study is recommended if

- None of the criteria are present, but the onset of symptoms has been very recent and there is strong clinical evidence for myocardial inflammation
- One of the criteria is present

The presence of LV dysfunction or pericardial effusion provides additional, supportive evidence for myocarditis

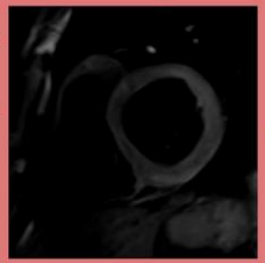
Table reprinted with permission from (20).
[a]Global signal intensity (SI) increase has to be quantified by an SI ratio of myocardium over skeletal muscle of ≥2.0. If the edema is more subendocardial or transmural in combination with a colocalized ischaemic (including the subendocardial layer) pattern of late gadolinium enhancement, acute myocardial infarction is more likely and should be reported.
[b]A global SI enhancement ratio of myocardium over skeletal muscle of ≥4.0 or an absolute myocardial enhancement of ≥45% is consistent with myocarditis.
[c]Images should be obtained at least 5 min after gadolinium injection; foci typically exclude the subendocardial layer, are often multifocal, and involve the subepicardium. If the late gadolinium enhancement pattern clearly indicates myocardial infarction and is colocalized with a transmural regional edema, acute myocardial infarction is more likely and should be reported.

Sensitivity 67%, specificity 91%, accuracy 78%, positive predictive value 91%, negative predictive value 69%

REVISED LAKE LOUISE CRITERIA FOR MYOCARDITIS

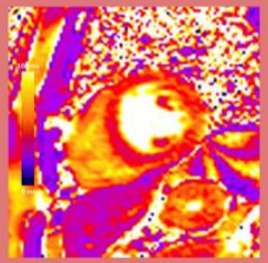
MAIN CRITERIA

T2 CRITERIA (EDEMA)



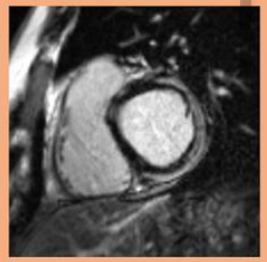
HIGH T2-SIGNAL INTENSITY

OR



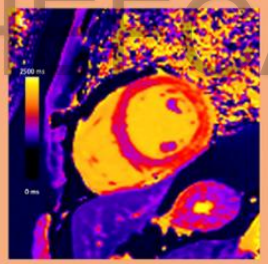
HIGH T2 VALUE

T1 CRITERIA (INJURY)



NON-ISCHEMIC LGE

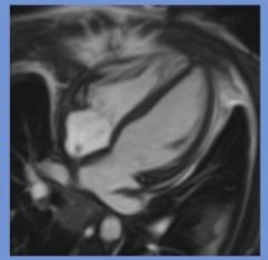
OR



HIGH T1 OR ECV

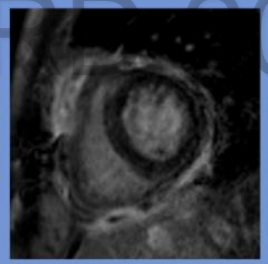
SUPPORTIVE CRITERIA

SYSTOLIC DYSFUNCTION



REGIONAL OR GLOBAL HYPOKINESIA

PERICARDITIS



PERICARDIAL ENHANCEMENT

In patients with high clinical pre-test probability of myocardial inflammation:

Fulfilment of any T2-criteria **AND** any T1-criteria → Strong evidence of myocardial inflammation

Fulfilment of any T2-criteria **OR** any T1-criteria → Possible evidence of myocardial inflammation

Left ventricular systolic dysfunction and pericarditis are supportive but are not required for diagnosis

• Myocardial Edema

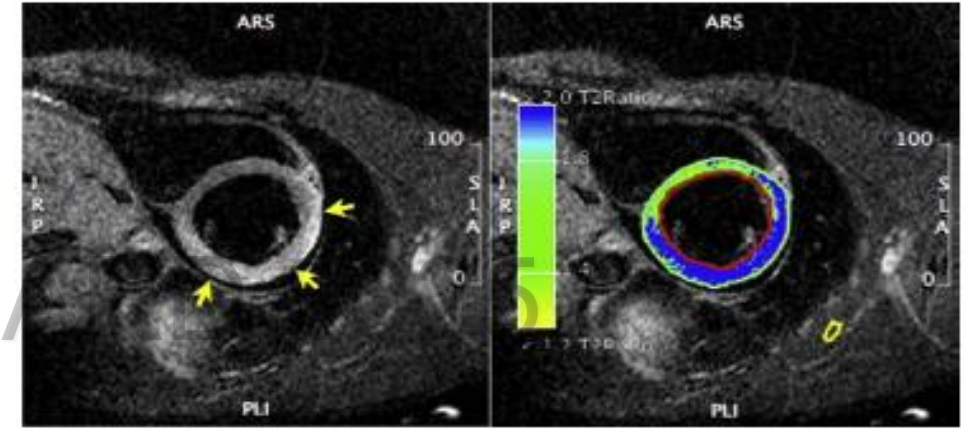
- **CMR:**

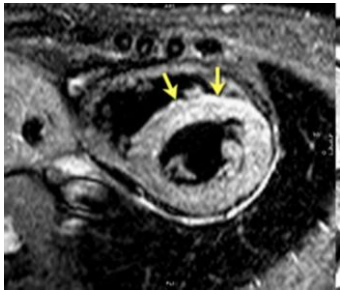
  the only imaging modality → assessing myocardial edema, feature of inflammation

- Despite scanner- and protocol-dependent variations of image quality, edema-sensitive CMR has shown **good diagnostic performance in clinically acute myocarditis**

- **Edema in the absence of necrosis or scar represents reversible injury and thus can predict functional recovery**.

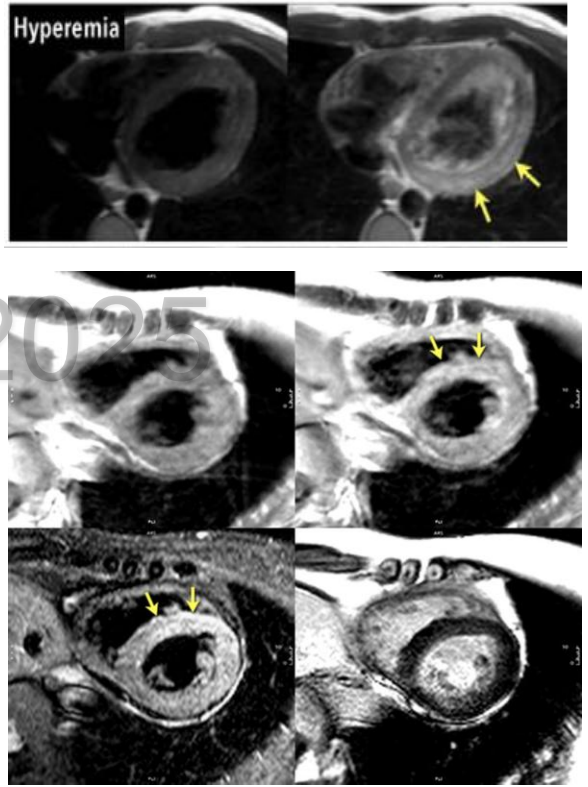
- Example of myocardial edema (water-sensitive T2-weighted sequence)





Hyperemia

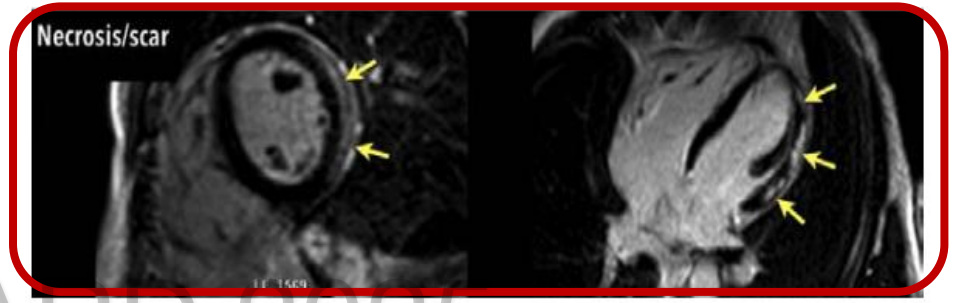
- **The first contrast-enhanced CMR technique applied** in patients with acute myocarditis
- **Targets myocardial hyperemia as another regular feature of inflammation**
- The **increase volume of Gadolinium distribution** can be visualized early after injection : T1-weighted, black-blood fast spin echo protocols



Myocarditis: imaging up to date, Liguori et al, 2020

Necrosis and Scar

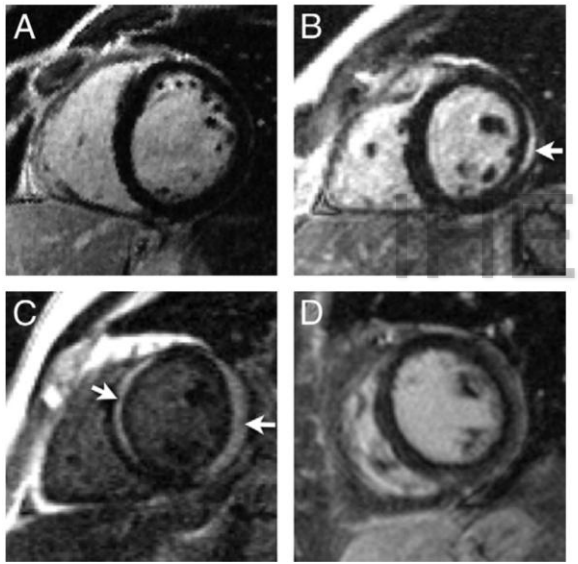
- **Late Gd enhancement imaging: visualize irreversible injury (necrosis in the acute setting and scar at a chronic stage)** as areas with high signal intensity
- More severe myocarditis: regional necrosis
- The **regional distribution is typically distinct from ischemic lesions**, which invariably include subendocardial layers, whereas **myocarditis typically exclude those zones**.



- LGE Imaging

Figure 2

Late Enhancement Patterns in Myocarditis



(A) Normal myocardium with no evidence of irreversible myocyte injury. **(B)** Regional subepicardial enhancement of the lateral wall **(arrow)**. **(C)** Subepicardial enhancement of lateral and midwall enhancement of the septal wall **(arrows)**. **(D)** Diffuse subepicardial enhancement.

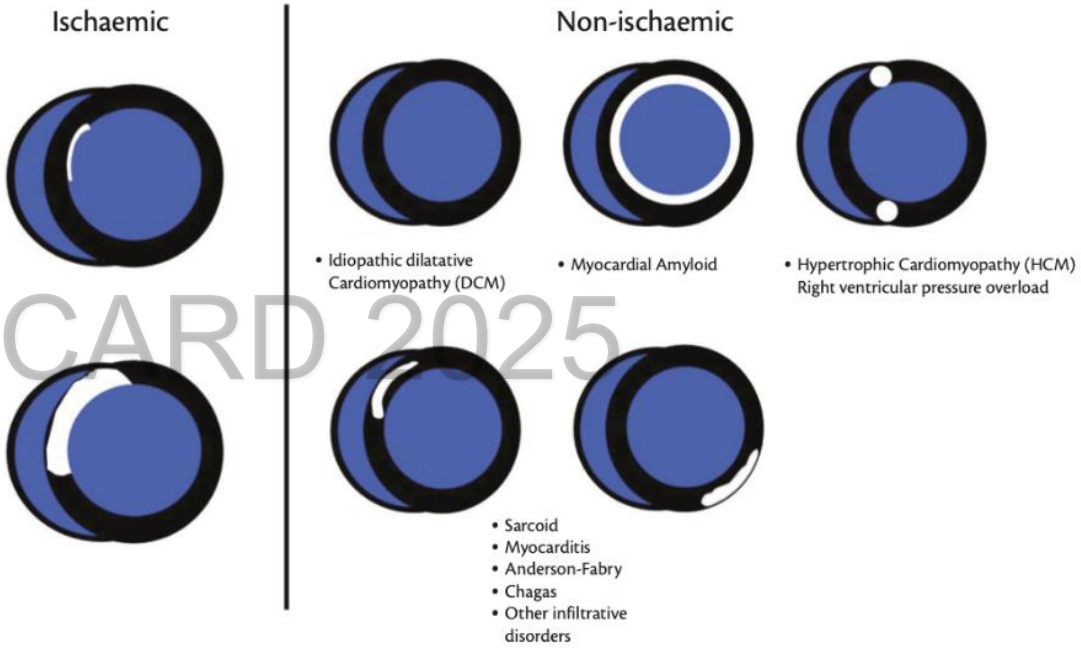


Fig. 48.6 Late gadolinium enhancement patterns that one may encounter in clinical practice. If hyperenhancement is present, the endocardium should be involved in patients with ischaemic disease. Isolated mid-wall or epicardial hyperenhancement strongly suggests a 'non-ischaemic' aetiology.

Reproduced from Mahrholdt H, Wagner A, Judd RM, Sechtem U, Kim RJ. Delayed enhancement cardiovascular magnetic resonance assessment of non-ischaemic cardiomyopathies. *Eur Heart J.* 2005;26(15):1461–74. doi:10.1093/eurheartj/ehi258 with permission from Oxford University Press.

Protocol

1. **Anatomy**
2. **LV function** (RV function)
3. **T1 mapping** (optional)
4. **T2 mapping** (optional)
5. **Oedema**
6. **LGE**

Report

1. **Dimensions** (corrected for BSA) and **function**
   - LV: EDV, ESV , SV, EF
   - RV: EDV, ESV , SV, EF
   - **Regional wall motion abnormalities**
2. Presence and location of **oedema**
3. Presence and location of **LGE**
4. **Pericardial effusion / enhancement**

Key Points

1. **Diagnostic CMR criteria**

   Myocardial inflammation (≥ 2 of the following criteria)

   Myocyte injury and / or scar (if focal lesion is present)
   - **Regional or global myocardial SI increase on T2w**
     SI ratio of myocardium over skeletal muscle of **≥2.0**
   - **Global myocardial SI increase on EGE**
     SI ratio of myocardium over skeletal muscle of **≥ 4.0** or absolute myocardial enhancement of **≥45%**
   - **At least 1 focal lesion with non-ischaemic regional distribution** (**sub-epicardial** layer or **mid-wall**)
     Infarction always involves sub-endocardial layer
2. Presence of **LV dysfunction** or **pericardial effusion** provides additional, supportive evidence
3. **Repeat scan** in 1-2 weeks after the first study, if
   - **None of the criteria** are present plus **very recent onset of symptoms** plus **strong clinical evidence**
   - **One of the criteria is present**

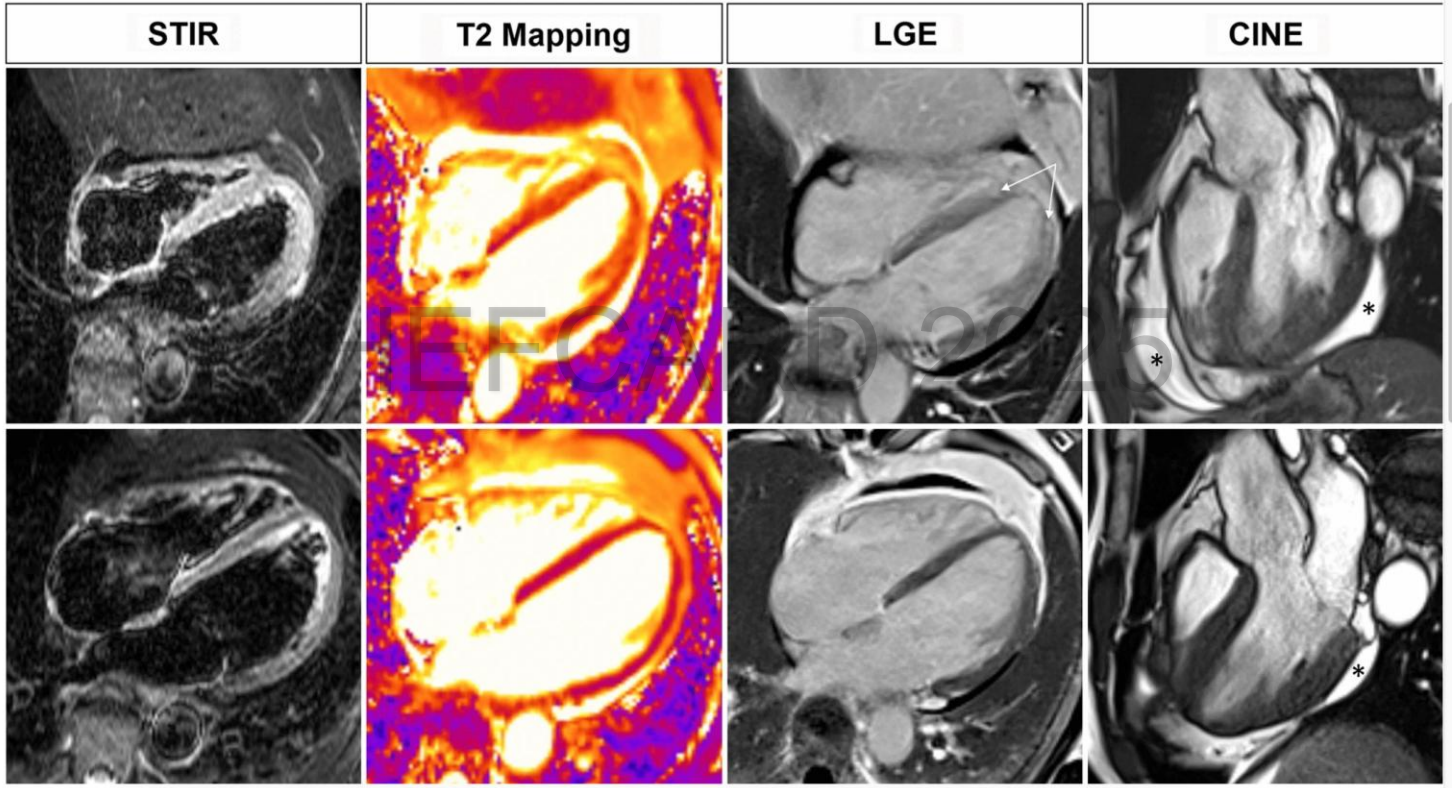
Tips & Tricks

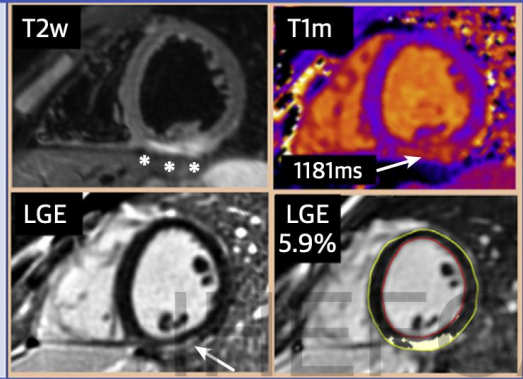
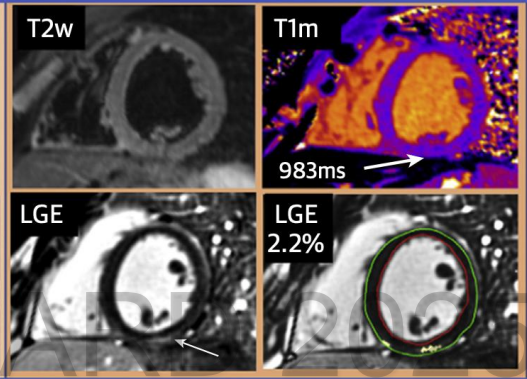
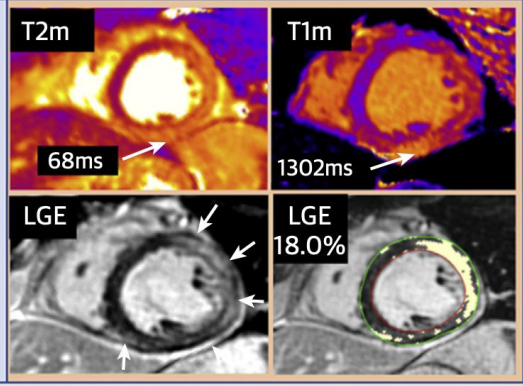
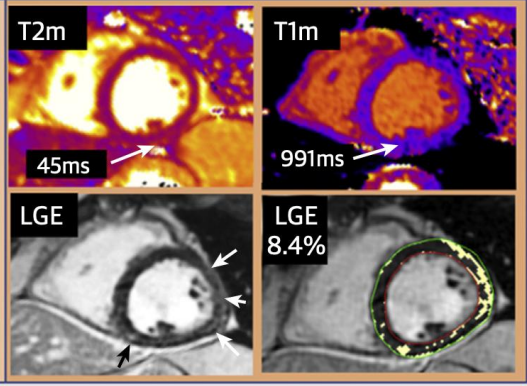
1. **Right ventricular dysfunction** seems to be the greatest predictor of mortality and cardiac transplantation

Diagnostic Modalities and Correlation

Targets	Sequences	Diagnostic criteria
Myocardial edema[a]	T2-weighted imaging	Regional high T2 SI
		Global T2 SI ratio ≥ 2.0 in T2W CMR images
	T2-mapping	Regional or global increase of myocardial T2 relaxation time
Hyperemia	T1-weighted imaging (EGE)	SI ratio myocardium/skeletal muscle (EGE ratio) of ≥ 4.0 in EGE images
	T1-mapping	Regional or global increase of native myocardial T1 relaxation time or ECV
Necrosis/fibrosis	T1-weighted imaging (LGE)	Areas with high SI in a nonischemic distribution pattern in LGE images
	T1-mapping	Regional or global increase of native myocardial T1 relaxation time or ECV

Myocarditis: imaging up to date, Liguori et al, 2020



	Baseline CMR	Follow-up CMR	Outcome
Patient A 21 y/o male presenting with clinically suspected myocarditis			No MACE
Patient B 30 y/o male presenting with clinically suspected myocarditis			MACE

Prognosis and Outcome

Table 2. Most Important Indications for CMR in Patients With Suspected Myocarditis

Clinical Presentation	Main Diagnostic Goal	Impact on Patient Management
Acute chest pain, normal coronary arteries, recent systemic viral disease, or other potential cause of myocarditis	Rule in/rule out of active inflammation, exclusion of ischemic injury	Modification of treatment (eg, discontinuation of anticoagulation)
Acute or progressive heart failure	Presence and character of myocardial injury (acuity, extent, ischemic vs nonischemic pattern, reversibility)	Gatekeeper for endomyocardial biopsy
Nonspecific cardiac symptoms	Rule in/rule out of myocarditis or other cardiomyopathies	Avoiding further diagnostic tests

CMR indicates cardiovascular magnetic resonance.

Conclusions

- Among available imaging techniques, **CMR is the most comprehensive and accurate diagnostic tool in patients with suspected myocarditis**
- CMR: **verifying or excluding myocardial inflammation** and **reversible/irreversible** injury and thus assessing the **activity and severity of myocarditis**
- Important roles in clinical routine include the **verification of myocarditis** in patients with ACS yet normal coronary arteries or with atypical symptoms, as well as **a gatekeeper** for endomyocardial biopsy in patients with **persisting symptoms and heart failure**
- In those diagnosed with acute myocarditis, we recommend **a follow-up scan at 3 months to identify persistent high-risk LGE extent or patterns and residual inflammation**