Consensus Criteria for the Diagnosis of Myocarditis

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>Grant/Research Support</td>
<td>Boston Scientific, Abbott Vascular</td>
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Prevalence, Etiology, Time Course of Myocarditis

**Prevalence**
- 220/million/year
- 358 in Manhattan/year

**Mortality** of Myocarditis or Cardiomyopathy

**Etiology**
- Virus, *Trypanosoma cruzi* (Chagas disease), Giant cell myocarditis, Autoimmune disease, Pheochromocytoma, Cardiac sarcoidosis, Hyperthyroidism

**Time course in virus myocarditis**
1. Acute (1-3 days) myocyte necrosis induced by virus replication
2. Subacute (few weeks-months) auto-immune myocarditis (activated T-lymphocytes) aimed to eliminate the virus in the myocardium
3. Chronic phase (DCM)

Heymans S. et al. JACC 2016;68:2348-64.
Myocardial Inflammation

1. Dilatation of the myocardial vascular bed with hyperemia, increased vascular permeability or capillary leak, edema (intracellular, extracellular space) → edema, hyperemia, increase of extracellular volume → T2 relaxation ↑ > T1 relaxation

2. Myocyte injury with loss of cell membrane integrity, myocyte necrosis, accumulation of debris in the extracellular space, infiltration of inflammatory cells or macrophages → myocardial damage, increase of extracellular volume → LGE (+)

3. Collagen deposition with formation of interstitial fibrosis and scar → increase of extracellular volume → LGE (+)
Lake Louise Criteria

1. Regional or global signal intensity increase in T2
2. Increased myocardial early enhancement ratio between myocardium and skeletal muscle in T1 with gadolinium.
3. ≥1 focal nonischemic LGE

Early enhancement:
A global SI enhancement ratio of myocardium/skeletal muscle ≥4.0 or absolute myocardial enhancement ≥45%

<table>
<thead>
<tr>
<th>Diagnostic Target</th>
<th>Original Lake Louise Criteria (Any 2 out of 3)</th>
<th>Updated Lake Louise Criteria (Any 2 out of 2)</th>
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<tbody>
<tr>
<td><strong>Myocardial Edema</strong></td>
<td><strong>T2-weighted imaging</strong>&lt;br&gt;Signal intensity↑</td>
<td><strong>T2-weighted imaging</strong>&lt;br&gt;Signal intensity↑&lt;br&gt;Relaxation time↑</td>
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<tr>
<td><strong>Myocardial Injury</strong></td>
<td>Hyperemia (Intra/extra cellular edema, capillary leak)&lt;br&gt;Early Gadolinium Enhancement</td>
<td>T1-weighted imaging&lt;br&gt;Native (non-contrast) relaxation time ↑&lt;br&gt;Extracellular volume↑&lt;br&gt;Non-ischemic pattern LGE</td>
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<td>Myocardial Necrosis, scar&lt;br&gt;Late Gadolinium Enhancement</td>
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<tr>
<td><strong>Supportive Criteria</strong></td>
<td>Pericardial effusion&lt;br&gt;Systolic LV wall motion abnormality</td>
<td>Pericardial effusion&lt;br&gt;High signal intensity of pericardium in LGE, T1, T2 mapping&lt;br&gt;Systolic LV wall motion abnormality</td>
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Ferreira VM. et al. JACC 2018;72:3158-76.
Diagnostic Performance Of CMR Criteria for Acute Myocarditis

Ferreira VM. et al. JACC 2018;72:3158-76.
Guideline Recommendation

- 2016 ESC for the acute and chronic heart failure
  - CMR is recommendation for the characterization of myocardial tissue in case of suspected myocarditis, amyloidosis, sarcoidosis, Chagas disease, Fabry disease, non-compaction cardiomyopathy, and haemochromatosis. (Class I, Level C Evidence).

- 2016 AHA Scientific Statement for specific DCM
  - CMR is reasonable for the diagnosis of myocarditis in clinically stable patients with clinically suspected myocarditis (Moderate level consensus, Level C Evidence).

- 2013 ESC Myocardial and Pericardial Disease
  - Reasonable to perform CMR in clinically stable patients prior to biopsy.

### MyoRacer-Trial

129 pts with suspicious myocarditis with biventricular biopsy, CMR (1.5T, 3T)

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<th>Acute Group (&lt;2 weeks)</th>
<th>Chronic Group (≥2 weeks)</th>
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<tr>
<td><strong>Age, yrs</strong></td>
<td>40 (29, 56)</td>
<td>46 (35, 57)</td>
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<tr>
<td><strong>Days since symptom onset</strong></td>
<td>6 (1, 13)</td>
<td>30 (21, 138)</td>
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<tr>
<td><strong>Symptoms, chest pain</strong></td>
<td>64%</td>
<td>41%</td>
</tr>
<tr>
<td><strong>ECG T-wave changes</strong></td>
<td>44%</td>
<td>49%</td>
</tr>
<tr>
<td><strong>Troponin positive</strong></td>
<td>77%</td>
<td>75%</td>
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<tr>
<td><strong>Biopsy findings</strong></td>
<td></td>
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<tr>
<td><strong>Myocardial inflammation</strong></td>
<td>70%</td>
<td>71%</td>
</tr>
<tr>
<td><strong>Presence of virus genome</strong></td>
<td>26%</td>
<td>28%</td>
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Acute Myocarditis

T1 Mapping

Extra Cellular Volume

T2 Mapping

Late Gadolinium Enhancement

T1 Relaxation time ↑

ECV ↑

T2 Relaxation time ↑

LGE (+)

MyoRacer-Trial, Diagnostic Accuracy

1.5T vs 3T (n=111) shows similar diagnostic accuracy.

Acute Symptoms (n=61)  Chronic Symptoms (n=61)

25-year-old, ST-elevation, Trop(+)

29-year-old, chest pain, Trop(+)

24-year-old, syncope, Trop(+)

T2 Mapping in Acute Myocarditis

LGE Pattern

Ischemic
Coronary territory related
- Transmural MI
- Non-Transmural MI

Non-Ishemic
Non coronary territory related
- Myocarditis
- Dilated Cardiomyopathy
- Hypertrophic Cardiomyopathy
- Amyloidosis
28 y.o. Male, Myocarditis with small LGE
Myocarditis with small LGE

Current Case

Normal Case
58 y.o. Male, Myopericarditis
68 y.o. Male, Cardiac Sarcoidosis
Cardiac Sarcoidosis

Current Case

Normal Case
Summary

1. New Lake Louise Criteria for myocarditis includes 1) edema by T2 and 2) myocardial injury by T1 image.
2. Diagnostic accuracy (area under the curve) of CMR for acute myocarditis is about 80% in the previous report.
3. However, this depends on the pre-test probability and timing/severity of myocarditis.