

SUPPLEMENTAL METHODS

The HRS consensus criteria and the 2016 JCS Guideline criteria are listed below:

HRS Expert Consensus Recommendations on Criteria for the Diagnosis of Cardiac Sarcoidosis¹⁰

There are two pathways to a diagnosis of cardiac sarcoidosis:

1. Histological diagnosis from myocardial tissue

Cardiac sarcoidosis is diagnosed in the presence of non-caseating granuloma on histological examination of myocardial tissue with no alternative cause identified (including negative organismal stains if applicable).

2. Clinical diagnosis from invasive and non-invasive studies

It is probable* that there is cardiac sarcoidosis if:

- a) There is a histological diagnosis of extra-cardiac sarcoidosis and
- b) One or more of following is present
 - Steroid ± immunosuppressant responsive cardiomyopathy or heart block
 - Unexplained left ventricular ejection fraction (<40%)
 - Unexplained sustained (spontaneous or induced) ventricular tachycardia
 - Mobitz type II second degree heart block or third-degree heart block
 - Patchy uptake on dedicated cardiac FDG-PET (in a pattern consistent with cardiac sarcoidosis)
 - Late gadolinium enhancement on CMR (in a pattern consistent with cardiac sarcoidosis)
 - Positive gallium uptake (in a pattern consistent with cardiac sarcoidosis)
- and
- c) Other causes for the cardiac manifestation(s) have been reasonably excluded

JCS 2016 Diagnostic Guidelines for Cardiac Sarcoidosis¹³

Clinical findings defining cardiac involvement

Cardiac findings should be assessed based on the major criteria and the minor criteria. Clinical findings that satisfy the following 1) or 2) strongly suggest the presence of cardiac involvement.

- 1) Two or more of the five major criteria (a) to (e) are satisfied
- 2) One in the five major criteria (a) to (e) and two or more of the three minor criteria (f) to (h) are satisfied.

Criteria for cardiac involvement

1. Major criteria

- (a) High-grade atrioventricular block (including complete atrioventricular block) or fatal ventricular arrhythmia (e.g., sustained ventricular tachycardia, and ventricular fibrillation)
- (b) Basal thinning of the ventricular septum or abnormal ventricular wall anatomy (ventricular aneurysm, thinning of the middle or upper ventricular septum, regional ventricular wall thickening)
- (c) Left ventricular contractile dysfunction (left ventricular ejection fraction less than 50%) or focal ventricular wall asynergy
- (d) ⁶⁷Ga citrate scintigraphy or ¹⁸F-FDG PET reveals abnormally high tracer accumulation in the heart
- (e) Gadolinium-enhanced MRI reveals delayed contrast enhancement of the myocardium

2. Minor criteria

- (f) Abnormal ECG findings: Ventricular arrhythmias (non-sustained ventricular tachycardia, multifocal or frequent premature ventricular contractions), bundle branch block, axis deviation, or abnormal Q waves
- (g) Perfusion defects on myocardial perfusion scintigraphy (SPECT)
- (h) Endomyocardial biopsy: Monocyte infiltration and moderate or severe myocardial interstitial fibrosis

Diagnostic guidelines for cardiac sarcoidosis

1) Histological diagnosis group (those with positive myocardial biopsy findings) - Cardiac sarcoidosis is diagnosed histologically when endomyocardial biopsy or surgical specimens demonstrate non-caseating epithelioid granulomas.

2) Clinical diagnosis group (those with negative myocardial biopsy findings or those not undergoing myocardial biopsy) - The patient is clinically diagnosed as cardiac sarcoidosis when epithelioid granulomas are found in organs other than the heart, and clinical findings strongly suggestive of the above-mentioned cardiac involvement are present and clinical findings strongly suggest the above-mentioned cardiac involvement.

Patients can also be clinically diagnosed as cardiac sarcoidosis when the patient shows clinical findings strongly suggestive of pulmonary or ophthalmic sarcoidosis; at least two of the five characteristic laboratory findings of sarcoidosis and clinical findings strongly suggest the above-mentioned cardiac involvement.

Note: The latter definition was noted used in our study since all included patients had histologically proven sarcoidosis.