


Recovery of Late Gadolinium Enhancement and T1-T2 Cardiac Mapping with Lake Louise Criteria in Patients with Acute Myocarditis

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ABSTRACT

Myocarditis is a condition characterized by inflammation in the myocardium. Myocarditis is difficult to diagnose, due to its multiple, heterogeneous manifestations with many differential diagnoses. T1 and T2 cardiac mapping were added as a criterion in the revised Lake Louise Criteria (LLC). The revised criteria have been reported to have higher sensitivity. We included two patients diagnosed with myocarditis based on the revised LLC. All patients were diagnosed using cardiac magnetic resonance (CMR), which includes late gadolinium enhancement (LGE) and T1-T2 mapping. LGE is a technique frequently used in CMR to visualize cardiac tissue, whichis most sensitive to fibrosis. Revised LLC includes quantitative measures of T1 and T2 value, and T1-T2 mapping is advantageously related to its ability to quantitatively assess myocardial abnormalities. CMR using LGE combined with T1-T2 mapping allows the diagnosis of myocarditis. Recovery of T1 and T2 values during follow-up allows quantitative measurement of patients' condition and treatment success.

Keywords: Acute myocarditis, cardiac magnetic resonance, late gadolinium enhancement, T1 mapping, T2 mapping.

ABSTRAK

Miokarditis adalah kondisi peradangan miokardium. Diagnosis miokarditis sulit karena manifestasinya bervariasi dan heterogen dengan banyak diagnosis diferensial. Pemetaan kardiovaskular T1 dan T2 ditambahkan dalam kriteria Lake Louise (LLC) yang direvisi. Kriteria yang direvisi ini dilaporkan memiliki sensitivitas yang lebih tinggi. Kami melaporkan 2 pasien dengan diagnosis miokarditis berdasarkan LLC yang direvisi. Semua pasien didiagnosis menggunakan resonansi magnetik jantung (CMR), yang mencakup pemeriksaan *late gadolinium enhancement* (LGE) dan pemetaan T1-T2. LGE adalah teknik yang sering digunakan dalam CMR untuk memvisualisasikan jaringan jantung yang paling sensitif terhadap fibrosis. LLC yang direvisi mencakup pengukuran kuantitatif nilai T1 dan T2, dan pemetaan T1-T2 memiliki keunggulan terkait kemampuannya untuk menilai secara kuantitatif kelainan miokardium. CMR menggunakan LGE dikombinasikan dengan pemetaan T1-T2 memungkinkan diagnosis miokarditis. Pemulihan nilai T1 dan T2 selama tindak lanjut memungkinkan pengukuran kuantitatif kondisi pasien dan keberhasilan pengobatan. **Prasetyo Andriono, Armand Achmadsyah. Pemulihan Penyangatan Gadolinium Akhir dan Pemetaan Jantung T1-T2 dengan Kriteria Lake Louise pada Pasien Miokarditis Akut.**

Kata Kunci: Miokarditis akut, resonansi magnetik jantung, penyangatan gadolinium akhir, pemetaan T1, pemetaan T2.

Introduction

Myocarditis is a condition characterized by inflammation in the cardiac muscle - myocardium. Myocarditis is an important cause of sudden cardiac death, with some mortality cases attributable to non-ischemic dilated cardiomyopathy.[1] However, the exact prevalence of myocarditis is still unknown due to difficulty in diagnosis. Patients may appear asymptomatic or with symptoms such as chest pain, palpitations, dyspnea, fatigue, decrease in exercise tolerance, and syncope.[1]

Evaluation for myocarditis includes electrocardiogram (ECG), echocardiography, and laboratory measures. An important diagnostic modality in myocarditis is radiology. Cardiac Magnetic Resonance (CMR) is a promising tool that may help differentiate an ischemic and non-ischemic etiology of dilated cardiomyopathy.[1] The Lake Louise Criteria (LLC) was established as a criterion in diagnosing patients suspected with myocarditis with a sensitivity and specificity of 74% and 86% respectively using early gadolinium enhancement (EGE), T2-weighted sequences, and late gadolinium enhancement (LGE).[1] However, due to no quantitative assessment requirement in this criterion, diffuse or subtle myocardial inflammation may be missed.[2,3] The revised LLC is based on one T1 criteria (increased T1 relaxation times, ECV fraction, or LGE) with one T2 criteria (increased T2 relaxation times, myocardial edema, or increased T2 signal ratio).[4] The new criteria have higher sensitivity with similar specificity.

Two patients with myocarditis diagnosed with CMR using LGE and T1-T2 mapping using

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revised LLC and their recovery was reported.

Case 1

A 17-year-old male came with a chief complaint of worsening palpitations. There was also mild dyspnea during strenuous exercise, as well as chest pain and shortness of breath for about 2 weeks, but worsened for the past 3 days. The patient had no history of cardiorespiratory symptoms. Physical examination revealed no rales or crackles. ECG showed normal sinus rhythm and chest radiograph showed unremarkable results. Laboratory examination showed normal NT-pro BNP value (98 ng/L; N: <125 ng/L), highly elevated leukocyte levels (19,800/uL; N:5,000-10,000/uL), segmented neutrophil count (83%; N:<50%), monocyte count (14%; N:<2%), and with normal hemoglobin levels (16 g/dL; N:13-18 g/dL). Glucose levels (124 mg/dL; N: <180 mg/dL) and glycosylated HbA1C were normal (4.7%; N: <5.7%). Ureum and creatinine were within normal limits, (17 mg/dL; N:9-21 mg/dL) and 0.9 mg/dL (N: 0.7-1.2 mg/dL) respectively. Liver function (SGOT: 34 U/L; N:0-40 U/L, SGPT: 23 U/L; N: 0-35 U/L, gamma GT: 44 U/L; N:11-50 U/L) were normal. Electrolytes were normal (sodium: 142 mmol/L; N: 137-150 mmol/L, potassium 4.3 mmol/L; N: 3.5-5.3 mmol/L, chloride 102 mmol/L; N: 94-111 mmol/L). He had an elevated hs-troponin level of 0.12 ng/mL (N: 0-0.04 ng/mL). Urine and blood culture results were negative. He was diagnosed with suspicion of myocarditis and started on a 7-day wide-spectrum antibiotic regimen with meropenem and moxifloxacin. Further examination with CMR revealed a left ventricle ejection fraction of 59.73%, with increased T1 and T2 values in T1-T2 mapping. The patient then came for a 3-month follow-up, which showed less significant hyperintensity and a decrease in extracellular volume (ECV) from 45±17% to 33±62% (normal). CMR examination is shown in **Figures 1** and **2**.

Case 2

A 33-year-old male presented with a chief complaint of three-day intermittent chest pain aggravated with exercise. He also reported palpitations and dyspnea. He had a history of NSTEMI and had been treated with percutaneous coronary intervention followed by dual antiplatelet therapy. A month before his current admission, he checked to our center with no symptoms, global normokinetic echocardiography, and

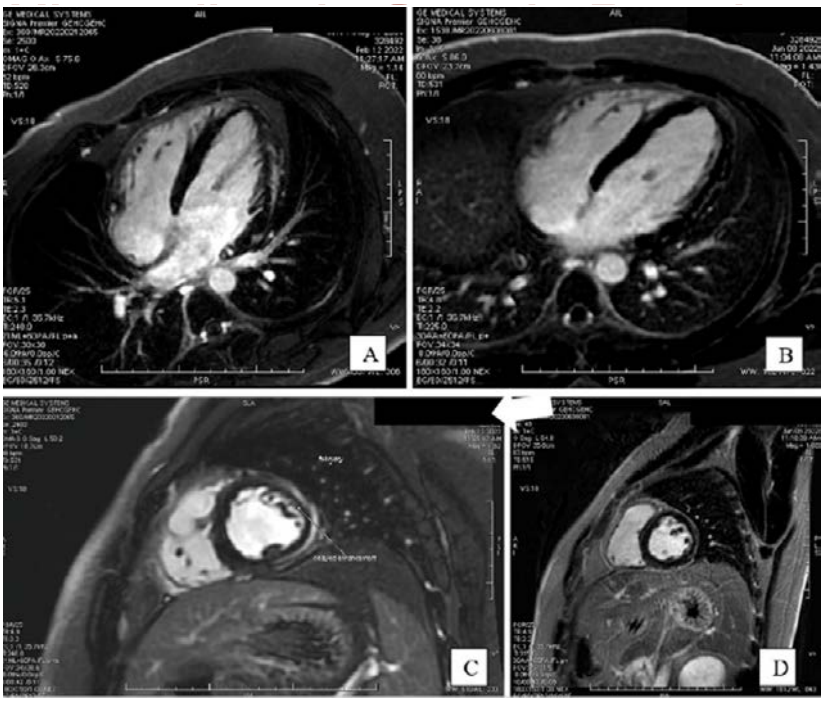

Figure 1. LGE in CMR. Figure 1a. Sagittal plane showing the apex in early disease showing hyperintensity area in the mid myocardium of lateral wall suggestive of myocarditis; Figure 1b. 3-months follow up showed significantly less hyperintensity area compared to previous CMR examinations; Figure 1c. White arrow showed LGE in lateral wall of left ventricular myocardium; Figure 1d. follow-up at 3 months showed recovery of LGE in lateral wall.

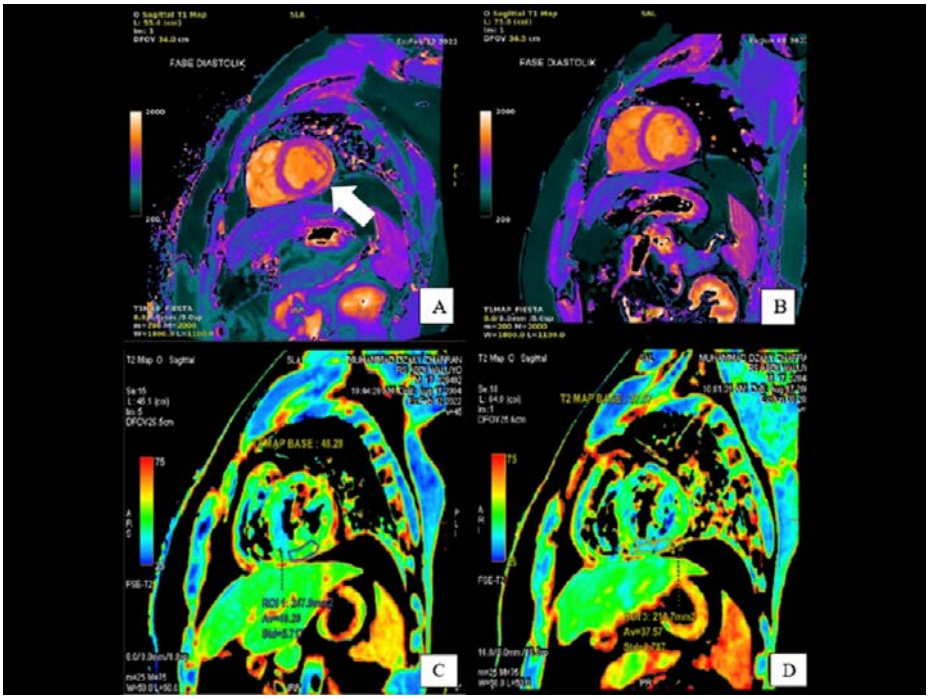

Figure 2. T1-T2 mapping. Figure 2a. White arrow in T1-mapping shows a high T1 value of 1,386 ms (N: 1,052±23 ms) in the mid myocardium of the lateral wall. There was also high T1 value of 1,235 ms (N: 1,052±23 ms) in anteroseptal wall, indicative of myocardial fibrosis; Figure 2b. 3-months follow-up; Figure 2c. T2-mapping shows high T2 value of 48.28 ± 5.72 ms (N: 45.1± 3.4 ms) in the lateral wall of left ventricle, indicative of acute myocardial edema; Figure 2d. 3-months follow-up showing lower T2 value of 37.57 ms (N: 45.1± 3.4 ms) in lateral wall of left ventricle.

no identifiable atherosclerotic plaque from CT angiography.

The chest pain persisted for one week after admission and multiple examinations were performed to confirm the patient's diagnosis. ECG findings were suggestive of atrial fibrillation. Laboratory findings were elevated leukocyte levels (14,800/uL; N: 5,000-10,000/uL), segmented neutrophil count (84%; N: <50%), and monocyte count (7%; N:<2%). He had a high NT-pro BNP value (853 ng/L; N: 125 ng/L) suggesting CHF, elevated hs-CRP value (4.3 mg/L; N: <1.0 mg/L), and normal troponin I levels (0.03 ng/mL; N: <0.1 ng/mL). Metabolic syndrome lab examinations showed normal lipid profile except for the slightly increased HDL levels (total cholesterol 159 mg/dL, N: <200 mg/dL; high-density lipoprotein 41 mg/dL, N: >55 mg/dL; low-density lipoprotein 113 mg/dL, N <150 mg/dL; triglyceride 143 mg/dL, N <150 mg/dL) and normal blood sugar levels (fasting blood glucose 88 mg/dL, N: <126 mg/dL; glycosylated HbA1C 5.0%; N: <5.7%). He had normal electrolyte levels (sodium: 138 mmol/L; N: 137-150 mmol/L, potassium 3.7 mmol/L; N: 3.5-5.3 mmol/L, chloride 1,058 mmol/L; N: 94-111 mmol/L). Ureum and creatinine were slightly elevated (24 mg/dL; N: 9-21 mg/dL) and 1.4 mg/dL (N: 0.7-1.2 mg/dL) respectively. Liver function (SGOT: 36 U/L; N:0-40 U/L, SGPT: 31 U/L; N: 0-35 U/L, gamma GT: 43 U/L; N: 11-50 U/L) were normal. A treadmill test was performed and showed negative (non-ischemic) results. Coronary calcium score showed a very low likelihood of significant coronary artery disease (<5%), which suggested symptoms and signs resulting from non-ischemic conditions. Initial diagnosis was suspected of myocarditis, chronic heart failure (CHF), and acute kidney injury (AKI). He was started on an antibiotic regimen with meropenem and moxifloxacin.

CMR was then performed, which revealed increased T1 and T2 value suggestive of acute myocarditis. After 3 months of follow-up, the patient reported no symptoms. CMR after 1-year follow-up showed partial resolution of myocarditis. The patient's CMR results can be seen in **Figures 3** and **4**.

Discussion

Acute myocarditis is defined as a period of less than 1 month between onset of symptoms and diagnosis. Symptoms may vary, ranging from chest pain (85-95% cases), fever (approximately 65% cases), to dyspnea (19-49% cases).[5] Acute myocarditis may present

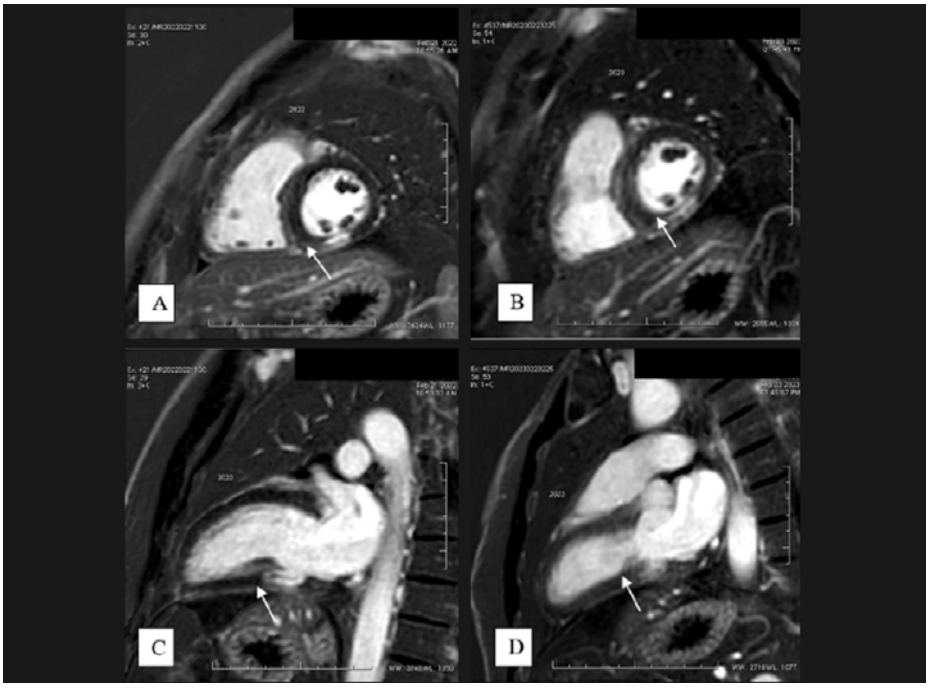

Figure 3. LGE showed improvement in areas of delayed enhancement and intensity of contrast enhancement from (Figure 3a) and (Figure 3c) to 1-year follow-up (Figure 3b) and (Figure 3d).

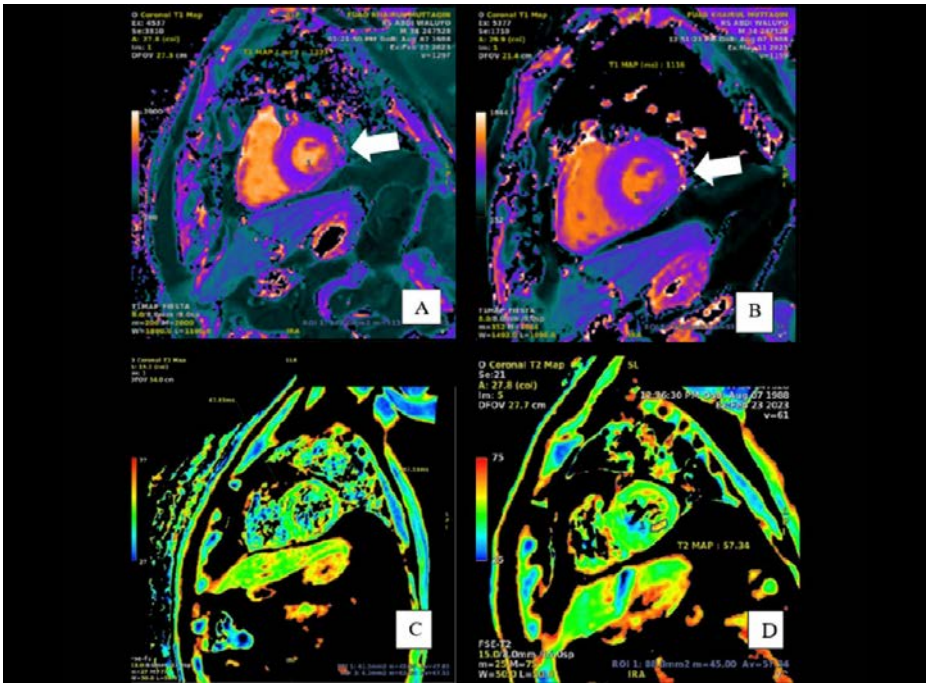

Figure 4. T1 mapping showed a decreased T1 value in the inferior region from the initial T1 value (Figure 4a) of 1,223 ms (N: 1,052±23 ms) to 1-year follow-up (Figure 4b) with a T1 value of 1,116 ms (N: 1052±23 ms). T2-mapping showed a decrease in native T2 value in the inferior region from the initial T2 value (Figure 4c) of 67.53 ms (N: 45.1±3.4 ms) to 1-year follow-up (Figure 4d) with T2 value of 57.34 ms (N: 45.1± 3.4 ms). Both parameters indicated partial resolution of myocarditis and subsequent myocardial edema (white arrow).

with palpitations and syncope as a symptom of arrhythmia in 18% of cases. However, myocarditis symptoms usually begin with prodromal symptoms in 80% patients, including flu-like symptoms, respiratory, and/or gastrointestinal illness.[6] This is similar to our patients, their symptoms varied from palpitation to classic CHF symptoms with concomitant dilated cardiomyopathy.

LGE is a technique that is frequently used in CMR to visualize cardiac tissue. Increasingly diffuse inflammation, commonly found in myocarditis after the first several days in transition from acute to subacute phase, is captured in homogenous signal intensity throughout the myocardium, which hinders detection of a discrete lesion by qualitative review and may lead to a missed diagnosis of myocarditis. Therefore, in the revised LLC, LGE was not the main diagnostic tool to confirm the diagnosis of myocarditis.[4] The revised LLC has a higher sensitivity and similar specificity, respectively 87.5% and 96.2% compared to 72.5% and 96.2% ($p = 0.031$).[7] In all of our patients, diagnosis of myocarditis can be achieved with revised LLC, based on the T1 and T2 criteria.

The major advantage of these sequences is their ability to quantitatively assess myocardial abnormalities. T1-T2 mapping allows comparison based on the normal value of the related tissues.[3] T1 mapping has been reported capable of detecting myocarditis in its various stages. However, it may be less sensitive in discriminating between the inflammatory and non-inflammatory conditions in chronic symptoms due to similar diffuse fibrosis characteristics.[2]

In contrast, T2 mapping is currently considered as the only technique that may adequately discriminate inflammatory (myocarditis) and non-inflammatory conditions in chronic cases (>2 weeks). They also allowed quantitative visualization of myocardial edema which correlates with injury and inflammatory conditions in the myocardium that usually appeared 4-6 weeks after onset of myocardial insult. Von Knobelsdorff-Brenkenhoff, *et al*, reported that a combination of T1 and T2 mapping resulted in a diagnostic accuracy of myocarditis to 86.1%.[8] Compared to LGE, T1 and T2 mapping allows more accurate quantification of edema and fibrosis compared to LGE.[2]

T2 mapping was also used regarding its capability to identify the presence of myocardial inflammation in patients with dilated cardiomyopathy. Furthermore, a cut-off T2 value of 65.3 ms has been reported to diagnose inflammatory conditions in dilated cardiomyopathy, with a sensitivity and specificity of 79% and 58% respectively. Regarding those findings, it is important to look for the regional elevation of T2 value.[9,10] In our patient, an increase in T2 value was seen in patients with dilated cardiomyopathy, which leads to our suspicion of inflammatory processes such as myocarditis. It needs to be highlighted that the high T2 value in the patient indicates the presence of chronic myocarditis, not healed nor "physiologic" dilated cardiac. Therefore, an increase in T2 value would be an indication of myocardial biopsy for further evaluation.

Conclusion

CMR using LGE combined with T1-T2 mapping allows the diagnosis of myocarditis. Recovery of T1 and T2 values during follow-up allows quantitative measurement of patients' condition and treatment success.

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