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ORIGINAL ARTICLE

Diagnostic values of edema-sensitive T2-weighted imaging, TSE T1-weighted early contrast-enhanced imaging, late gadolinium enhancement, and the Lake Louise criteria in assessing acute myocarditis: A single-center cardiac magnetic resonance study

Akut miyokardit tanısında kardiyak MRG incelemede T2-ağırlıklı ödem duyarlı incelemenin, TSE T1-ağırlıklı erken kontrastlı incelemenin, geç kontrast tutulumunun ve Lake Louise konsensüs kriterlerinin tanısal değeri

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ABSTRACT

Objective: The aim of this study was to evaluate the diagnostic accuracy of the Lake Louise consensus criteria using cardiac magnetic resonance (CMR) imaging assessment of edema, hyperemia, and late gadolinium enhancement (LGE) in the diagnostic determination of acute myocarditis.

Methods: A total of 44 patients with acute myocarditis and 24 healthy controls were included in this retrospective study. The presence of edema was defined as a myocardial mean signal intensity >1.9 times that of the skeletal muscle in the same slice on T2-weighted short tau inversion-recovery sequences. Hyperemia was defined as an early gadolinium enhancement ratio (EGEr) ≥4 calculated using the contrast-enhancement of the myocardium and skeletal muscle on TSE T1-weighted sequences, and LGE was assessed by visual examination. The reference methods used to determine the presence of myocarditis were based on the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases guidelines for clinical and biochemical findings.

Results: The diagnostic accuracy of edema, hyperemia, LGE, and the Lake Louise criteria (at least 2 of 3 components) was 75.7%, 64.2%, 88.5%, and 84.2%, respectively. Among the 3 components of the Lake Louise criteria, edema had the highest specificity (100%), and LGE had the highest sensitivity (86%). The use of LGE and/or edema as a criterion for acute myocarditis revealed the highest diagnostic accuracy (92.8%) among the CMR sequences and combinations of components examined.

Conclusion: LGE and/or edema as a sole criterion for the diagnosis of acute myocarditis demonstrated better diagnostic accuracy than the Lake Louise criteria. The use of EGEr did not improve the performance of CMR-based diagnosis. Alternatives to the use of EGEr are recommended for the diagnosis of acute myocarditis.

ÖZET

Amaç: Akut miyokardit tanısında kardiyak manyetik rezonans görüntülemede (MRG) “Lake Louise konsensüs” kriterlerinin üç ana komponenti olan ödem, hiperemi ve geç kontrast tutulumunun (GKT) tanısal etkinliğini araştırmak.

Yöntemler: Geriye dönük olarak yürütülen bu çalışmaya akut miyokardit tanılı 44 hasta ve 24 sağlıklı kontrol dahil edildi. Kardiyak MRG’de ödem varlığı T2-ağırlıklı STIR imajlarda miyokart üzerinde yaygın veya fokal olarak normal görünümdeki kas dokusundan 1.9 kat daha fazla sinyal artışı olarak tanımlandı. Hiperemi T1-ağırlıklı turbo spin eko sekanslarda miyokardın erken kontrast tutulum oranının aynı kesitteki kaslardan 4 kat veya daha fazla olması olarak tanımlandı. GKT ise görsel olarak değerlendirildi. Akut miyokardit tanısı için referans yöntem Avrupa Kardiyoloji Derneği’nin kılavuzlarına uyumlu olacak şekilde klinik ve biyokimyasal belirteçler olarak kabul edildi.

Bulgular: Ödem, hiperemi, GKT ve Lake Louise kriterinin (3 bulgudan en az ikisi) tanısal doğruluğu sırasıyla %75.7, %64.2, %88.5 ve %84.2 idi. Lake Louise kriterlerinden özgüllüğü en yüksek olan %100 ile ödemdi. Duyarlılığı en yüksek kriter ise GKT idi (%86). Akut miyokardit tanısı için GKT ve/veya ödem varlığı kriter olarak kabul edildiğinde en yüksek tanısal doğruluk değeri elde edildi (%92.8).

Sonuç: Akut miyokardit tanısında GKT ve/veya ödem varlığı tanı kriteri olarak kabul edildiğinde Lake Louise kriterlerine göre daha yüksek tanısal doğruluk elde edildi. Bu çalışmada erken kontrast tutulum oranının kardiak MRG incelemenin akut miyokardit tanısını koymada tanısal doğruluğa katkıda bulunmadığı saptanmıştır. Bu nedenle kardiyak MRG’de erken kontrast tutulum oranının akut miyokardit tanısındaki katkısının sorgulanmasını ve tanı için alternatif yöntemlerin geliştirilmesini öneriyoruz.

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Acute myocarditis refers to inflammation of the myocardium.[1,2] Acute myocarditis has been reported to be the cause of sudden cardiac death in as many as 12% of young adults.[3] The underlying cause of acute myocarditis remains undetermined in the vast majority of patients, in part because a broad range of agents, including viral infections, toxins, autoimmunity, and drugs, can lead to acute myocarditis.[4] Acute myocarditis patients may present with a variety of symptoms and signs, ranging from mild chest pain to heart failure and cardiogenic shock.[5–7] The diverse clinical pictures make diagnosis challenging. The gold standard method to diagnose acute myocarditis is endomyocardial biopsy (EMB); however, given the invasiveness of the technique and its potential complications, EMB is not routinely used in daily practice.[4,8,9] Furthermore, sampling error is a substantial limitation factor for EMB.[9]

Cardiac magnetic resonance (CMR) imaging plays a significant role in the diagnosis of acute myocarditis due to its ability to identify functional and structural abnormalities of the heart and to indirectly identify and characterize underlying histopathological changes in the myocardium.[2,10,11] A 2009 white paper proposed an initial set of criteria to identify acute myocarditis using CMR that are referred to as the Lake Louise consensus criteria.[2] The confirmation of 2 of the 3 major criteria was sufficient to diagnose the condition: hyperemia, identified according to the early gadolinium enhancement ratio (EGEr); edema, identified by edema-sensitive CMR sequences; and late gadolinium enhancement (LGE).[2] However, the robustness of the criteria components, particularly the assessment of edema on T2-weighted images and hyperemia on T1-weighted images, has been a subject of debate.[10–12]

The objective of this study was to assess the diagnostic accuracy of the Lake Louise consensus criteria and evaluations of hyperemia, edema, and LGE to diagnose acute myocarditis.

METHODS

The local ethics committee approved this retrospective study and the institutional board waived the need for informed consent for the use of de-identified medical and clinical patient data. The hospital picture archiving and communicating system (PACS; ExtremePacs, Ankara, Turkey) records were reviewed for CMR requests with a diagnosis of acute myocarditis based on clinical and biochemical results. EMB is not routinely performed in our hospital in cases of suspected acute myocarditis; therefore, histopathological analyses were not available. CMR findings were not taken into account while forming the eligibility criteria of the study since the primary purpose of the present work was to assess the diagnostic performance of CMR sequences in assessing acute myocarditis. The inclusion criteria were contrast-enhanced magnetic resonance images (MRI), a 24-hour Holter monitoring report, and a clinical diagnosis of acute myocarditis based on the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases recommendations,[13] that is, any of the clinical presentation criteria in addition to any of the diagnostic criteria, in the absence of angiographically detectable coronary artery disease or known pre-existing cardiovascular disease or extra-cardiac causes that could explain the syndrome. The clinical presentations compatible with acute myocarditis are acute chest pain; new or worsening dyspnea at rest or exercise, and/or fatigue, with or without left and/or right heart failure present for up to 3 months; palpitations or unexplained arrhythmia symptoms, and/or syncope, and/or aborted sudden cardiac death; or unexplained cardiogenic shock. In addition, new results of an abnormal 12-lead electrocardiogram and/or Holter and/or stress test that includes a I to III degree atrioventricular block, bundle branch block, ST/T wave change (ST elevation or non-ST elevation, T wave inversion), sinus arrest, ventricular tachycardia or fibrillation and asystole, atrial fibrillation, reduced R wave height, intraventricular conduction delay (widened QRS complex), abnormal Q waves, low voltage, frequent premature

Abbreviations:

AUC	*Area under the curve*
CIn	*Cardiac index*
CI	*Confidence interval*
CMR	*Cardiac magnetic resonance*
CO	*Cardiac output*
EDV	*End diastolic volume*
EF	*Ejection fraction*
EGEr	*Early gadolinium enhancement ratio*
EMB	*Endomyocardial biopsy*
ESV	*End-systolic volume*
LGE	*Late gadolinium enhancement*
LV	*Left ventricle*
MRI	*Magnetic resonance imaging*
NPV	*Negative predictive value*
PPV	*Positive predictive value*
ROC	*Receiver operating characteristic*
ROI	*Region of interest*
RV	*Right ventricle*
SSFP	*Steady-state free precession*
STIR	*Short tau inversion- recovery*
SV	*Stroke volume*
TLVM	*Total left ventricular mass*
TSE	*Turbo spin-echo*

beats, supraventricular tachycardia) are required. The criteria also include elevated myocardiocytolysis markers (cardiac troponins) or otherwise unexplained left ventricle (LV) and/or right ventricle (RV) structural and functional abnormality detected by cardiac imaging (regional wall motion or global systolic or diastolic function abnormality, with or without ventricular dilatation, with or without increased wall thickness, with or without pericardial effusion, with or without intraventricular or atrial thrombus).

Elevated inflammatory serum markers (e.g., C-reactive protein) and the presence of pericardial effusion are used as ancillary findings to support clinical diagnosis. The exclusion criteria are hypertrophic cardiomyopathy, storage disorders, a congenital heart disorder, and coronary artery disease.

CMR acquisition

All of the MRI studies were acquired with a 1.5 T scanner (Magnetom Aera; Siemens Healthineers GmbH, Erlangen, Germany). All of the CMR acquisitions were performed using phased-array body coils. All of the sequences were obtained using prospective cardiac gating. The CMR protocol for myocarditis consisted of a 9–12 stack of short-axis breath-hold cine images using balanced steady-state free precession imaging (SSFP) with the corresponding 4-chamber SSFP images for visual evaluation of focal ventricular functions and quantitative calculation of ejection fraction (EF), end diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), cardiac output (CO), cardiac index (CIn), and total left ventricular mass (TLVM); edema-sensitive, black-blood T2-weighted short tau inversion-recovery sequences (STIR); pre-contrast turbo spin-echo (TSE) breath-hold T1-weighted imaging; and post-contrast TSE breath-hold T1 weighted imaging using 0.10–0.12 mmol/kg gadolinium-diethylenetriamine pentaacetic acid (Magnevist; Bayer-Schering Pharma AG, Berlin, Germany) obtained within 2–3 minutes after contrast injection; and late gadolinium enhancement (LGE) sequences obtained in 4-chamber, 2-chamber, and short-axis views covering the entire LV myocardium approximately 12 minutes (range: 10–15 minutes) after the administration of the initial contrast material. The parameters were adjusted according to the manufacturer's standard parameters. Total acquisition time ranged between 40–60 minutes.

Image analysis

A single radiologist (D.A.) with 4 years of CMR interpretation experience evaluated all of the CMR images. First, the observer calculated EF, ESV, EDV, SV, CIn, CO, and TLVM with a modified Simpson's method on short-axis cine images using software (Argus; Siemens Healthineers GmbH, Erlangen, Germany). The LV myocardium was divided into 16 segments: 6 regions at the basal level, 6 regions at the midventricular level, and 4 regions at the apical level, as recommended by the American Heart Association segmentation model for the LV.[15]

Black-blood T2-weighted STIR sequence images were examined for the presence of edema, and inversion-recovery gradient-echo sequences were analyzed for the presence of LGE. Visual assessment according to existing guidelines was used to review axial, short--axis images to confirm the presence of edema and LGE on axial 4-chamber images. The observer placed a region of interest (ROI) on the LGE-positive areas as evaluated according to the initial visual examination. The final assessment of whether the area was LGE(+) or LGE(-) was determined by comparing the signal intensity of the area with the normal appearance of the myocardium. A signal intensity that was greater than the mean signal intensity plus 6 SD of the normal myocardium was accepted as LGE(+). To evaluate the presence of edema, the observer repeated the same procedure, but the mean signal intensity of the myocardial ROI was compared with the mean signal intensity of the ROI location on the skeletal muscle in the same slice, and the ratio >1.9 was accepted as edema positivity. After a focal edema assessment, to avoid overlooking global edema, the observer manually traced the borders of the myocardium and calculated a global mean signal of the myocardium and compared that signal with the skeletal muscle and the same ratio was accepted as the presence of global edema. Figure 1 shows the focal area of edema and LGE in the LV free wall in a patient with acute myocarditis.

To assess myocardial hyperemia, the observer manually traced the endocardial and epicardial borders on a pre-contrast T1-weighted image and overlaid these predefined contours on the post-contrast T1-weighted images. An ROI was noted on the skeletal muscle structure on the same slide for pre- and post-contrast T1-weighted images. The EGEr was calculated by evaluating the enhancement of the myocardium to

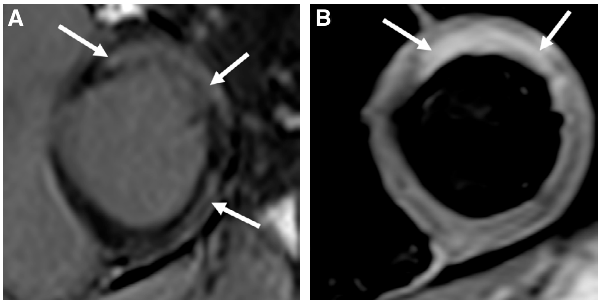

Figure 1. An 18-year-old male patient with acute myocarditis. (A) Late gadolinium enhancement (LGE) image shows an increased signal in the anterior and anterolateral wall extending from the midmyocardial to the subendocardial area, as well as the subepicardial area in the inferolateral wall (arrows). (B) TRIM T2-weighted image of the same patient shows midmyocardial to subendocardial signal increase in the anterior wall (arrows).

skeletal muscle as previously described.[2] The cutoff value of ≥4 was used for a binary classification of the patients as EGEr(+) and EGEr(-). Figure 2 shows the EGEr assessment of a patient with acute myocarditis.

Furthermore, to evaluate the image quality and interpretability of each sequence, 2 readers, each with approximately 2 years of CMR experience, were asked to categorize the T2-weighted STIR, EGEr, and LGE images of the patients as "poor quality," "acceptable quality," or "excellent quality." Inter-observer reliability was calculated for each sequence using the Kappa test.

Statistical analyses

All of the statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). All continuous variables were presented as mean±SD unless otherwise specified. The EF, EDV, ESV, CO, and SV values of patients with myocarditis and the healthy controls were compared using an independent samples t-test. The sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and diagnostic accuracy of the edema-sensitive T2-weighted STIR sequence, the TSE T1-weighted sequence, the LGE sequence, and the Lake Louise criteria were calculated using the clinical and biochemical diagnosis of myocarditis as a reference method. Receiver operating curve (ROC) analysis was used to assess the performance of the Lake Louise criteria and the edema, hyperemia, and LGE assessments in the diagnosis of acute myocarditis.

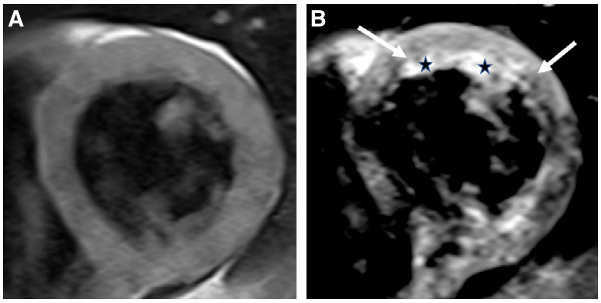

Figure 2. T1-weighted turbo spin echo (A) pre- and (B) post-contrast images of another patient with acute myocarditis. The signal increase depicted in the anterolateral wall of the left ventricle on post-contrast image (arrows) compared with pre-contrast image reflects hyperemia. Note: asterisks indicate blood pool enhancement, not myocardial hyperemia.

RESULTS

A total of 44 patients with myocarditis, 30 male and 14 female, and 24 age- and sex-matched healthy controls, 16 male and 8 female, were included in the study. The mean age of the patients was 38.15±10.82 years and the mean age of the healthy controls was 35.12±8.88 years ($p>0.05$). CMR examinations were performed within 5.67±2.95 days (range: 1–14 days) after the onset of symptoms. Table 1 provides details of the CMR findings of the study patients and healthy controls. The first observer rated the T2-weighted STIR image quality as poor in 2 cases, acceptable in 19 cases, and excellent in 22 cases, while the second observer rated the image quality as poor in 2 cases, acceptable in 20 cases, and excellent in 21 (Kappa value: 0.8, indicating excellent inter-observer agreement). The first observer rated the T1-weighted TSE pre- and post-contrast image quality as poor in 7 cases, acceptable in 26 cases, and excellent in 10 cases, while the second observer rated the image quality as poor in 10 cases, acceptable in 23 cases, and excellent in 10 (Kappa value: 0.62, indicating substantial inter-observer agreement). The first observer rated LGE image quality as poor in 3 cases, acceptable in 17 cases, and excellent in 23 cases, while the second observer rated the image quality as poor in 4 cases, acceptable in 16 cases, and excellent in 23 (Kappa value: 0.8, indicating excellent inter-observer agreement).

Myocardial edema

Of 44 patients, focal myocardial edema was seen in 27 cases according to the visual assessments. Notably, none of the healthy controls had focal myocardial edema; hence, the specificity of myocardial edema was 100% in the present study. Figure 1 is an image of a patient with myocardial edema in the lateral wall. The sensitivity, specificity, NPV, PPV, and diagnostic accuracy of LGE in diagnosing myocarditis are shown in Table 2. Figure 3 shows a ROC curve analysis of myocardial hyperemia for the diagnosis of acute myocarditis (area under the curve [AUC]: 0.80; 95% confidence interval [CI]: 0.70–0.90)

Myocardial hyperemia

Of 44 patients, only 27 (61.4%) cases revealed an EGEr above the cut-off value of 1.9. Figure 2 is an image of a myocarditis patient with an EGEr above the cut-off value. The sensitivity, specificity, NPV, PPV, and diagnostic accuracy of LGE to diagnose myocarditis are shown in Table 2. Figure 3 shows a ROC curve analysis of myocardial hyperemia for the diagnosis of acute myocarditis (AUC: 0.65; 95% CI: 0.52–0.78).

Late gadolinium enhancement

Of 44 patients, 38 (86.4%) had LGE to some extent. LGE was most commonly located in the lateral myocardial wall (74%), followed by inferior (33%), septal (22%), and anterior (12%) locations. LGE can have a mid-myocardial, subepicardial, mid-myocardial and subepicardial, or a transmural pattern. No pure subendocardial LGE was observed in this study cohort. We identified LGE in 2 of 24 (8.3%) healthy controls, located in the junction points of the left and right ventricles in both cases. The sensitivity, specificity, NPV, PPV, and diagnostic accuracy of LGE in diagnosing myocarditis are shown in Table 2. Figure 3 shows a ROC curve analysis of LGE for the diagnosis of acute myocarditis (AUC: 0.89; 95% CI: 0.80–0.97).

Table 1. Cardiac magnetic resonance imaging findings of myocarditis (+) patients and healthy controls, and comparison of findings between the groups

Variables	Myocarditis (+)	Healthy controls	*p* value
	Mean±SD	Mean±SD	
Age (years)	38.15±10.82	35.12±8.88	NS
Myocardial mass (g/m²)	73.61±16.71	67.92±8.84	NS
Ejection fraction (%)	52.77±15.29	59.73±6.22	0.001
End systolic volume (mL/m²)	50.75±39.92	31.15±8.29	<0.0001
End diastolic volume (mL/m²)	97.82±38.87	75.31±8.84	<0.0001
Cardiac index (L/min/m²)	3.46±0.81	3.74±0.82	NS
Stroke volume (mL/m²)	46.34±9.16	51.1±6.63	NS
Cardiac output	6.33±1.64	6.72±1.25	NS

*All variables are expressed as mean±SD unless otherwise specified. SD: Standard deviation.

Table 2. Sensitivity, specificity, negative predictive value, positive predictive value, and diagnostic accuracy of CMR parameters and combinations in assessing acute myocarditis

	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Diagnostic accuracy (%)
LGE	86	92	80	95	88.5
EGEr	61.4	51.4	69.2	77.1	64.2
Edema	61.4	100	60.5	100	75.7
LGE and/or edema	93.2	92.3	88.9	95.3	92.8
LGE and/or EGEr	93.2	65.4	85	82	82.8
Lake Louise criteria	77.3	96.2	71.4	97.1	84.2

CMR: Cardiac magnetic resonance imaging; EGEr: Early gadolinium enhancement ratio; LGE: Late gadolinium enhancement; NPV: Negative predictive value; PPV: Positive predictive value.

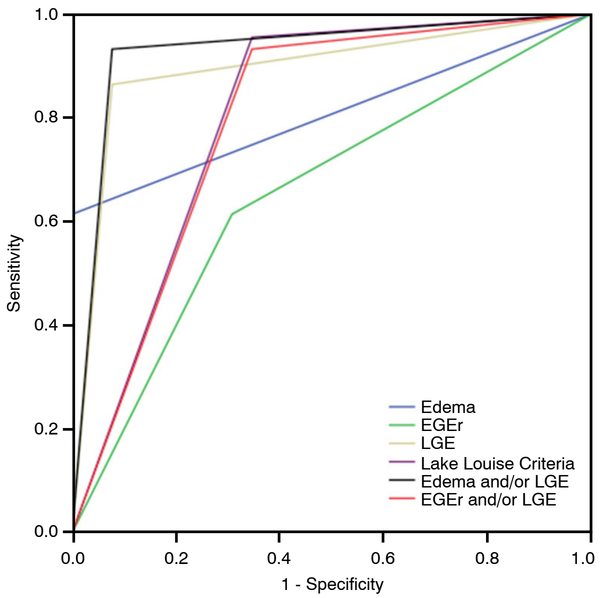

Figure 3. Receiver operating characteristic curve analysis of edema, late gadolinium enhancement (LGE), early gadolinium enhancement ratio (EGEr), and the Lake Louise criteria, LGE and/or edema, and LGE and/or EGEr for the diagnosis of acute myocarditis. LGE: Area under the curve (AUC): 0.89, 95% confidence interval (CI): 0.80–0.97; edema: AUC: 0.80, 95% CI: 0.70–0.90; EGEr: AUC: 0.65, 95% CI: 0.52–0.78; Lake Louise criteria: AUC: 0.80, 95% CI: 0.68–0.92; LGE and/or edema: AUC: 0.92.7, 95% CI: 0.85–1; LGE and/or EGEr : AUC: 0.79, 95% CI: 0.67–0.91.

Lake Louise criteria

Among 44 patients, 34 (77.3%) met the Lake Louise criteria definition for diagnosis (2 of 3 major criteria). The sensitivity of the Lake Louise criteria was lower than that of LGE assessment (77.3% vs. 86.4%). The Lake Louise criteria misdiagnosed 1 healthy control (3.8%) as myocarditis, while LGE misclassified 2 healthy controls (7.6%) as myocarditis. The sensitivity of the Lake Louise criteria was higher than that of edema or hyperemia evaluation alone (77.3% vs. 61.4% for each), while the specificity of edema was slightly higher than the Lake Louise criteria (100% vs. 96.2%). The patient with a misdiagnosis of acute myocarditis according to the Lake Louise criteria had hyperemia and LGE. The sensitivity, specificity, NPV, PPV, and diagnostic accuracy of the Lake Louise criteria in diagnosing myocarditis are shown in Table 2. Figure 3 shows a ROC curve analysis of the Lake Louise criteria for the diagnosis of acute myocarditis (AUC: 0.80; 95% CI: 0.68–0.92).

We evaluated different combinations of assessments to diagnose acute myocarditis against the Lake Louise criteria. Accepting the presence of myocardial edema or LGE, or both of them as a CMR criterion of acute myocarditis revealed a higher diagnostic accuracy compared with the Lake Louise criteria (93.2% vs. 84.2%), but with slightly lower specificity (92.3% vs. 96.2%). On the other hand, accepting the presence of hyperemia or LGE, or both of them as a CMR criterion of acute myocarditis revealed lower diagnostic accuracy than the Lake Louise criteria (84.2% vs. 82.8%) with low specificity (65.4%) (Table 2). Figure 3 shows a ROC curve of LGE and/or edema and LGE and/or EGEr for the diagnosis of acute myocarditis.

DISCUSSION

The findings of the present study show that LGE demonstrated better sensitivity in diagnosing acute myocarditis compared with myocardial edema, myocardial hyperemia, and the Lake Louise criteria. The Lake Louise criteria had only a slightly higher specificity compared with LGE, while using the presence of LGE or myocardial edema as a criterion for an acute myocarditis diagnosis provided superior sensitivity, specificity, and diagnostic accuracy than the other methods.

Myocardial edema

Edema, which represents underlying inflammation, is one of the hallmark CMR findings of acute myocarditis.[15,16] A black-blood T2-weighted STIR sequence is a validated method to identify edema in acute myocarditis.[2] However, it is susceptible to arrhythmia and respiratory motion, which might lead to overlooking the underlying inflammation.[2] Furthermore, mild inflammation might not be detectable on black-blood T2 weighted STIR sequences.[17,18] The sensitivity of myocardial edema assessment was rather low compared with LGE and the Lake Louise criteria in the present study. The relatively low sensitivity of edema (61.4%) was comparable with the results of several previous studies,[13,19] while substantially lower than others.[11] The mean time interval between the onset of myocarditis symptoms and the CMR examinations was 5.67±2.95 days (range: 1–14 days) in this study. It is well known that edema may resolve during the course of the disease; hence, these circumstances, particularly in patients who underwent CMR later, might have contributed to the relatively low sensitivity of the T2-weighted STIR sequences in detecting edema. Notably, none of the healthy controls had increased signal intensity above the cut-off value of 1.9 in our study cohort, yielding a specificity of edema of 100%. Chu et al.[12] also found that the presence of edema had 100% specificity for acute myocarditis. Since black-blood T2-weighted STIR sequence CMR is prone to artifacts, we tried to eliminate potential false-positive signals on STIR images by confirming the presence of edema in 2 different planes. Nevertheless, we should acknowledge that the specificity of black-blood T2-weighted STIR is still questionable and should be interpreted with caution in daily practice.[20]

Myocardial hyperemia

EGEr is a surrogate marker of underlying inflammation-induced hyperemia in acute myocarditis.[21,22] However, of the 3 Lake Louise criteria, EGEr assessment is the most debatable.[12,19] Initial studies evaluating EGEr as an indicator of acute myocarditis had promising results.[11,17] However, later studies reported diagnostic accuracy rates as low as 60%, which is consistent with the diagnostic accuracy of our findings (64.2%).[12,19] However, the susceptibility of the technique to motion artifacts, the need for quantitative measurements, and the potential misdiagnosis of normal EGEr in cases of accompanying myositis, which is quite common in systemic viral infections, limit the utility.[2] Therefore, drawing on our findings and those of previous reports, we suggest that the reliability of EGEr as a marker for acute myocarditis seems to be vague compared with the other 2 criteria.

Late gadolinium enhancement

LGE is a relatively novel CMR sequence with an ability to non-invasively characterize pathological alterations in the myocardium.[23–25] LGE is a validated tool for the assessment of myocardial fibrosis.[26,27] In cases of acute myocarditis, an increased signal on LGE sequences is more likely to occur due to necrosis and irreversible myocyte damage, rather than fibrosis.[16,27] The present study revealed that LGE demonstrated excellent diagnostic accuracy for the assessment of acute myocarditis, higher than that of the Lake Louise criteria (88.5% vs. 84.2). Previous research has reported an incidence of LGE that varied from 44% to 84%, and the results of the present study are in the upper end of the spectrum with 84.2% sensitivity.[11,18,28] LGE might also serve to differentiate between acute myocarditis and acute myocardial infarct, since the former is almost always located in the epicardial/midmyocardial layer, while the latter is typically seen in the subendocardial area.[29]

Lake Louise criteria and LGE and/or edema

The Lake Louise criteria were proposed for the diagnosis of acute myocarditis in a white paper by Friedrich et al.[2] in 2009. Since then, many studies have evaluated and validated the diagnostic value of the criteria.[11,12,17,19] The robustness of the Lake Louise criteria was also established in histopathological studies.[30] The diagnostic accuracy of the criteria was 78% in the initial report (white paper) derived from the pooled data of 130 patients, while the diagnostic accuracy of LGE and/or edema was quite low (62%). [2] Further studies revealed that the Lake Louise criteria had a diagnostic accuracy ranging from 77% to 85% for the diagnosis of, acute myocarditis, which is comparable to the diagnostic accuracy of the present study (84.2%).[12,19,30,31] Notably, when LGE and/or edema were used as a sole criterion for the diagnosis, we obtained a better diagnostic accuracy compared with the Lake Louise criteria (92.8% vs. 84.2%), with slightly lower specificity (92.3% vs. 96.2%). Chu et al.[12] also noted better diagnostic accuracy using LGE and/or edema as a sole criterion compared with the Lake Louise criteria.

Limitations

First and foremost, our study was retrospective in design, with a relatively small sample size, which might affect the reliability of our results. Second, we did not obtain EMB results; the acute myocarditis diagnosis was established based on clinical and biochemical findings. Many other studies have also not included the use of EMB, and EMB, while a reference method for the diagnosis of acute myocarditis, is not routinely employed in daily practice.[12,19] Third, we did not use novel quantitative CMR methods, such as quantitative T1 and T2 mapping, which have yielded promising results in other studies.[19] Despite these limitations, the existing evidence regarding the use of the Lake Louise criteria and its main components of edema, hyperemia, and LGE in the diagnosis of acute myocarditis is scarce in Turkish population. This study should be seen as another step in exploring the diagnostic accuracy of the Lake Louise criteria for the diagnosis of acute myocarditis. However, our results should be validated by additional multicenter research.

Conclusion

LGE and/or edema as a sole criterion for the diagnosis of acute myocarditis had better diagnostic accuracy compared with the Lake Louise criteria. EGEr had the lowest diagnostic accuracy of the other 2 criteria, and the use of EGEr did not improve the performance of CMR-based diagnosis. We suggest that prospective future research is needed to explore alternative approaches other than EGEr for the diagnosis of acute myocarditis.

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Data Statement: According to our institute policy, the data of the present work available from the corresponding author on reasonable request.

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Anahtar sözcükler: Akut miyokardit; geç kontrast tutulumu; hiperemi; MRG; Ödem.