Original Article | Cardiovascular Imaging

eISSN 2005-8330
https://doi.org/10.3348/kjr.2022.0898
Korean J Radiol 2023;24(6):512-521

Korean Journal of Radiology
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Left Atrial Strain Derived From Cardiac Magnetic Resonance Imaging Can Predict Outcomes of Patients With Acute Myocarditis

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Objective: There is increasing recognition that left atrial (LA) strain can be a prognostic marker of various cardiac diseases. However, its prognostic value in acute myocarditis remains unclear. Therefore, this study aimed to evaluate whether cardiovascular magnetic resonance (CMR)-derived parameters of LA strain can predict outcomes in patients with acute myocarditis.
Materials and Methods: We retrospectively analyzed the data of 47 consecutive patients (44.2 ± 18.3 years; 29 males) with acute myocarditis who underwent CMR in 13.5 ± 9.7 days (range, 0–31 days) of symptom onset. Various parameters, including feature-tracked CMR-derived LA strain, were measured using CMR. The composite endpoints included cardiac death, heart transplantation, implantable cardioverter-defibrillator or pacemaker implantation, rehospitalization following a cardiac event, atrial fibrillation, or embolic stroke. The Cox regression analysis was performed to identify associations between the variables derived from CMR and the composite endpoints.
Results: After a median follow-up of 37 months, 20 of the 47 (42.6%) patients experienced the composite events. In the multivariable Cox regression analysis, LA reservoir and conduit strains were independent predictors of the composite endpoints, with an adjusted hazard ratio per 1% increase of 0.90 (95% confidence interval [CI], 0.84–0.96; $P = 0.002$) and 0.91 (95% CI, 0.84–0.98; $P = 0.013$), respectively.
Conclusion: LA reservoir and conduit strains derived from CMR are independent predictors of adverse clinical outcomes in patients with acute myocarditis.
Keywords: Myocarditis; Magnetic resonance imaging; Major adverse cardiovascular events; Left atrium

INTRODUCTION

Myocarditis is an acute or chronic inflammatory disease of the myocardium that can be caused by infection, immune-mediated responses, or toxic insults [1]. The clinical presentation of myocarditis is heterogeneous, ranging from chest pain or palpitations to life-threatening ventricular shock or malignant arrhythmias [1-3]. Furthermore, myocarditis is an important cause of sudden cardiac death and dilated cardiomyopathy [3,4]. Predictors of poor outcome in myocarditis include advanced New York Heart Association functional class, the presence of certain viruses, or immunohistological signs of inflammation identified by endomyocardial biopsy, decreased left ventricular (LV) function, and the presence and anteroseptal location of late gadolinium enhancement (LGE) [5-8].

Cardiovascular magnetic resonance (CMR) imaging has emerged as a primary noninvasive method for the diagnosis

Received: November 16, 2022 **Revised:** February 20, 2023
Accepted: March 10 2023
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and risk stratification of myocarditis [9]. A recent meta-analysis demonstrated that the presence and anteroseptal location of LGE are independent prognostic markers of adverse cardiac outcomes in patients with acute myocarditis [8]. Several investigators recently reported the role of CMR-derived LV strain in patients with myocarditis [10,11]. Lee et al. [10] evaluated the relationship between CMR-derived LV strain parameters and adverse cardiac events (cardiac death, transplantation, implantable cardioverter-defibrillator or pacemaker insertion, hospitalization, or stroke) during a 41-month follow-up period. The authors suggested the possibility of an independent association between reduced LV strain and adverse events.

Left atrial (LA) strain is a parameter used to quantify LA phasic function and is a potentially more sensitive indicator of real-time filling pressure than LA volume [12]. LA strain can be obtained using cine images of CMR as well as echocardiographic images and has recently demonstrated incremental diagnostic and prognostic value in a number of common cardiac diseases [13-16]. To our knowledge, few studies have examined the predictive value of LA strain measurements in predicting poor outcomes in patients with acute myocarditis [17]. Pastore et al. [17] assessed the prognostic role of echocardiography-derived LA strain in 30 patients with acute myocarditis. They suggested that lower LA strain values may characterize patients at higher risk of incident atrial fibrillation. However, echocardiography-derived LA strain parameters were compared without adjusting for clinical or other echocardiographic parameters. Furthermore, the study did not include a control group. Therefore, this study aimed to evaluate whether CMR-derived LA strain parameters can predict outcomes in patients with acute myocarditis.

MATERIALS AND METHODS

This retrospective study was approved by the Institutional Review Board (IRB) of Pusan National University Hospital, which waived the requirement for written informed consent (IRB No. 2208-019-118).

Study Population

Patients were considered eligible for inclusion if they met the clinical and imaging diagnostic criteria for myocarditis. The clinical diagnosis was based on the position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases [18]. Patients with symptoms suggestive of acute myocarditis who fulfilled at least one of the following diagnostic criteria, including electrocardiogram abnormalities, elevated troponins, functional and structural abnormalities on cardiac imaging, and tissue characterization by CMR, were included in this study. The imaging diagnosis was based on the presence of ≥ 2 of the 3 Lake Louise criteria (T2-weighted ratio, ≥ 2.0; early gadolinium enhancement ratio, ≥ 4.0; and nonischemic LGE pattern) [19]. Patients were excluded if: 1) they had any prior evidence or CMR characteristics of other cardiac comorbidities; 2) they had poor CMR image quality; 3) the duration between symptom onset and CMR performance was > 1 month; or 4) they were lost to follow-up (Fig. 1).

To compare the CMR parameters between patients and healthy controls, CMR findings were retrospectively analyzed in 10 prospectively collected healthy participants with no cardiac symptoms, no history of cardiovascular disease, unremarkable findings on physical examination, and a low probability of heart disease. All healthy controls had normal CMR results, without any structural abnormalities.

CMR

CMR examinations were performed using a 1.5-T (Magnetom Sonata; Siemens Healthcare) or 3.0-T scanner (Achieva, Philips Healthcare; Magnetom Skyra, Siemens Healthcare). All cine images were acquired using a balanced steady-state free precession sequence during a gentle expiratory breath hold. In all patients and controls, short-axis cine images were obtained from the cardiac base to the apex as well as long-axis cine images in two- and four-chamber views following image parameters (time to echo [TE]/repetition time [TR]/flip-angle = 1.1 ms/54.8 ms/50°, slice thickness = 8 mm, gap = 2 mm, matrix = 192 x 119, temporal resolution = 25 frame per beat [Magnetom Sonata]; TE/TR/flip-angle = 1.5 ms/2.9 ms/40°, slice thickness = 10 mm, no gap, matrix = 176 x 168, temporal resolution = 25 frame per beat [Achieva]; TE/TR/flip-angle = 1.1 ms/57.9 ms/79°, slice thickness = 8 mm, gap = 2 mm, matrix = 192 x 109, temporal resolution = 25 frame per beat [Magnetom Skyra]). All patients underwent LGE imaging with whole-heart coverage of the short axis following the administration of 0.2 mmoL/kg gadobutrol (Gadovist; Bayer Schering Pharma), using a T1-weighted middiastolic inversion recovery sequence and a patient-adapted prepulse. Detailed CMR protocols have been described previously [10].

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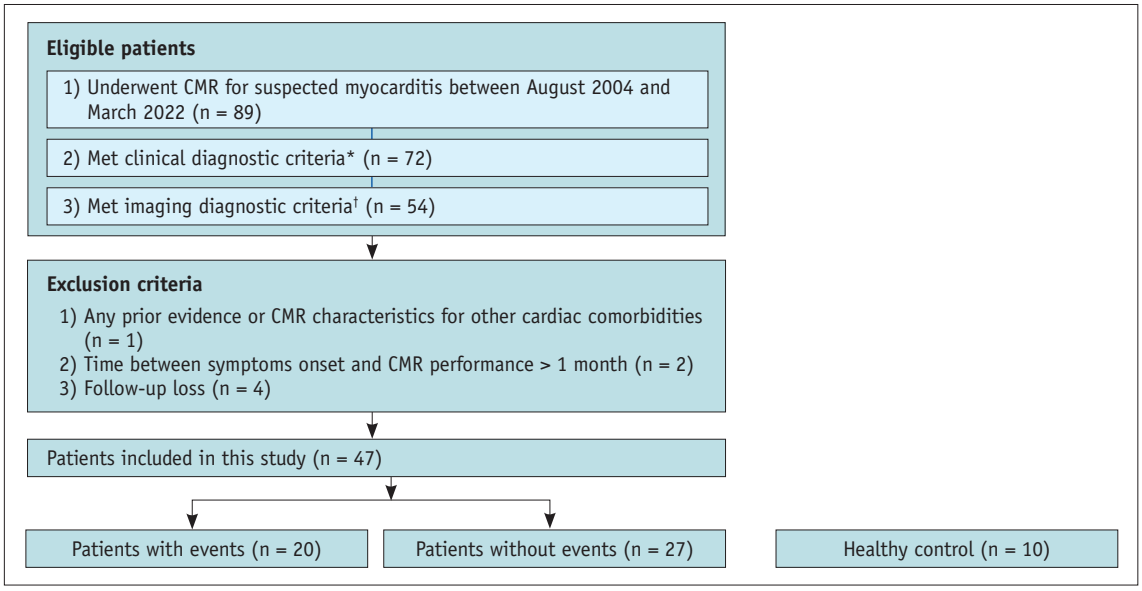

Fig. 1. Flowchart of study population. *The clinical diagnosis was based on the position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases (Caforio et al. *Eur Heart J* 2013;34:2636-2648, 2648a-2648d) [18], †The imaging diagnosis was based on the presence of ≥ 2 of 3 Lake Louise criteria (T2-weighted ratio ≥ 2.0, early gadolinium enhancement ratio ≥ 4.0, and nonischemic late gadolinium enhancement pattern) (Friedrich et al. *J Am Coll Cardiol* 2009;53:1475-1487) [19]. CMR = cardiovascular magnetic resonance

Image Analysis

Image analyses were performed by a blinded radiologist (JWL) with 12 years' experience performing cardiac imaging. All routine CMR analyses except strain were performed using commercially available software (cvi42; Circle Cardiovascular Imaging Inc.). The extent of myocardial LGE was assessed through the use of a semiquantitative analysis. The presence of LGE was evaluated in each of the 17 LV segments according to the consensus of the North American Society of Myocardial Imaging. The pattern of LGE was defined as anteroseptal, inferolateral, and other LGE [20].

QStrain v4.0 (Medis Suite v4.0; Medical Imaging Systems) was used for strain analysis. The feature-tracking CMR-derived LV strain was obtained based on two- and four-chamber long-axis cine images. The endo- and epicardial contours of the LV were manually drawn in the end-diastolic and end-systolic phases. The LV was automatically tracked over the cardiac cycle with subsequent averaging of the peak strain values to derive the LV global longitudinal strain. The feature tracking of the CMR-derived LA strain was obtained based on two- and four-chamber long-axis cine images. LA endocardial contours were drawn manually on the end-diastolic and end-systolic images, excluding the LA appendage and pulmonary veins (Fig. 2). The software automatically propagated the contours throughout the cardiac cycle. We checked the automatic tracking quality and manually adjusted the contours, as required. The values of the two- and four-chamber images were averaged for further analyses. Three aspects of LA strain were analyzed as previously described [21]: reservoir strain (corresponding to total strain), contractile strain (corresponding to active strain), and conduit strain (corresponding to passive strain). LA maximal volume (LAVmax) at ventricular end-systole and LA minimal volume (LAVmin) at ventricular end-diastole were also acquired. The LA ejection fraction was calculated using the following equation: LA ejection fraction = ([LAVmax – LAVmin]/LAVmax) x 100%. To assess intraobserver reproducibility, LA function measurements were repeated after 1 month in 20 randomly selected participants.

Clinical Outcomes

Outcomes were assessed through a chart review. Composite endpoints were defined as cardiac death, heart transplantation, implantable cardioverter-defibrillator or pacemaker implantation, rehospitalization following a cardiac event, atrial fibrillation, or embolic stroke.

Statistical Analysis

Categorical and continuous variables were compared using chi-square and independent student's *t*-test, respectively. After setting the cut-off value using receiver operating characteristic analysis, the Kaplan–Meier plots were

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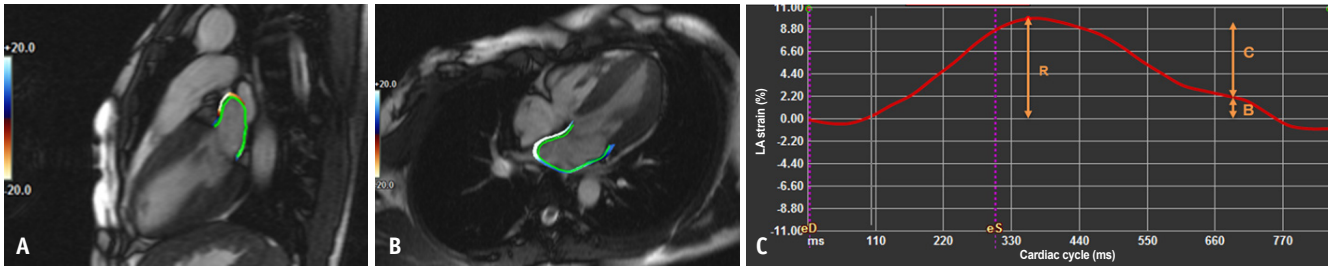

Fig. 2. Sample measurement of cardiac magnetic resonance-derived left atrial (LA) strain using the feature tracking method from two- and four-chamber cine images. **A, B:** Semiautomated tracking of the LA was performed on two- and four-chamber cine images, excluding the LA appendage and pulmonary veins. **C:** Representative plots of LA strain, along with measurements of reservoir (R), conduit (C), and contractile (B) function.

obtained to visualize event-free survival for the composite endpoints and were compared using the log-rank test [22]. Uni- and multivariable Cox proportional hazards models were used to assess independent associations between CMR-derived parameters and the composite endpoints. Parameters with values of $P < 0.05$ on the univariable analysis were incorporated into the multivariable analysis. All LA strain parameters were entered separately into models 1–3. To avoid collinearity, we measured the variance inflation factor, and one variable was included in the multivariable analysis among the parameters with a variance inflation factor greater than 3 [13].

Intraobserver reproducibility was calculated using the intraclass correlation coefficient (ICC), where an ICC < 0.4 represented poor reliability; ICC 0.4–0.75, fair to good reliability; and ICC > 0.75, excellent reliability. Statistical analysis was performed using the Statistical Package for the Social Sciences software (version 22; IBM SPSS Inc.). Statistical significance was set at $P < 0.05$.

RESULTS

Patient Characteristics

From the initial cohort of 89 consecutive patients who underwent CMR for suspected myocarditis between August, 2004 and March, 2022, 72 met the clinical diagnostic criteria proposed by the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases [18]. Of these, 54 met the diagnostic imaging criteria. Patients with any prior evidence or CMR characteristics of other cardiac comorbidities (n = 1), time between symptom onset and CMR performance > 1 month (n = 2), or follow-up loss (n = 4) were excluded. Therefore, 47 patients were included in the final analysis (Fig. 1). Ten healthy controls were separately included in this study. Among the study participants, 24 patients and 10 healthy controls were included in our previous study [10]. CMR was performed within 13.5 ± 9.7 days (range, 0–31 days) of symptom onset in patients with myocarditis. After a median follow-up of 37 months (interquartile range, 5–82 months), 20 (42.6%) of the 47 patients experienced composite events. Cardiac death occurred in four (10.8%), heart transplantation in one (2.1%), implantable cardioverter defibrillator or pacemaker implantation in two (4.3%), hospitalization following a cardiac event in seven (14.9%), new-onset atrial fibrillation in one (2.1%), and embolic stroke in five (10.6%) patients. Table 1 compares the baseline clinical and CMR characteristics between patients with myocarditis and healthy controls and between myocarditis patients with and without composite endpoints.

Prognostic Value of LA Strain

The Kaplan–Meier survival curves for the composite endpoint obtained before the multivariable Cox regression analysis are shown in Figure 3. In the Kaplan–Meier survival analysis, patients with an LA reservoir strain ≤ 19.9% or conduit strain ≤ 11.1% showed a higher rate of reaching the composite endpoint (log-rank, $P < 0.001$).

Table 2 displays the univariable Cox regression analysis results for the predictors of composite endpoints. The analysis revealed that left ventricle end-diastolic volume index (LV EDVI) (hazard ratio [HR], 1.01; 95% confidence interval [CI], 1.0–1.02; $P = 0.023$), left ventricle end-systolic volume index (LV ESVI) (HR, 1.01; 95% CI, 1.0–1.02; $P = 0.011$), LV mass index (LVMI) (HR, 1.03; 95% CI, 1.01–1.04; $P = 0.005$), LV ejection fraction (HR, 0.96; 95% CI, 0.94–0.98; $P < 0.001$), right ventricular (RV) ejection fraction (HR, 0.97; 95% CI, 0.94–0.99; $P = 0.019$), left atrium (LA) volume index (HR, 1.02; 95% CI, 1.0–1.05; $P = 0.042$), LA ejection fraction (HR, 0.94; 95% CI, 0.91–0.97; $P < 0.001$), LA reservoir

https://doi.org/10.3348/kjr.2022.0898

Table 1. Patient Characteristics

	Myocarditis (n = 47)	Healthy Control (n = 10)	*P*	Myocarditis with Composite Endpoints (n = 20)	Myocarditis without Composite Endpoints (n = 27)	*P*
Age, yr	44.2 ± 18.3	36.4 ± 9.8	0.197	51.1 ± 19.3	39.1 ± 16.0	0.026
Sex, female	18 (38.3)	5 (50.0)	0.724	6 (30.0)	12 (44.4)	0.242
Body mass index, kg/m^2	22.7 ± 3.5	22.0 ± 3.2	0.562	22.4 ± 2.9	22.9 ± 3.9	0.623
CMR findings						
LV EDVI, mL/m^2	87.5 ± 37.8	67.2 ± 10.7	0.002	103.9 ± 47.7	75.3 ± 22.5	0.020
LV ESVI, mL/m^2	51.8 ± 39.9	26.6 ± 5.3	< 0.001	72.2 ± 49.8	36.8 ± 21.3	0.007
LVMI, g/m^2	70.9 ± 23.9	46.4 ± 11.2	0.003	81.1 ± 29.4	63.4 ± 15.5	0.021
LV ejection fraction, %	45.7 ± 18.3	60.7 ± 3.0	< 0.001	34.8 ± 18.3	53.9 ± 13.6	< 0.001
LV global longitudinal strain, %	12.8 ± 7.0	22.5 ± 4.4	< 0.001	8.5 ± 5.4	16.1 ± 6.3	< 0.001
RV EDVI, mL/m^2	58.9 ± 18.9	67.1 ± 13.4	0.200	62.2 ± 22.5	56.5 ± 15.8	0.319
RV ESVI, mL/m^2	37.5 ± 54.6	27.6 ± 7.0	0.569	54.7 ± 80.8	24.8 ± 10.0	0.115
RV ejection fraction, %	51.3 ± 15.2	59.1 ± 5.3	0.008	44.1 ± 16.2	56.4 ± 12.5	0.006
Presence of LGE	40 (85.1)	N/A	N/A	19 (95.0)	21 (77.8)	0.108
Location of LGE						0.194
Anteoseptal LGE	23 (48.9)	N/A	N/A	13 (65.0)	10 (37.0)	
Inferolateral LGE	4 (8.5)	N/A	N/A	1 (5.0)	3 (11.1)	
Other LGE	13 (27.7)	N/A	N/A	5 (25.0)	8 (29.6)	
No LGE	7 (14.9)	N/A	N/A	1 (5.0)	6 (22.2)	
Number of LGE segments	4.2 ± 3.9	N/A	N/A	4.5 ± 4.6	4.0 ± 3.5	0.695
LA volume index, mL/m^2	39.3 ± 20.7	29.7 ± 5.2	0.007	45.0 ± 24.4	35.1 ± 16.8	0.107
LA ejection fraction, %	44.3 ± 17.2	60.3 ± 5.9	< 0.001	31.9 ± 14.9	53.5 ± 12.4	< 0.001
LA reservoir strain, %	23.7 ± 14.2	35.1 ± 4.0	< 0.001	13.5 ± 9.1	31.3 ± 12.5	< 0.001
LA contractile strain, %	9.6 ± 8.8	16.0 ± 3.7	0.001	6.0 ± 7.5	12.3 ± 8.8	0.014
LA conduit strain, %	14.1 ± 11.0	19.2 ± 5.4	0.040	7.5 ± 6.5	19.0 ± 11.2	< 0.001

Values are shown as n (%) or mean ± standard deviation unless otherwise indicated. CMR = cardiovascular magnetic resonance, EDVI = end-diastolic volume index, ESVI = end-systolic volume index, LA = left atrial, LGE = late gadolinium enhancement, LV = left ventricular, LVMI = LV mass index, RV = right ventricular, N/A = not applicable

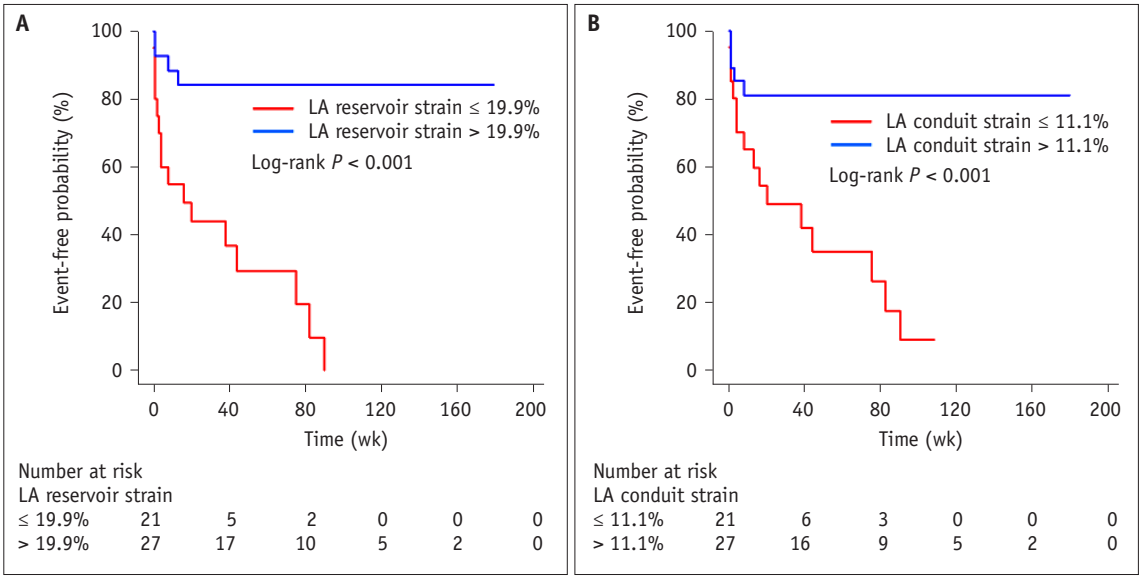

Fig. 3. The Kaplan–Meier curves according to left atrial (LA) strain. **A:** The Kaplan–Meier curves grouped according to LA reservoir strain cut-off value. **B:** The Kaplan-Meier curves grouped according to LA conduit strain cut-off value.

https://doi.org/10.3348/kjr.2022.0898

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strain (HR, 0.90; 95% CI, 0.86–0.95; $P < 0.001$), LA contractile strain (HR, 0.92; 95% CI, 0.86–1.0; $P = 0.040$), and LA conduit strain (HR, 0.90; 95% CI, 0.85–0.96; $P = 0.001$) were significantly associated with the composite endpoint.

In the multivariable analysis, all LA strain parameters were individually placed into the model. To avoid collinearity,

Table 2. Cox Proportional Hazards Regression Analysis of the Association with the Composite Endpoints

	Univariable Analysis		Model 1 Multivariable Analysis		Model 2 Multivariable Analysis		Model 3 Multivariable Analysis	
	HR (95% CI)	*P*	Adjusted HR (95% CI)	*P*	Adjusted HR (95% CI)	*P*	Adjusted HR (95% CI)	*P*
Age, yr†	1.03 (1.0–1.05)	0.046	1.0 (0.97–1.03)	0.795	1.02 (0.99–1.05)	0.249	1.0 (0.97–1.04)	0.842
Sex (female vs. male*)	1.60 (0.61–4.17)	0.341						
Body mass index, kg/m²†	0.97 (0.85–1.11)	0.662						
CMR findings								
LV EDVI, mL/m²†	1.01 (1.0–1.02)	0.023			1.0 (0.98–1.01)	0.756	1.0 (0.98–1.01)	0.504
LV ESVI, mL/m²†	1.01 (1.0–1.02)	0.011						
LVMI, g/m²†	1.03 (1.01–1.04)	0.005	1.0 (0.97–1.03)	0.862	1.02 (0.98–1.05)	0.321	1.01 (0.98–1.04)	0.764
LV ejection fraction, %†	0.96 (0.94–0.98)	< 0.001						
LV global longitudinal strain, %†	0.85 (0.78–0.92)	< 0.001						
RV EDVI, mL/m²†	1.01 (0.99–1.04)	0.290						
RV ESVI, mL/m²†	1.0 (1.0–1.01)	0.332						
RV ejection fraction, %	0.97 (0.94–0.99)	0.019	1.0 (0.96–1.04)	0.958	0.99 (0.95–1.04)	0.696	0.97 (0.93–1.01)	0.185
Presence vs. absence* of LGE	0.24 (0.03–1.76)	0.159						
Location of LGE								
Anteoseptal LGE	0.29 (0.34–2.47)	0.256						
Inferolateral LGE	1.52 (0.54–4.26)	0.430						
Other LGE	0.55 (0.06–4.68)	0.580						
No LGE	Reference							
Number of LGE segments†	1.02 (0.92–1.13)	0.719						
LA volume index, mL/m²†	1.02 (1.0–1.05)	0.042						
LA ejection fraction, %†	0.94 (0.91–0.97)	< 0.001						
LA reservoir strain, %†	0.90 (0.86–0.95)	< 0.001	0.90 (0.84–0.96)	0.002				
LA contractile strain, %†	0.92 (0.86–1.0)	0.040			0.94 (0.85–1.03)	0.163		
LA conduit strain, %†	0.90 (0.85–0.96)	0.001					0.91 (0.84–0.98)	0.013

Values are shown as n (%) or mean ± standard deviation unless otherwise indicated. *For the categorical variables, the asterisked category was the reference, †For continuous variables, an increased by 1 was considered when calculating HRs and 95% CIs. CMR = cardiovascular magnetic resonance, CI = confidence interval, EDVI = end-diastolic volume index, ESVI = end-systolic volume index, HR = hazard ratio, LA = left atrial, LGE = late gadolinium enhancement, LV = left ventricle, LVMI = LV mass index, RV = right ventricle

Table 3. Correlation between Left Atrial Strain and Clinical and CMR Parameters

Parameter	LA Reservoir Strain		LA Contractile Strain		LA Conduit Strain	
	r	*P*	*r*	*P*	*r*	*P*
Age, yr	-0.29	0.051	0.01	0.963	-0.38	0.009
LV ejection fraction, %	0.66	< 0.001	0.49	0.001	0.47	0.001
LV EDVI, mL/m²	-0.53	< 0.001	-0.30	0.039	-0.44	0.002
LV ESVI, mL/m²	-0.58	< 0.001	-0.40	0.006	-0.43	0.003
LVMI, g/m²	-0.40	0.006	-0.06	0.703	-0.47	0.001
RV ejection fraction, %	0.48	0.001	0.50	< 0.001	0.22	0.142
LA volume index, mL/m²	-0.48	0.001	-0.30	0.043	-0.38	0.008
LA ejection fraction, %	0.94	< 0.001	0.67	< 0.001	0.67	< 0.001

CMR = cardiovascular magnetic resonance, EDVI = end-diastolic volume index, ESVI = end-systolic volume index, LA = left atrium, LV = left ventricle, LVMI = LV mass index, RV = right ventricle

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one variable among the parameters with a variance inflation factor greater than 3 was included in the multivariable analysis. LA reservoir (adjusted HR, 0.90; 95% CI, 0.84–0.96; P = 0.002) and conduit strain (adjusted HR, 0.91; 95% CI, 0.84–0.98; P = 0.013) were independent predictors of the composite endpoint.

Correlation between LA Strain and Other CMR Parameters

Table 3 shows the correlations between LA strain parameters and other CMR parameters. All LA strain parameters were associated with LV ejection fraction, LV EDVI, LV ESVI, LA volume index, and LA ejection fraction (all P < 0.05). LA reservoir and contractile strains were associated with RV ejection fraction (all P < 0.05).

Intraobserver Reproducibility of LA Function Measurement

Excellent intraobserver reproducibility was observed between the first and second evaluations of LA function measurements (ICC, 0.88–0.95, all P < 0.001) (Table 4).

DISCUSSION

The major findings of this retrospective study were as follows: 1) all LA strain parameters were lower in acute myocarditis patients than in healthy controls; 2) LA reservoir and conduit strain independently predicted the outcomes of patients with acute myocarditis; and 3) every LA strain parameter was associated with LV function, LA volume index, and LA ejection fraction. LA reservoir and contractile strains were associated with RV ejection fraction.

LA strain is a measurement of LA myocardial deformation and is expressed as a percentage. It can be divided into three strain parameters according to the cardiac cycle phase: reservoir, conduit, and contractile strains. LA strain parameters can reflect the degree of LV diastolic dysfunction, even in the absence of LA dilation, and are more sensitive than LAVI [23,24]. The main role of LA is to modulate LV filling via its reservoir, conduit, and contractile functions. During ventricular systole and isovolumetric relaxation, the LA relaxes and receives blood from the pulmonary veins, thereby functioning as a reservoir of energy in the form of pressure. Therefore, the LA reservoir strain may reflect changes in LA compliance. After opening the atrioventricular valves during early ventricular diastole, the LA operates as a conduit for blood transfer from the pulmonary veins to the LV. Therefore, LA conduit strain may be sensitive to LV changes, such as heart failure and long-standing hypertensive heart disease [25]. In late ventricular diastole, the LA operates as a pump to augment LV filling by 20%–25%. Therefore, LA contractile strain is a measure of LA contractile function and may be affected by changes in the LA and LV [25].

Table 4. Intra-observer Reproducibility of LA Function Measurement

	ICC (95% CI)	P
LA volume index	0.95 (0.87–0.98)	< 0.001
LA ejection fraction	0.91 (0.78–0.97)	< 0.001
LA reservoir strain	0.88 (0.70–0.95)	< 0.001
LA contractile strain	0.88 (0.68–0.95)	< 0.001
LA conduit strain	0.93 (0.83–0.97)	< 0.001

CI = confidence interval, ICC = intraclass correlation coefficient, LA = left atrial

Several studies have demonstrated that LA strain has a potential role in the diagnosis of variable heart diseases [15,16,26,27]. Dick et al. [27] compared CMR-derived LA strains of 30 patients with acute myocarditis, with preserved LV ejection fraction and 25 controls. They revealed that the LA reservoir and conduit strain were significantly lower in patients with myocarditis than in controls, suggesting LV diastolic dysfunction. This finding is consistent with the results of the present study. Interestingly, contractile strain was reduced in patients with acute myocarditis in our study, in contrast to the results of a previous study [27].

Previous studies demonstrated that impaired LA strain is associated with poor outcomes in patients with myocardial infarction, hypertrophic cardiomyopathy, valvular heart diseases, and heart failure as well as in the general population [13,14,28-31]. Schneider et al. [32] demonstrated that the recovery of biatrial function by feature-tracking CMR strain analyses after acute myocarditis was independent of the clinical presentation. The study included 35 patients with acute myocarditis and compared the CMR-derived LA reservoir strain at baseline and 3 months follow-up. The median LA reservoir strain increased from 33.2% at baseline to 37.0% at follow-up. However, to our knowledge, no study has examined the clinical significance of LA strain in predicting the outcomes of patients with acute myocarditis. Therefore, this study introduced the prognostic role of CMR-derived LA strains in patients with acute myocarditis. In this study, the LA reservoir and conduit strains independently predicted the composite endpoint in patients with acute myocarditis, similar to the results of studies on patients with heart failure [13].

https://doi.org/10.3348/kjr.2022.0898

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Tissue Doppler imaging and speckle tracking echocardiography have been used to assess atrial strain [33]. However, they have several limitations, including the far-field location of the atrium, dependence on the scanning angle, and low signal-to-noise ratio [34]. The CMR-derived feature tracking method was recently used to assess LA strain. The feature tracking method using CMR is analogous to the speckle tracking method used in echocardiography to assess LA wall motion [18]. The CMR-derived feature tracking method has several advantages: 1) CMR provides higher spatial resolution, rendering more reliable and accurate for LA evaluation [35]; 2) CMR has been used to diagnose acute myocarditis [19]; and 3) CMR-derived LA strains using feature tracking can be acquired retrospectively using cine images. Therefore, CMR may be used as a one-stop shop for the diagnosis and risk stratification of acute myocarditis.

This study had several limitations. First, this was a single-center retrospective study with a relatively small sample size, which might have caused a type II error. In this study, the presence and location of LGE were not associated with poor outcomes, and this result is not consistent with previous studies [8,20]. This is probably due to the small sample size and relatively small percentage of LGE-negative individuals (14.9%) in this study. Second, CMR scanners with different field strengths were used in this study, which might have affected imaging analyses. However, previous studies have indicated no significant differences in global strain parameters, volumes, or ejection fractions in accordance with the differences in field strength [36]. In addition, we did not perform T1 or T2 mapping in most of the study population. Therefore, T1 and T2 mapping parameters were not included in this study and could not be used for the diagnosis of acute myocarditis. Finally, because of the relatively small sample size, we had to use a composite endpoint only. Despite these limitations, this study suggests the potential role of LA strain as a predictor of poor outcomes. Further studies with larger patient populations are needed to confirm these results.

In conclusion, LA reservoir and conduit strains derived from CMR are independent predictors of adverse clinical outcomes in patients with acute myocarditis. However, larger longitudinal follow-up studies are required to confirm these results.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Ji Won Lee. Data curation: Jimin Lee, Ki Seok Choo, Yeon Joo Jeong, Minhee Hwang, Ji Won Lee. Formal analysis: Jimin Lee, Ji Won Lee. Funding acquisition: Ji Won Lee. Investigation: Jimin Lee, Minhee Hwang, Ki Seok Choo, Ji Won Lee. Methodology: Jimin Lee, Ji Won Lee. Resources: Yeon Joo Jeong. Software: Jimin Lee, Minhee Hwang, Ki Seok Choo, Ji Won Lee. Supervision: Ji Won Lee. Validation: Ji Won Lee. Visualization: Geewon Lee. Writing—original draft: Jimin Lee, Ji Won Lee. Writing—review & editing: Jimin Lee, Maria Roselle Abraham, Ki Seok Choo, Ji Won Lee.

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Funding Statement

This study is supported by the 2021 overseas training grant from Pusan National University Hospital.

Acknowledgments

We acknowledge the assistance of Kwang Min Lee (KM consulting) with the statistical analysis.

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