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Dynamic Change of Left Ventricular Mechanics in Patients with Acute Myocarditis with Preserved Left Ventricular Systolic Function: A 2-Year Follow-up Study

Sol Ventrikül Sistolik Fonksiyonu Korunmuş Akut Miyokarditli Hastaların Sol Ventrikül Mekaniklerinin Dinamik Değişimi: İki Yıllık Takip Çalışması

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

ABSTRACT

Objective: Acute myocarditis mimics acute coronary syndrome due to its clinical course and presentation. This study aimed to evaluate left ventricular longitudinal and circumferential functions during the acute phase and late phase of acute myocarditis with preserved left ventricular ejection fraction using 2-dimensional speckle tracking echocardiography.

Methods: Forty-one consecutive acute myocarditis patients with preserved left ventricular ejection fraction confirmed by cardiac magnetic resonance imaging underwent 2-dimensional speckle tracking echocardiography within the first week of hospital admission. Findings were compared with age and sex-matched 40 healthy controls. Left ventricular mechanics of the study group were reevaluated by 2-dimensional speckle tracking echocardiography during follow-up (23.85 ± 6.65 months later).

Results: Myocardial lesions with late gadolinium enhancement on cardiac magnetic resonance imaging were mostly localized in the subepicardial layer (91.40%) and commonly observed in the inferolateral wall (42.94%). Consistent with the cardiac magnetic resonance imaging findings, 2-dimensional speckle tracking echocardiography showed the localization of the involved myocardial segments with prominent impairment in global longitudinal peak systolic strain and global circumferential strain of the inferolateral wall of the left ventricle. In the acute phase, global longitudinal peak systolic strain (−17.32 ± 2.02 vs −20.59 ± 2.38) and global circumferential strain (−22.33 ± 2.27 vs −24.85 ± 3.19) were found to be lower in patients with acute myocarditis compared to healthy controls (both $P < .001$). While global circumferential strain was improved in the late phase compared with the acute phase (from −22.28 ± 2.32 to −22.90 ± 2.65; $P = .003$), global longitudinal peak systolic strain was not significantly changed during follow-up (from −17.30 ± 2.09 to −17.62 ± 2.19; $P = .072$).

Conclusion: Subtle left ventricular systolic function impairment can be detected by the 2-dimensional speckle tracking echocardiography technique in patients with acute myocarditis with preserved left ventricular ejection fraction and improvement in circumferential function could be observed during follow-up.

Keywords: Acute myocarditis, global circumferential strain, global longitudinal strain, speckle tracking echocardiography

ÖZET

Amaç: Akut miyokardit (AM), klinik seyri ve prezentasyonu nedeniyle akut koroner sendromu taklit eder. Bu çalışmada, iki boyutlu benek takibi ekokardiyografisi kullanarak (2D-STE), korunmuş sol ventriküler ejeksiyon fraksiyonlu (pLVEF) AM'in akut fazı ve geç fazı sırasında sol ventriküler (LV) longitudinal ve sirkumferansiyel fonksiyonlarının değerlendirilmesi amaçlandı.

Yöntemler: Kardiyak manyetik rezonans (KMR) görüntüleme ile doğrulanmış pLVEF'li 41 AM hastası, hastaneye yatışlarının ilk haftasında 2D-STE ile incelendi. Bulgular, yaş ve cinsiyet açısından uyumlu 40 sağlıklı kontrol hastası ile karşılaştırıldı. Çalışma grubunun sol ventrikül mekaniği 2D-STE ile izlemde (23,85 ± 6,65 ay sonra) yeniden değerlendirildi.

Bulgular: KMR'de geç gadolinyum tutulumlu (LGE) miyokardiyal lezyonlar en çok subepikardiyal tabakada (%91,40) olup yaygın olarak inferolateral duvarda (%42,94) gözlendi. 2D-STE, sol ventrikül inferolateral duvarın global longitudinal zirve sistolik gerilim (GLPS) ve global sirkumferansiyel gerilim (GCS) fonksiyonlarında belirgin bozulma ile etkilenen miyokardiyal segmentini kardiyak manyetik rezonans görüntüleme bulgularıyla uyumlu olarak gösterdi. Akut fazda

Esra Poyraz, M.D.
Lale Dinç Asarcıklı, M.D.

Department of Cardiology, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center, İstanbul, Turkey

Corresponding author:
Lale Dinç Asarcıklı
✉ mdlaledinc@gmail.com

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GLPS (−17,32 ± 2,02 vs −20,59 ± 2,38) ve GCS (−22,33 ± 2,27 vs −24,85 ± 3,19) AM'li hastalarda sağlıklı bireylere göre daha düşük bulundu (her ikisi için *P* < ,001). Akut faza kıyasla geç fazda, GCS fonksiyonunda anlamlı düzelme gözlenirken (−22,28 ± 2.32'den −22,90 ± 2.65'e, *P* = ,003), GLPS'de anlamlı değişiklik izlenmedi (−17,30 ± 2,09'dan −17,62 ± 2,19'a, *P* = ,072).

Sonuç: Korunmuş sol ventrikül sistolik fonksiyonlu AM'li hastalarda 2D-STE tekniği ile subklinik LV sistolik fonksiyon bozukluğu saptanabilir ve takip sırasında sirkumferansiyel fonksiyonda iyileşme gözlenebilir.

Anahtar Kelimeler: Global longitudinal strain, global sirkumferansiyel strain, korunmuş ejeksiyon fraksiyonlu akut miyokardit

Myocarditis refers to any inflammation of the myocardium. The pathogenesis of myocarditis is cardiac injury followed by an immunologic response from the host as cardiac inflammation. Myocarditis is responsible for 6%-7% of sudden cardiac deaths in young adults according to autopsy studies.[1,2] The dilated cardiomyopathy may appear in up to 30% of acute myocarditis (AM) cases.[3] However, a benign prognosis can be observed for AM patients with preserved left ventricular ejection fraction (pLVEF).[4]

Due to the lack of clear noninvasive clinical diagnostic criteria, diagnosing myocarditis can be difficult. Although endomyocardial biopsy result is the gold standard for the diagnosis of AM, it is only used for patients presenting with acute heart failure or LV systolic dysfunction due to its serious complication related to invasive strategy.[5,6] According to the Lake Louise consensus criteria, cardiac magnetic resonance imaging (CMR) is the current reference method for noninvasive diagnosis of myocarditis.[7] But it is costly and not widely available. However, 2-dimensional speckle tracking echocardiography (2D-STE), novel imaging modality, has played an important role for assessing global and regional LV functions in AM. Therefore, the aim of the study was to compare LV mechanics (GLPS (global longitudinal peak systolic strain) and global circumferential strain [GCS]) during acute phase and late phase of AM with pLVEF using 2D-STE.

Methods

Study Population

Patients admitted to Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Center between December 2017 and December 2019 with a clinical diagnosis of suspected AM[5,6] were included in the study and the inclusion criteria were (i) clinical symptoms consistent with AM, such as a history of flu-like symptoms within 8 weeks, chest pain, dyspnea, and fatigue palpitations; (ii) evidence of myocardial damage as indicated by elevated biomarkers (high-sensitive troponin [hs-Trop] T level >0.1 ng/mL [reference value 0.03 ng/mL]); and (iii) acute myocarditis confirmed by the Lake Louise CMR criteria.[7] Exclusion criteria were patients younger than 18 years, recurrent myocarditis, unattainable patients, hypertension, diabetes, hyperlipidemia, preexisting coronary artery disease, myocardial infarction, severe valvular disease, cardiac rhythms other than sinus, and poor echocardiographic windows. A total of 108 clinically suspected AM patients have undergone echocardiographic evaluation and have planned for a CMR scan (Figure 1). Fifty-four clinically suspected AM patients were excluded since CMR examination could not be performed (due to claustrophobia, presence of metallic implant, and unwillingness to scan) and 8 cases were excluded as CMR results could not confirm the diagnosis of AM. During follow-up, 5 patients were excluded due to rehospitalization with recurrent AM. The study group (n=41) was created following CMR examination, and the definitive diagnosis of AM patients with pLVEF was made with Lake Louise CMR criteria. The control group (n=40) consisted of asymptomatic individuals with no history of cardiovascular disease with unremarkable findings on physical examination and normal echocardiograms.

Enrolled patients with AM and pLVEF received guideline-directed medical therapy, for example, nonsteroid anti-inflammatory drugs/acetylsalicylic acid medications, and they were routinely followed up for cardiac evaluation. The mean duration of follow-up was 23.85 ± 6.65 months.

The study protocol was approved by the Ethic Committee of Haydarpaşa Numune Education and Research Hospital (October 6, 2017/593) and conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all individual participants included in the study.

Standard Echocardiography

Two-dimensional transthoracic echocardiography was performed during hospital admission. An EPIQ 7 ultrasound platform (Philips, Bothell, WA, USA) with an X5-1 matrix transducer was used for transthoracic echocardiographic evaluation. Three consecutive cycles were averaged for each parameter. The thickness of the LV walls and LV systolic and diastolic diameters were measured from the parasternal long-axis view. The biplane modified Simpson's method was used to determine the LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LVEF from apical 4-chamber (A4C) and 2-chamber (A2C) views. Two-dimensional speckle tracking analysis was performed offline by using QLAB (QLab 13, Tomtec AutoStrain LV, Philips, The Netherlands).

Two-Dimensional Speckle Tracking Echocardiography

Left ventricular GLPS and GCS were analyzed in the AM group within the first week before the hospital discharge. For late

ABBREVIATIONS

2D-STE	Two-dimensional speckle tracking echocardiography
A2C	Apical two-chamber
A4C	Apical four-chamber
AM	Acute myocarditis
CMR	Cardiac magnetic resonance
EGEr	Early-gadolinium enhancement ratio
GCS	Global circumferential strain
GLPS	Global longitudinal peak systolic strain
LGE	Late gadolinium enhancement
LV	Left ventricle
LVEDV	Left ventricular end-diastolic
LVEF	Left ventricular ejection fraction
LVESV	Left ventricular end-systolic volume
pLVEF	Preserved left ventricular ejection fraction volume

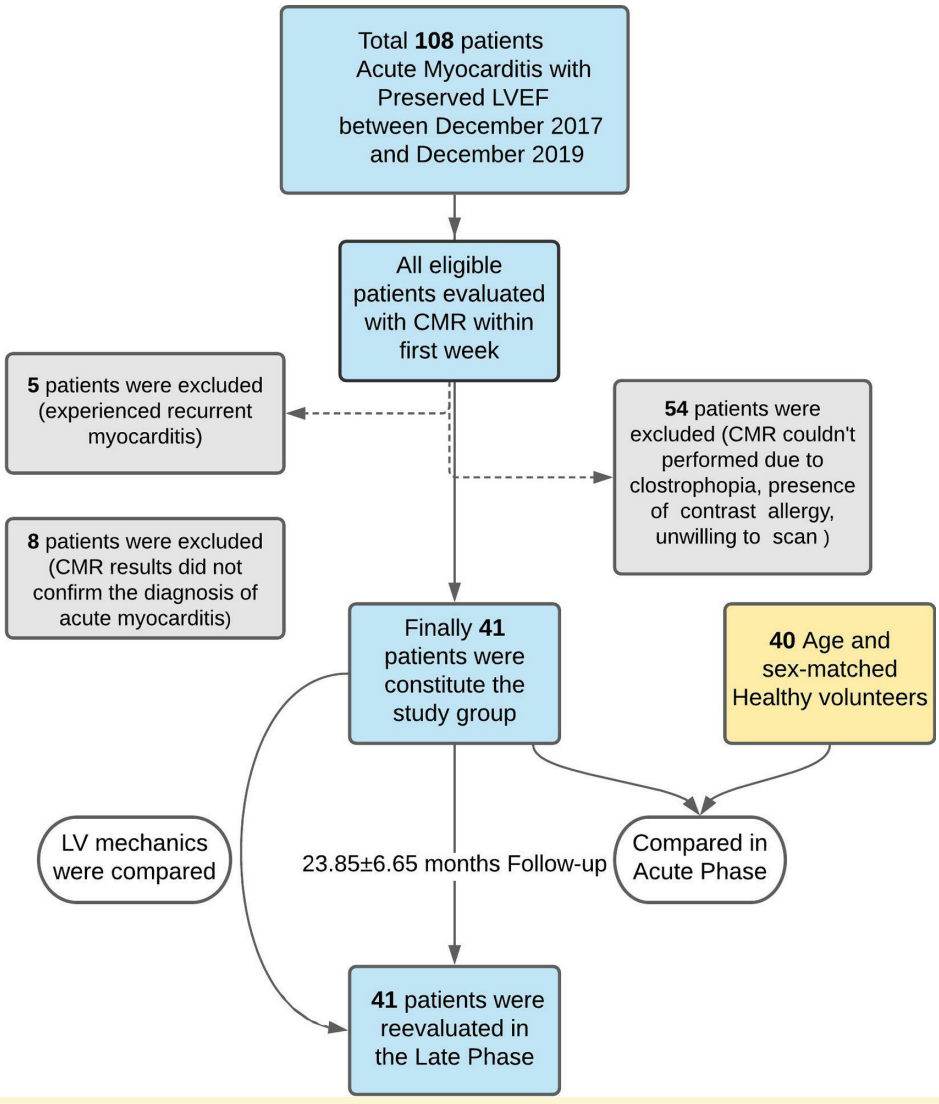

Figure 1. Allocation of study groups. LVEF, left ventricular ejection fraction; CMR, cardiac magnetic resonance.

phase, LV mechanics were reevaluated 23.85 ± 6.65 months following discharge. Acquired images were digitally stored, and data were subsequently transferred to the external computer for offline analysis using dedicated software (TMQA, Q-lab, Philips). For the 2D longitudinal speckle tracking analysis, 3 endocardial markers were put in an end-systolic frame at apical 4, 3, and 2 chamber views. The software automatically traced the endocardial contour to cover the full thickness of the LV wall. Adequate manual tracking was made for correcting the contour to ensure optimal tracking (Figure 2).

Global circumferential strain was obtained from parasternal short-axis views from LV basal, mid, and apical levels. During end-systole, the markers were manually placed along the endocardium. The software subsequently created a region of interest (ROI) to cover the LV wall. In short-axis view, the wall was divided into 6 segments. The ROI was manually adjusted to ensure that the LV endocardial border inner margin tracing covered the whole thickness of the LV myocardium (Figure 3).

Cardiac Magnetic Resonance Imaging

Cardiac magnetic resonance imaging was performed on all patients for the diagnosis of AM. Cardiac magnetic resonance imaging examination was performed within 6.34 ± 2.72 days (range: 2-12 days) of the acute phase of AM using 1.5 Tesla (SignaHDxt 1.5T system, GE Medical Systems, Milwaukee, Wis, USA) according to the Lake Louise criteria.[7] Cardiac magnetic resonance imaging protocol involved T2-weighted sequences for assessing myocardial edema, post-contrast early gadolinium enhancement (EGE) T1-weighed fast spin-echo sequences for assessing hyperemia, and late gadolinium enhancement (LGE) inversion recovery sequences for assessing necrosis/fibrosis. The localization of LGE was defined using a standard 17-segment tomographic model.[8] Since the diagnosis of AM was not verified by CMR results, 8 patients with clinically suspected AM were excluded.

Statistical Analysis

Continuous variables were represented by mean ± standard deviation, while categorical variables were represented by the number of subjects and percentages. Depending on the estimated cell

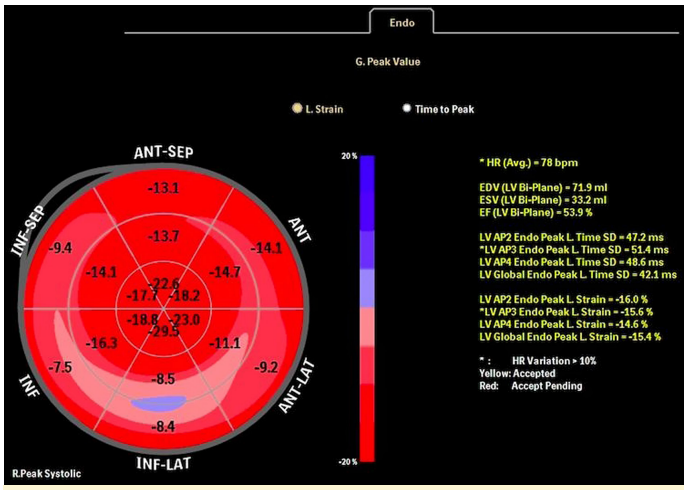

Figure 2. Bull's eye global longitudinal peak systolic strain diagram of AM patients with pLVEF. Red color denotes preserved strain values and blue color denotes decreased strain values. AM, acute myocarditis; pLVEF, preserved left ventricular ejection fraction.

value, categorical data were evaluated using the χ^2 test or Fisher's exact test. The Kolmogorov–Smirnov and Levene's tests were used to determine the normality and homogeneity of the variances. For continuous variables, the Student's *t*-test was applied for homogeneous data, whereas the Mann–Whitney *U* test was applied for heterogeneous data. Paired-sample test was performed for the comparison of speckle tracking data between acute phase and late phases of the AM group. $P < .05$ was considered significant. Statistical Package for the Social Sciences software 22 version (IBM Corp.; Armonk, NY, USA) was used for the analyses.

For LV mechanics (GLPS and GCS), intraclass correlation coefficients for intra- and interobserver variability were obtained for 40 participants during the acute phase and 20 participants during the late phase. Intraclass correlation coefficients were determined using a 2-way mixed method to examine intra- and interobserver variability.

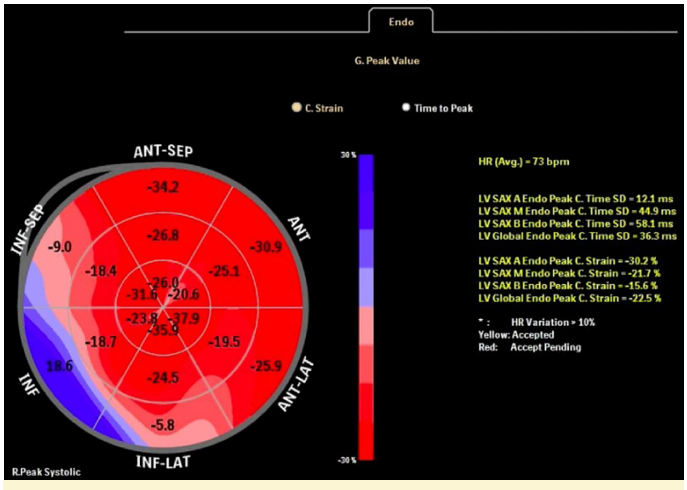

Figure 3. Bull's eye global circumferential strain diagram of AM patients with pLVEF. Red color denotes preserved strain values and blue color denotes decreased strain values. AM, acute myocarditis; pLVEF, preserved left ventricular ejection fraction.

Results

Clinical characteristics data of the study groups were presented in Table 1. There were no significant differences between AM group and age and sex-matched control group in terms of blood pressure values and body surface area.

Echocardiographic Data

In acute phase, EDV (58.79 ± 12.57 mL/m^2 vs 62.13 ± 17.13 mL/m^2), ESV (23.79 ± 4.88 ml/m^2 vs 24.35 ± 5.48 mL/m^2), and LVEF (59.1 ± 4.44 vs 60.2 ± 4.18) were similar in the AM and healthy controls group ($P = .320$; $P = .634$; $P = .244$, respectively) (Table 2).

Acute myocarditis group had significantly lower GLPS (−17.30 ± 2.09 vs −20.59 ± 2.38, $P < .001$) and GCS (−22.28 ± 2.32 vs 24.85 ± 3.19, $P < .001$) compared to healthy controls (Table 2). A prominent impairment in LV GLPS was observed in the inferolateral wall of the LV, as shown in the bull's eye diagram (Figure 2). Left ventricular deformation values of the affected segments of the LV in CMR are shown in Supplementary Table 1.

End-diastolic volume (58.79 ± 12.57 mL/m^2 vs 61.16 ± 14.14 mL/m^2; $P = .035$) was significantly increased in the late phase compared to acute phase. But ESV (23.79 ± 4.88 vs 24.39 ± 4.84; $P = .144$) and LVEF (59.1 ± 4.44 vs 60.1 ± 4.72; $P = .178$) were similar between the groups (Table 3).

In the late phase, no significant change was observed in GLPS (−17.30 ± 2.09 vs −17.62 ± 2.19; $P = .072$) comparing the acute phase. However, significant increase was observed in GCS (−22.28 ± 2.32 vs −22.90 ± 2.65; $P = .003$) compared to the acute phase (Table 3).

Cardiac Magnetic Resonance Imaging Data

The diagnosis of AM was verified in 41 patients by CMR. Cardiac magnetic resonance imaging findings of the study group is presented in Table 4. Mean EDV was 80.08 mL/m^2 ± 18.06, mean ESV was 34.28 mL/m^2 ± 7.41, and mean LVEF was 57 ± 4.96%, respectively. T1-weighted EGE ratio was 4.22 ± 2.09. T2-weighted edema on CMR was present in 30 (68.18%) patients. Late gadolinium enhancement (necrosis) on CMR was observed in 38 (92.7%) patients. Late gadolinium enhancement pattern on CMR was subepicardial in 170 segments and midmural in 16 segments. Myocardial lesions with LGE on CMR were commonly observed in inferolateral wall (42.94%).

Intraobserver and Interobserver Variabilities for 2D-STE

For LV mechanics of acute phase, ICCs for intra- and interobserver variabilities were found as 0.971 (95% CI: 0.946-0.985) and 0.944 (0.894-0.970) for GLPS and 0.960 (95% CI: 0.925-0.979) and 0.913 (95% CI: 0.936-0.954) for GCS, respectively. Intraclass correlation coefficients for intra- and interobserver variabilities for LV mechanics of late phase were as follows: 0.974 (95% CI: 0.935-0.990) and 0.937 (0.842-0.975) for GLPS and 0.952 (95% CI: 0.881-0.981) and 0.928 (95% CI: 0.818-0.971) for GCS, respectively.

Table 1. Clinical Characteristics Data of the Study Groups

Variables	Acute Myocarditis (n=41)	Healthy Controls (n=40)	*P*
Age (years)	30.48 ± 6.83	29.85 ± 6.19	.661
Gender (male, %)	32 (78.3)	28 (70.0)	.409
BSA (m^2)	1.77 ± 0.20	1.71 ± 0.16	.158
SBP (mmHg)	117.17 ± 14.98	111.47 ± 15.01	.091
DBP (mmHg)	70.70 ± 11.50	68.40 ± 9.86	.336
Elevated Hs-Trop T (>0.1 ng/mL)(n, %)	41 (100)	-	NA
Elevated Hs-CRP (>0.5 mg/L) (n, %)	41 (100)	-	NA
Prodromal symptoms within 8 weeks (n, %)	41 (100)	-	NA
Chest pain (n, %)	39 (95.1)	0	<.001
Dyspnea (n, %)	11 (26.8)	0	<.001
Fatigue (n, %)	12 (29.3)	0	<.001
Palpitation (n, %)	12 (29.3)	0	<.001
ST segment elevation (n, %)	27 (65.9)	0	<0.001
ST segment depression (n, %)	2 (4.9)	0	.494
T wave abnormalities (n, %)	8 (19.5)	0	.005
Normal ECG (n, %)	4 (9.8)	41 (100)	<.001

BSA, body surface area; CRP, C-reactive protein; DBP, diastolic blood pressure; hs-Trop, high-sensitive troponin; SBP, systolic blood pressure; ECG, electrocardiogram; NA, not applicable.

Table 2. Conventional and Speckle Tracking Echocardiographic Data of the Study Groups

Variables	Acute Myocarditis (n=41)	Healthy Controls (n=40)	*P*
EDV (mL/BSA)	58.79 ± 12.57	62.13 ± 17.13	.320
ESV (mL/BSA)	23.79 ± 4.88	24.35 ± 5.48	.634
EF (%)	59.1 ± 4.44	60.2 ± 4.18	.244
Interventricular septum (cm)	1.10 ± 0.11	0.98 ± 0.08	<.001
Posterior wall (cm)	0.95 ± 0.09	0.95 ± 0.09	.203
Right ventricle basal diameter (cm)	3.13 ± 0.22	3.08 ± 0.19	.274
SPAP (mmHg)	18.68 ± 5.44	17.35 ± 4.28	.354
GLPS (%)	−17.30 ± 2.09	−20.59 ± 2.38	<.001
GCS (%)	−22.28 ± 2.32	−24.85 ± 3.19	<.001

BSA, body surface area; EDV, end-diastolic volume; ESV, end-systolic volume; EF, ejection fraction; SPAP, systolic pulmonary artery pressure; GCS, global circumferential strain; GLPS, global longitudinal peak systolic strain.

Discussion

Our study has revealed several new findings by comparing LV mechanics during the acute phase and the late phase in AM with pLVEF: (i) GLPS and GCS values were impaired in AM with pLVEF compared to healthy controls, (ii) GCS values were recovered at the late phase but not GLPS, and (iii) the inferolateral wall of the LV was the most affected segment in speckle tracking echocardiography analysis, consistent with the CMR findings.

Subepicardial lesions are the most commonly observed lesion on CMR in patients with AM.[9-11] Subepicardial inflammatory lesion was seen in histological postmortem examinations and CMR.[10,12] Consistent with previous findings, in the present study, patients with AM had subepicardial lesions on CMR most commonly. Furthermore, strain analysis of AM patients with the 2D-STE imaging technique revealed the localization of the most involved segments as consistent with CMR findings of the patients with AM. Myocardial strain analysis using echocardiography is easy to use, a widely available technique, and it is of low cost compared to CMR. Non-ischemic myocardial involvement in AM, especially in the lateral wall of the LV can be detected with 2D-STE imaging. In another study from our country, analyzing AM patients with CMR, it was reported that LGE was observed mostly in thw lateral wall followed by the inferior wall, similar to the present study.[13] Cardiac magnetic resonance imaging appears to be the most accurate noninvasive diagnostic modality for myocarditis; however, it is still in scarce supply. These findings revealed the excellent correlation between global strain assessment and CMR, and the high reproducibility suggests that strain techniques may be very useful not only in diagnosis but also in the follow-up of a patient's illness progress.

Previous data revealed that GLPS values were reduced in both acute and chronic myocarditis with pLVEF.[14,15] Additionally, GLPS and GCS have been shown to be diagnostic and prognostic tools, even in patients with pLVEF.[16] In the present study, GLPS was significantly reduced in the AM group compared with controls. Caspar et al[14] demonstrated that longitudinal dysfunction that persisted for up to 2 years corresponds to the late phase following AM. Di Bella et al[17] analyzed the longitudinal deformation parameters of AM patients with 2 years of follow-up. They found that longitudinal dysfunction, particularly in endo-layer longitudinal deformation, persisted in the late phase,[17] while they did not assess

Table 3. Conventional and Speckle Tracking Echocardiographic Data of the Acute Phase and the Late Phase in Patients with Acute Myocarditis

Variables	Acute Phase (n=41)	Late Phase (n=41)	*P*
EDV/BSA	58.79 ± 12.57	61.16 ± 14.14	.035
ESV/BSA	23.79 ± 4.88	24.39 ± 4.84	.144
LVEF (%)	59.1 ± 4.44	60.1 ± 4.72	.178
GLPS (%)	17.30 ± 2.09	17.62 ± 2.19	.072
GCS (%)	22.28 ± 2.323	22.90 ± 2.65	.003

EDV, end-diastolic volume; BSA, body surface area; ESV, end-systolic volume; LVEF, left ventricular ejection fraction; GLPS: global longitudinal peak systolic strain; GCS, global circumferential strain.

Table 4. Cardiac Magnetic Resonance Imaging Data of Patients with Acute Myocarditis

Parameters	Acute Myocarditis Patients (n=41)
LV EDV (mL/m²)	80.08 ± 18.06
LV ESV (mL/m²)	34.28 ± 7.41
LVEF (%)	57 ± 4.96
LV mass (g/m²)	58.47 ± 12.47
Edema (T2-weighted images) (n, %)	30 (68.18)
EGEr	4.22 ± 2.09
Number of segments with LGE (%)	186 (26.68%)
Segments mid-wall LGE (%)	16/186 (8.60%)
Segments with subepicardial LGE (%)	170/186 (91.40%)
Localization of the subepicardial LGE	
Inferolateral segment (%)	73/170 (42.94%)
Anterolateral segment (%)	42/170 (24.70%)
Inferior segment (%)	32/170 (18.82%)
Anterior segment (%)	10/170 (5.88%)
Anterior and Inferior septum (%)	13/170 (7.65%)

LV EDV, left ventricular end-diastolic volume; LV ESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; EGEr, early gadolinium enhancement ratio; LGE, late gadolinium enhancement.

LV circumferential deformation parameter. Unfortunately, in our study, we did not evaluate LV longitudinal function in a layer-based manner such as endo- and epi-longitudinal mechanics. In the present study, frequently observed subepicardial inflammatory lesions in CMR of patients with AM may be responsible for the impairment of LV longitudinal functions, because fibers in the subepicardial region are mainly arranged in a longitudinal direction.[18] While the acute phase of AM is considered in the presence of both impairment in GLPS and GCS, it can be used to predict the late phase of AM in the presence of isolated GLPS impairment. Strain measurement has prognostic value, so it can facilitate the clinical decision-making process by contributing to distinguishing between acute and chronic phases.

The mid-wall LV fibers have a circumferential direction, and contraction of mid-wall fibers results in LV circumferential shortening.[19] Contrary to the findings of Di Bella et al[9] of the presence preserved circumferential function in patients with AM and pLVEF in the acute phase, in our study, GCS was lower in the AM group than in healthy subjects. However, the number of patients with AM was quite low compared to the present study. Although the involvement is not as widespread as the subepicardial fibers, segmental involvement of the mid-wall fibers was observed by CMR in the present study. Compared with the acute phase, the recovery of circumferential function in spite of persisting longitudinal dysfunction in the late phase may be related to less involvement of mid-wall fibers compared to subepicardial fibers in our study. In another study, comparing deformation parameters of patients with AM and healthy controls by using 3-dimensional speckle tracking echocardiography (3D-STE), it was found that GCS impairment persisted for up to 2 years.[14] The 3D-STE technique has some limitations in assessing the basal parts of LV, even affected segments were more often located in the basal region. This discrepancy between these two studies can be explained by the different analyzing techniques that were used and the different size of the studies.

The presence of several limitations should be taken into account when interpreting the results of our study. First, the study was conducted in a single center with small sample size, so generalizability was poor. Second, CMR was not performed on the control group, because the control group consisted of healthy people and they had no symptoms suggesting myocarditis. Third, CMR was not performed in the late phase of AM to elucidate the status of lesions related to the late phase of myocarditis on CMR. Unfortunately, all included AM cases were CMR-confirmed AM cases as they were not biopsy-proven. If the study population would be larger, the change in LV GLPS during the late phase could have been statistically significant. Since myocardial contraction is 3-dimensional, in addition to longitudinal and circumferential strain, radial strain and twist and untwist movement also contribute to the movement of the heart in all dimensions. The effect of myocardial involvement in acute myocarditis can be evaluated more clearly with radial strain and twist and untwist data. Unfortunately, we could not perform radial strain analysis since the software that we analyzed did not have a radial strain analysis program. Furthermore, twist and untwist movements were not analyzed as study data.

Conclusion

In patients with AM, subtle LV systolic function impairment can be detected by 2D-STE technique. Deformation imaging with transthoracic echocardiography also allows us to determine the affected segments of LV wall that was consistent with CMR. The degree of dysfunction observed in left ventricular mechanics in the acute phase depends on the extent of myocardial involvement and the segment involved. And this situation also determines whether this change will recover in the late phase. Further studies are needed to elucidate the changes of LV mechanics by time in patients with AM.

Visual summary of the article can be seen in Figure 4.

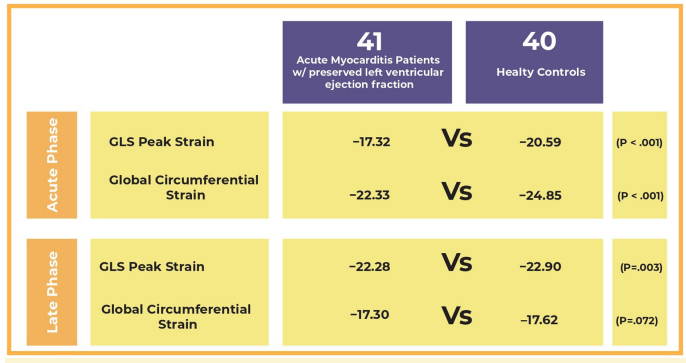

Figure 4. A visual summary of the article.

Ethics Committee Approval: The study was approved by the medical ethics committee of Haydarpaşa Numune Education and Research Hospital (No:09.2017.593 06/10/2017).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – E.P., L.D.A.; Design – E.P.; Data Collection and/or Processing – E.P.; Analysis and/or Interpretation – L.D.A.; Literature Search – L.D.A.; Writing Manuscript – E.P., L.D.A.; Critical Review – L.D.A.

Declaration of Interests: The authors have no conflict of interest to declare.

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Supplementary Table 1. Left Ventricular Strain Values of Corresponding Affected Myocardial Segments in Cardiac Magnetic Resonance Imaging of Patients with Acute Myocarditis

Localization of the Subepicardial LGE	GLPS	GCS
Inferolateral segment (%)	9.8 ± 3.6	11.2 ± 3.1
Anterolateral segment (%)	8.3 ± 2.8	15.3 ± 3.9
Inferior segment (%)	7.2 ± 2.6	13.2 ± 4.4
Anterior segment (%)	11.6 ± 3.8	14.1 ± 4.7
Anterior septum (%)	10.2 ± 3.4	14.2 ± 4.3
Inferior septum (%)	9.7 ± 2.1	10.7 ± 2.8

LGE, late gadolinium enhancement; GLPS, global longitudinal peak systolic strain; GCS, global circumferential strain.