ORIGINAL ARTICLE

# Utility of segmental and regional left ventricular longitudinal strain in identifying localization and extent of myocardial injury in patients with acute myocarditis confirmed by cardiac magnetic resonance

## Intérêt du Strain longitudinal segmentaire et régional ventriculaire gauche dans la détermination de la localisation et l'étendue de l'atteinte myocardique en cas de myocardite aigue confirmée par résonance magnétique cardiaque

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**Abstract**

**Introduction-Aim**: This study aimed to evaluate the role of echocardiographic left ventricular (LV) longitudinal strain (LS) in identifying the localization and extent of myocardial injury compared to edema and late gadolinium enhancement (LGE) detected on cardiac magnetic resonance (CMR) imaging in patients with acute myocarditis (AM).

**Methods**: Patients >18years-old, with informed consent, and AM confirmed by CMR were prospectively enrolled between 1st November 2023 and 30th September 2024. Strain echocardiography with measurements of global (GLS) and segmental longitudinal strains (SLS) was performed. Number and localization of segments with impaired LS were compared with those with edema and/or LGE on CMR.

**Results**: 19 patients, 31.6±12.0 years old and 84.2% male were enrolled. Although LV ejection fraction (EF) was preserved in all patients, GLS was impaired in 63.2% of them. Impairment in regional LS was identified mainly in the anterolateral, inferolateral and inferior regions, in concordance with localization of edema and LGE detected by CMR, with strong correlation between extent of myocardial injury on CMR and number of segments with impaired SLS per patient (r=0.76; p=0.0002). Performance of SLS in the diagnosis of edema in AM patients was satisfactory with an AUC=0.725, CI 95% [0.67-0.78] and p<0.001. Cut-off value was -17.5% with a sensitivity of 71% and specificity of 65%.

**Conclusion**: In AM patients, analysis of LS identified impairment in LV myocardial deformation in patients with a normal LVEF. Comparison with CMR showed a very close topographical distribution between regions with impaired myocardial deformation and those of inflammatory tissue injury detected on CMR.

**Key words**: strain echocardiography, segmental longitudinal strain, late gadolinium enhancement, myocardial edema.

**Résumé**

**Introduction-Objectif**: Cette étude visait à évaluer le rôle de l'échocardiographie du strain longitudinal (SL) ventriculaire gauche (VG) dans la détermination de la localisation et l'étendue de l'atteinte myocardique par rapport à l'œdème et au rehaussement tardif (RT) au gadolinium détectés par l'imagerie par résonance magnétique cardiaque (IRMc) chez les patients avec myocardite aigue (MA).

**Méthodes**: Les patients >18ans, avec MA confirmée à l'IRMc étaient inclus prospectivement. Une mesure du strain longitudinal global (SLG) et segmentaire (SLS) était réalisée. Le nombre et la localisation des segments avec SLS altéré étaient comparés à ceux présentant de l'œdème et/ou RT à l'IRMc.

**Résultats**:19 patients, d'âge 31,6±12,0ans et 84,2% de sexe masculin étaient recrutés. Malgré une FEVG préservée, le SLG était altéré chez 63,2% des patients. Le SL régional était altéré principalement dans les régions antéro-latérale, inféro-latérale et inférieure, en concordance avec la localisation de l'œdème et du RT à l'IRMc, avec une forte corrélation entre l'étendue de l'atteinte myocardique en IRMc et le nombre de SLS altérés par patient (r=0,76;p=0,0002). La performance du SLS dans le diagnostic de l'œdème dans la MA était satisfaisante avec une AUC=0,725, IC95%[0,67-0,78] et p<0,001. La valeur seuil était de -17,5% avec une sensibilité de 71% et une spécificité de 65%.

**Conclusion**: Chez les patients avec MA, l'analyse du SL a permis d'identifier une altération de la déformation myocardique VG chez des patients avec FEVG normale. La comparaison avec l'IRMc a montré une distribution topographique très proche entre les régions avec un SL altéré et celles où des lésions tissulaires inflammatoires étaient détectées en IRMc.

**Mots clés**: échocardiographie de strain, strain longitudinal segmentaire, rehaussement tardif au gadolinium, œdème myocardique.

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## Introduction

Presentation of acute myocarditis (AM) can vary widely, and establishing the diagnostic can be difficult, especially when there is no impairment in left ventricular (LV) systolic function.
Historically, endomyocardial biopsy served as gold standard for diagnosing AM, while recently, cardiac magnetic resonance (CMR) based on Lake Louise criteria has gained prominence. Nonetheless, performing CMR faces limitations, as it may be unavailable during the acute-phase myocarditis or can be contraindicated due to specific conditions or patient intolerance. Two-dimensional (2D) speckle tracking echocardiography (STE) could assess subclinical LV dysfunction, detect segmental myocardial involvement in AM patients and exhibit greater accuracy than traditional echocardiography with its global function assessment. When available, the criteria from CMR for AM can supplement findings obtained by 2D-STE.
The aim of this study was to evaluate the role of echocardiographic 2D LV longitudinal strain (LS) imaging in identifying the localization and extent of myocardial injury compared to that detected on CMR in patients with AM.
We hypothesized that LS analysis could identify myocardial segments or regions involved in AM and thus provides information on localization and extent of myocardial injury.

## Methods

We performed a prospective study of echocardiographic evaluation in patients with CMR-confirmed AM between 1st November 2023 and 30th September 2024.
The primary objective was to investigate the role of LV segmental and regional LS in identifying localization and extent of myocardial injury in AM patients compared to edema and late gadolinium enhancement (LGE) detected by CMR.
We included consecutive patients >18 years-old, who gave their informed consent to participate in the study, with clinical presentation compatible with AM diagnosis according to European Society of Cardiology (4,5) and elevated troponin, with or without ECG anomalies, structural or functional abnormalities by standard TTE, with absence of coronary artery disease, and CMR evidence of AM according to 2018 Lake Louise Criteria (6).
We didn't include patients with history of hypertension, diabetes mellitus, hyperlipidemia, and cardiovascular or chronic kidney disease (eGFR<60ml/min/1.73 $m^2$) in order to reduce potential confounders that may impact on strain measurement, patients with poor echocardiographic image quality, greater than mild valvular heart disease, more than mild pericardial effusion, arrhythmia on ECG and those with angiographically coronary stenosis ≥50%.
Patients who didn't undergo or tolerate CMR and patients in whom CMR wasn't consistent with acute-phase myocarditis or didn't show myocardial involvement (edema and/or LGE) were excluded.
The primary endpoint of this study was to compare the number and localization of impaired SLS on STE with the number and localization of segments with edema and/or LGE on CMR.
Each patient underwent a detailed assessment of clinical parameters and baseline laboratory tests. TTE was performed using General Electric Vivid E9 ultrasound echocardiogram equipped with M5Sc transducer, involving comprehensive analysis of standard and LV strain parameters.

### Standard trans-thoracic echocardiography

Parasternal long-axis view was used for M-Mode measurements: Interventricular septal and LV posterior wall thicknesses, LV diameters and LV mass index. LV ejection fraction was assessed by biplane Simpson's method from apical 4-and 2-chamber views in addition to LV and left atrial volumes (7).
Doppler and tissue Doppler measurements for cardiac valves were performed: peak early (E) and late (A) diastolic velocities of mitral valve and early diastolic peak velocities (e') of septal and lateral mitral annulus.

### Two-dimensional speckle tracking Echocardiography

2D-grayscale images were recorded using a frame rate >55 frames-per-second. Three consecutive cardiac cycles were recorded. Echocardiographic images were sent to a single software station (EchoPAC Clinical Workstation Software, GE Vingmed Ultrasound) and strain analyses were performed offline.
For LV GLS assessment, apical 3-, 2-and 4-chamber views were acquired. Segmental LSs (SLS) were demonstrated automatically in bull's eye plot according to the 17-myocardial segment model of the American Heart Association (AHA) (8). All STE parameters were measured by the same trained operator.
LS values depend on many parameters and there's no real definition of impaired LS. In this study, the prevalence of impaired LV LS was defined in relation to previously reported strain values obtained from Nagata et al, defined in 254 healthy subjects according to subgroup analysis by age (3rd, 4th, 5th , 6th and >7th decade of life) and using the same echocardiogram as the one used in our study (9).
We distinguished three anatomical zones: basal (segments 1 to 6), median (segments 7 to 12) and apical (segments 13 to 17). We used previously established cut-off values (9) to define alteration in LS for a myocardial segment (-16.8% to -15.1% for basal segments, -17.9% to -17.2% for median segments and -17.7% to -19.2% for apical segments); cut-off values corresponding to the mean LS + standard deviation, according to age and distribution into basal, median or apical segment obtained from the 254 healthy subjects (9).

### Cardiac magnetic resonance

CMR was performed in the first few days of AM on a 1.5 Tesla scanner, by experienced radiologists specialized in the assessment of cardiac images. CMR images were acquired during breath hold and with ECG-gating. 2018 expert recommendation for updated CMR criteria in AM inflammation was evaluated in each case. CMR imaging protocol included searching for myocardial edema and detection of myocardial injury. All CMR scans were reviewed by the same experienced radiologist to identify myocardial segments with edema and/or LGE with their topography described according to AHA standardized myocardial segmentation model (8): segments 1 to 6 for basal segments, segments 7 to 12 for median segments and segments 13 to 17 for apical segments.

### Statistical analysis

All statistical analyses were carried out using SPSS software (IBM SPSS Statistics, version 26). The numeric variables were depicted through mean±Standard Deviation or median (interquartile range), whereas categorical variables were represented as frequencies and percentages. To assess the relationship between extent of myocardial injury in CMR and STE parameters, linear Pearson or Spearman correlation coefficients were employed. The performance of segmental LV strain in predicting the presence of edema in AM was studied using the ROC curve method and threshold value of segmental LV strain was determined. A p value < 0.05 or the 95% confidence interval (CI) of the odds ratio (OR) excluded the value of 1 were considered as statistically significant.

## Results

During the study period, 19 patients (mean age 31.6±12.0 years; 84.2% male) were enrolled. The flow chart of the study is represented in figure 1. Clinical baseline characteristics and laboratory data of the study population are shown in table 1

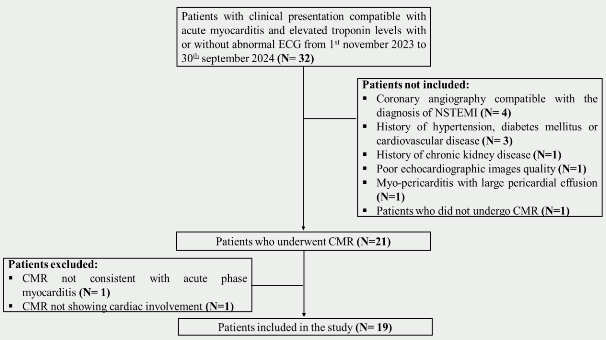


**Figure 1**. Flow chart of the study

**CMR**: cardiac magnetic resonance, NSTEMI: non-ST elevation myocardial infarction.

All patients presented with chest pain and one (5.3%) presented with a syncope. A total of 14 (73.7%) patients had preceding signs of infection and 7 (36%) had fever at admission. Median time from symptoms onset was 4 (2–7) days. C-reactive protein was elevated in 13 (68.4%) patients and white blood cells were elevated in 11 (57.9%) out of the 19 patients. Furthermore, ST-segment elevation was observed in 12 (63.2%) patients and high-sensitive troponin was increased in all patients.

Coronary imaging was performed in 14 (73.6%) patients and all of them had normal coronary arteries which were diagnosed on coronary angiography in 12 (63.2%) cases and gated cardiac CT-scan in 2 (10.5%) others. The remaining 5 (26.3%) patients underwent CMR within 24 hours and ischemic heart disease was ruled out in all of them.

**Table 1.** Clinical, laboratory baseline characteristics, and standard echocardiographic parameters of the study population.

| Parameters | Statistics |
|---|---|
| Age (years) | 31.6 ± 12.0 |
| Gender (male, N %) | 16 (84.2%) |
| Smoking (%) | 11 (57,9%) |
| Preceding signs of infection N (%) | 14 (73.7%) |
| Chest pain N (%) | 19 (100%) |
| Syncope N (%) | 1 (5.3%) |
| ECG abnormalities N (%) | 19 (100%) |
| • ST segment elevation | 12 (63.2%) |
| • Non-specific abnormal T waves | 12 (63.2%) |
| Systolic blood pressure (mmHg) | 117.9 ± 22.2 |
| Diastolic blood pressure (mmHg) | 68.9 ± 11.0 |
| Heart rate (bpm) | 73.4 ± 10.3 |
| Peak C-reactive protein (mg/L) (N=13) | 39 (20 – 66) |
| WBC ($10^3$E/mm$^3$) (N=11) | 11.7 ± 4.1 |
| Hemoglobin (g/dL) | 14.2 ± 1.3 |
| Hematocrit (%) | 40.8 ± 3.7 |
| Peak high sensitive troponin (ng/L) | 6789 (3200 – 11600) |
| eGFR (ml/min/1.73m$^2$) | 121.5 ± 25.6 |
| Coronary imaging N (%) | 14 (73.6%) |
| • Coronary angiography | 12 (63.2%) |
| • Cardiac CT scan | 2 (10.5%) |
| TTE standard parameters N (%) | 19 (100%) |
| Posterior wall thickness (mm) | 8.8 ± 1.4 |
| Interventricular septum thickness (mm) | 9.0 ± 1.7 |
| LV end-diastolic diameter/BSA (mm/m$^2$) | 26.2 ± 3.8 |
| LV end-systolic diameter/BSA (mm/m$^2$) | 17.2 ± 2.5 |
| LV end-diastolic volume/BSA (ml/m$^2$) | 54.8 ± 13.4 |
| LV end-systolic volume/BSA (ml/m$^2$) | 20.9 ± 7.4 |
| Left ventricular ejection fraction (%) | 62.0 ± 6.4 |
| Left atrial volume/BSA (ml/m$^2$) | 24.7 ± 4.6 |
| LV mass/BSA (g/m$^2$) | 80.9 ± 10.6 |
| Mitral peak E velocity (cm/s) | 80.8 ± 16.4 |
| Mitral peak A velocity (cm/s) | 56.3 ± 15.0 |
| Mitral E/A ratio | 1.5 ± 0.5 |
| E’ average velocity (cm/s) | 12.4 ± 3.4 |
| E/ e’ average ratio | 6.8 ± 2.6 |

**LV**: left ventricular, **TTE**: transthoracic echocardiography, **WBC**: white blood cells

### Standard echocardiography analysis

All patients underwent TTE. Standard 2D and Doppler echocardiographic parameters are shown in table 1. The median time from admission to TTE was 1 (1-1) day. Global LV function was preserved with mean LVEF measured by Biplane Simpson 62.0±6.4%. LV and left atrial chamber diameters and volumes as well as Doppler Tissue parameters of the mitral annulus were in normal range by gender according to the American society of echocardiography and the European association of cardiovascular imaging.

### Left ventricular 2D speckle tracking echocardiography analysis

A total of 323 myocardial segments out of 323 were analyzed in STE. Global and segmental LV LS parameters are represented in table 2.

Although LVEF was preserved in all patients, GLS was impaired in 12 (63.2%) of them and the mean GLS was -17.5±2.6% (Table 2).

Thus, we were able to determine the number of altered SLS in our patients: a total of 157 segments and a mean of 8.3 segments per patient.

**Table 2**. Global and segmental left ventricular longitudinal strain parameters in the study population.

| Parameters | Mean ± SD (%) | Segments with impaired SLS; n (%) (n=19) |
|---|---|---|
| GLS | -17.5 ± 2.6 | |
| **Segmental longitudinal strain** | | |
| Basal anterior | -17.0 ± 4.6 | 7 (36.8%) |
| Basal anteroseptal | -17.6 ± 4.1 | 2 (10.5%) |
| Basal inferoseptal | -15.7 ± 1.7 | 12 (63.2%) |
| Basal inferior | -14.7 ± 6.1 | 12 (63.2%) |
| Basal inferolateral | -14.4 ± 3.3 | 17 (89.5%) |
| Basal anterolateral | -14.8 ± 5.9 | 13 (68.4%) |
| Mid anterior | -17.5 ± 3.6 | 8 (42.1%) |
| Mid anteroseptal | -19.6 ± 4.5 | 3 (15.8%) |
| Mid inferoseptal | -18.7 ± 1.8 | 4 (21.1%) |
| Mid inferior | -17.5 ± 2.5 | 14 (73.7%) |
| Mid inferolateral | -16.2 ± 3.8 | 15 (78.9%) |
| Mid anterolateral | -16.5 ± 3.9 | 12 (63.2%) |
| Apical anterior | -19.3 ± 4.5 | 7 (36.8%) |
| Apical septal | -21.2 ± 3.2 | 2 (10.5%) |
| Apical inferior | -19.4 ± 4.5 | 11 (57.9%) |
| Apical lateral | -18.7 ± 5.4 | 11 (57.9%) |
| Apex | -19.2 ± 4.9 | 7 (36.8%) |

**GLS**: global longitudinal strain, **SLS**: segmental longitudinal strain.

The topography of myocardial involvement on STE is detailed in figure 2. Lower regional LS values were detected predominantly in anterolateral, inferolateral, and inferior segments in patients with AM (Figure 2).

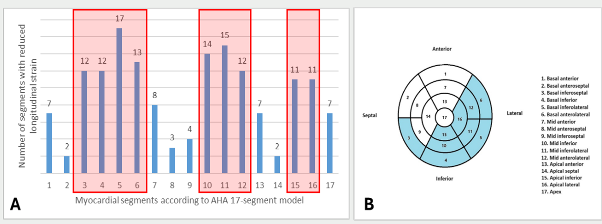


**Figure 2.A.** Topography of impaired segmental longitudinal strain according to the 17-segment model of the American Heart Association, **B**: Bull's eye plot showing localization of lower regional longitudinal strains (represented in blue color) by speckle tracking echocardiography in the study population.

### Cardiac magnetic resonance analysis

Median time between TTE and CMR was 3 (2-5) days. Mean LVEF in our patients calculated on CMR was 56.1±9.8%. Edema was diagnosed in 18 (94.7%) out of the 19 patients of the study and LGE was detected in all of them.

Distribution of edema and LGE in myocardial segments according to 17-segment model of AHA is shown in figure 3. Myocardial injury in CMR was detected predominantly in anterolateral, inferolateral, and inferior segments in patients with AM (Figure 3).

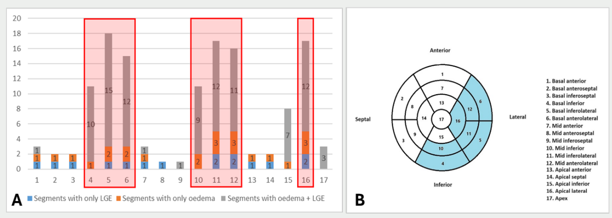


**Figure 3.A.** Distribution of edema and late gadolinium enhancement in myocardial segments according to the American Heart Association 17-segment model, **B.** Bull's eye plot showing distribution of myocardial involvement on cardiac magnetic resonance according to the American Heart Association 17-segment model.

Figure 4 demonstrated an example of comparison between myocardial injury localization using CMR and strain echocardiography in the same patient with AM.

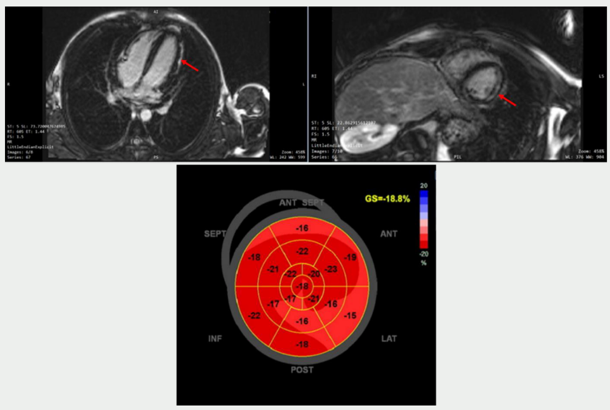

**Figure 4.** Example of comparison of myocardial injury localization in the same patient with acute myocarditis using CMR and Strain echocardiography.

On the top: CMR T1 sequence image of late gadolinium enhancement in 4-cavity view on the left and in short axis on the right showing the presence of late enhancement throughout anterolateral and inferolateral wall.

On the bottom: bull's-eye view of LV longitudinal strain with distribution of impaired regional longitudinal strain corresponding to the CMR territory affected.

### Performance of segmental left ventricular strain in the diagnosis of edema in acute myocarditis

In AM patients with edema presence (94.7% of patients), performance of SLS in predicting the diagnosis of myocardial edema was assessed.

Diagnostic performance of SLS was satisfactory with area under the curve: (AUC)=0.725, CI95% [0.67-0.78] and p<0.001. The cut-off value was -17.5% with sensitivity and specificity of 71 and 65% respectively for detecting myocardial edema in AM.

### Correlations

Correlation between the number of myocardial segments with edema and/or LGE on CMR and GLS was moderate (r=0.58; p=0.009), however, there was strong correlation between the extent of myocardial injury in CMR and the number of segments with impaired SLS per patient (r=0.76; p=0.0002).

## Discussion

The main findings of this STE study among patients with AM confirmed by CMR and without cardiovascular risk factors or cardiovascular or renal disease were:

- Although LVEF was preserved in all patients, GLS was impaired in 63.2% of them.
- Our study suggested that STE was able to detect the extent and localization of myocardial involvement similarly to CMR in these patients with AM. STE, was able to identify an impairment in segmental and regional strains mainly in the anterolateral, inferolateral and inferior regions, in concordance with the localization of edema and LGE detected by CMR in patients with AM with a strong correlation between the extent of myocardial injury on CMR and the number of segments with impaired SLS per patient (r=0.76; p=0.0002).
- The performance of SLS in the diagnosis of edema in AM patients with myocardial edema was satisfactory with an area under the curve=0.725, confidence interval IC95%[0.67-0.78] and p<0.001. The cut-off value was -17.5% with a sensitivity and specificity of 71% and 65%.

A retrospective study by Meindel et al. including 31 AM patients and 20 healthy controls, investigated the diagnostic value of GLS compared with edema and LGE assessed by CMR (12). In this study, despite normal LVEF, GLS was lower in AM patients compared to controls suggesting subclinical dysfunction. Reduction in regional strain was predominant in lateral, inferolateral, and inferior segments with significant association between regional LS and a semi-quantitative analysis of myocardial injury by CMR (12) .

In the same way, in 28 patients with CMR-confirmed AM, myocardial edema was mostly found in the basal inferior and inferolateral, mid anterior and anterolateral, and inferolateral segments. GLS was significantly associated to the amount of edema in CMR (r=0.65, p<0.004) and no differences in strain values were obtained according to layer-specific myocardial deformation (13).

To assess systolic function in AM patients, its correlation to CMR findings, and its prognostic value for recovery and arrhythmias during follow-up, strain analysis was performed at admission and after 6 months in 115 patients with CMR-confirmed AM, and 70 healthy controls. GLS was lower in AM group compared to controls with significant correlation with the extent of myocardial injury (r=0.67, p<0.0001). GLS impairment had also prognostic role with a value of −12% predicting myocardial scar with sensitivity of 79% and specificity of 84% (p<0.001, AUC=0,91) and non-sustained ventricular tachycardias (sensitivity of 84% and specificity of 74.4%, AUC=0,75) (14).

In another retrospective cohort of 45 patients with AM and 83 healthy subjects, AM patients had a reduction in their global circumferential strain and GLS and these reductions were associated with increased risk of clinical deterioration that may require the use of LV assistance device, cardiac defibrillator implantation, or lead to acute pulmonary edema, cardiogenic shock, rehospitalization for cardiac events and cardiac arrest. This study concluded that global circumferential and longitudinal strains may have diagnostic and prognostic implications in AM patients (15).

In a pediatric population with CMR-confirmed AM, GLS was reduced in 51% of segments with LGE presence with a moderate correlation between GLS and LGE presence, suggesting that 2D-STE could be useful as a non-invasive method for diagnostic and potentially aiding in the prognosis in the pediatric population (13).

Association between 2D-STE and edema in CMR was studied in 47 patients with suspected AM. In CMR-edema patients (53%) mild reductions in GLS and transmural CS were noted. Moreover, epicardial CS ≤-13.0% (AUC=0.747, p=0.0005) was an indicator of edema. Twenty-two patients (all but 3) with AM and epicardial CS ≤-13.0% had edema confirmed by CMR. Epicardial CS can serve as a diagnostic marker for edema in early-stage AM (17).

Currently, novel techniques such as CMR-feature tracking allows quantitative strain analysis of myocardial function. Myocardial strain using CMR-feature tracking provides incremental prognostic value over clinical features, LVEF, and LGE and may serve as a novel marker to improve risk stratification in myocarditis (18,19).

It is highlighted that a single non-invasive imaging technique may not always be adequate to confirm AM diagnosis. 2D-STE can serve as an initial approach to detect subtle but clinically relevant LV dysfunction. This can be further supported by CMR findings if it is available and the patient's condition permits.

**Study limits:**

This study had several limitations. First, a single-center study with small sample of patients may represent a limitation for the validation of results accuracy. Second, we didn't use circumferential strain, as epicardial circumferential strain could be more sensitive in detecting edema and LGE given the epicardial topography of myocardial injury in AM, as demonstrated in previous studies. Third, the absence in the published recommendations of a cut-off value for impaired GLS as well as segmental and regional strains, allowing more accurate definition of myocardial injury in STE. Finally, we didn't assess reproducibility of strain measurements by calculating interobserver and intra-observer variability.

## Conclusion

In this population of AM patients, STE identified impairment in LV LS myocardial deformation in patients with a normal LVEF. Comparison with CMR showed a very close topographical distribution between regions with impaired myocardial deformation seen on TTE and those of inflammatory tissue injury detected on CMR.

STE is not a substitute for CMR for the diagnosis of AM, since LS impairment is not specific to inflammatory pathology, however 2D-STE can help to set the diagnosis of AM in patients with acute chest pain, elevated cardiac biomarkers, with normal coronary arteries, especially when LVEF is normal and when there are few abnormalities in segmental wall motion detected by conventional TTE.

**Abbreviation list:**
**2D**: two-dimensional
**AHA**: American Heart Association
**AM**: acute myocarditis
**CMR**: cardiac magnetic resonance
**GLS**: global longitudinal strain
**LV**: left ventricular
**LS**: longitudinal strain
**LVEF**: left ventricular ejection fraction
**SLS**: segmental longitudinal strain
**STE**: speckle tracking echocardiography
**TTE**: trans-thoracic echocardiography

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