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# Relationship of Left Atrial Global Peak Systolic Strain with Left Ventricular Diastolic Dysfunction and Brain Natriuretic Peptide Level in Patients Presenting with Non-ST Elevation Myocardial Infarction

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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**Background:** In patients presenting with non-ST elevation myocardial infarction, we investigated the relationship of left atrial deformational parameters evaluated by 2-dimensional speckle tracking imaging (2D-STI) with conventional echocardiographic diastolic dysfunction parameters and brain natriuretic peptide level.

**Material/Methods:** We enrolled 74 non-ST segment elevation myocardial infarction patients who were treated with percutaneous coronary intervention and 58 healthy control subjects. Non-ST segment elevation myocardial infarction patients had echocardiographic examination 48 h after the percutaneous coronary intervention procedure and venous blood samples were drawn simultaneously. In addition to conventional echocardiographic parameters, left atrial strain curves were obtained for each patient. Average peak left atrial strain values during left ventricular systole were measured.

**Results:** BNP values were higher in non-ST segment elevation myocardial infarction patients compared to controls. Mean left atrium peak systolic global longitudinal strain in Group 2 (the control group) was higher than in the non-ST segment elevation myocardial infarction group. Left atrium peak systolic global longitudinal strain was significantly correlated with left ventricular ejection fraction. There was a significant inverse correlation between left atrium peak systolic global longitudinal strain and brain natriuretic peptide level, left atrium volume maximum, and left atrium volume minimum.

**Conclusions:** Our study shows that Left atrium peak systolic global longitudinal strain values decreased consistently with deteriorating systolic and diastolic function in non-ST segment elevation myocardial infarction patients treated with percutaneous coronary intervention. Left atrium peak systolic global longitudinal strain measurements may be helpful as a complimentary method to evaluate diastolic function in this patient population.

**MeSH Keywords:** **Echocardiography • Myocardial Infarction • Natriuretic Peptide, Brain**

**Abbreviations:** **A** – mitral inflow velocity during atrial contraction; **BNP** – brain natriuretic peptide; **E** – early mitral inflow velocity; **Em** – early mitral annular tissue Doppler diastolic velocity; **LA** – left atrium; **LAVmax** – left atrium maximum volume; **LAVmin** – left atrium minimum volume; **LAVreservoir** – left atrium reservoir volume; **LAGLSs** – left atrium peak systolic global longitudinal strain; **LARF** – left atrium reservoir function; **LV** – left ventricle; **LVEDV** – left ventricular end-diastolic volume; **LVEDP** – left ventricular end-diastolic pressure; **LVEF** – left ventricular ejection fraction; **LVESD** – left ventricular end-systolic diameter; **LVEDD** – left ventricular end-diastolic diameter; **LVESV** – left ventricular end-systolic volume; **MI** – myocardial infarction; **NSTEMI** – non-ST segment elevation myocardial infarction

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## Background

Left atrial (LA) function has been associated with adverse outcomes in patients after myocardial infarction (MI). MI results in left ventricular (LV) systolic and diastolic dysfunction. During the early phases of MI, 38% of patients have impaired relaxation and 24% of patients have restrictive LV filling pattern [1]. The important consequence of diastolic dysfunction is elevated filling pressures [2,3]. LV diastolic dysfunction was related to morbidity and death independently from systolic function in MI [4,5]. Therefore, assessment of diastolic function and LV filling pressures after non-ST segment elevation myocardial infarction (NSTEMI) has important prognostic implications. Diastolic function can be evaluated with several noninvasive and invasive techniques. Tissue Doppler imaging (TDI)-derived indices, including systolic velocity (S), early (Em), and late (Am) diastolic velocities of mitral annulus and early mitral inflow peak velocity (E)/Em ratio, are sensitive and widely used parameters to estimate LV filling pressures [6]. Increased B-type natriuretic peptide (BNP) levels also provide reliable estimation of LV filling pressures, particularly for left ventricular end diastolic pressure (LVEDP) and pulmonary capillary wedge pressure (PCWP) [7–9]. LA function and morphology is affected by increased LV filling pressures. Compared with Doppler and 2-D echocardiography, 2-dimensional speckle tracking imaging (2D-STI) has the advantage of angle independence, and is also less affected by reverberations, side lobes, or drop-out artifacts. While this novel echocardiographic method has been frequently used to assess LV function, it has more recently been used to evaluate atrial function in normal subjects and in conditions with atrial dysfunction. Assessment of LA strain using 2-D STI is a recently introduced and accurate method for evaluating LA functions. Current studies have shown the clinical importance of LA strain in atrial fibrillation and cardiomyopathy [10]. Moreover, decreased LA peak strain during LV systole (LAGLSs) was related to increased LVEDP, [11]. In the setting of NSTEMI treated with percutaneous coronary intervention (PCI) and medical treatment, we aimed to investigate the effects of diastolic dysfunction detected by echocardiography and BNP on LA deformational parameters evaluated with 2-D STI. We also measured phasic LA volumes and assessed their relation to diastolic dysfunction and LA strain.

## Material and Methods

The study was conducted in the cardiology clinic in accordance with the Helsinki Declaration after the approval of the hospital ethics committee. All patients were informed before the study and they gave consent.

### Study population

The study group consisted of 74 (65 male, 9 female) consecutive NSTEMI patients who were treated with PCI in our institution (Group 1) and the control group (Group 2) consisted of 58 healthy subjects (48 male, 10 female) with no known history of cardiovascular disease, hypertension, or diabetes mellitus, and with normal treadmill exercise stress echocardiography. Patients with critical stenosis in coronary angiography were included in the study. We excluded patients with atrial fibrillation or moderate-to-severe valvular stenosis or regurgitation, as well as patients whose LA had an insufficient imaging quality.

### Study design

There were 2 groups: Group 1 consisted of 74 patients with NSTEMI and Group 2 consisted of 58 healthy control subjects. NSTEMI patients had an echocardiographic examination 48 h after the PCI procedure and venous blood samples were drawn simultaneously.

### Conventional echocardiographic evaluation

All patients underwent an echocardiographic evaluation in the left lateral position, using the GE Vivid 7 system (GE Vingmed Ultrasound AS, Horten, Norway) with a 3.5-MHz transducer. Heart rate and blood pressure were continually monitored during the transthoracic evaluation. All data were transferred to a workstation for offline analyses (EchoPac PC). The Group 1 patients had echocardiographic evaluation 48 h after PCI. Transmitral early (E) and atrial contraction (A) flow wave velocities were attained by pulsed-wave Doppler echocardiography in the apical 4-chamber image. The ratio of E/A and E wave deceleration time were evaluated. For tissue Doppler imaging, the same echocardiography was used to achieve tissue Doppler imaging data at high frame rates. The myocardial systolic (Sm), early diastolic (Em), and late diastolic (Am) wave velocities were attained at the septal and lateral mitral annulus. The E/Em for septal and lateral annulus, as well as E/A ratios, were calculated. LA dimensions and LV end-systolic (LVESD) and end-diastolic diameters (LVEDD) were evaluated. LV ejection fraction (LVEF) was anticipated by Simpson's biplane method using apical 4-chamber and 2-chamber images. LA volumes were evaluated using the biplane "area-length" method from apical 4- and 2-chamber images and their averages were calculated. LA maximum volume (LAVmax) was measured when the mitral valve was completely opened, LA minimum volume (LAVmin) was measured when the mitral valve was completely closed, and following parameters were calculated using these measurements:

LAVreservoir (ml): LAVmax–LAVmin, LAEF (%): LAVmax–LAVmin/LAVmax





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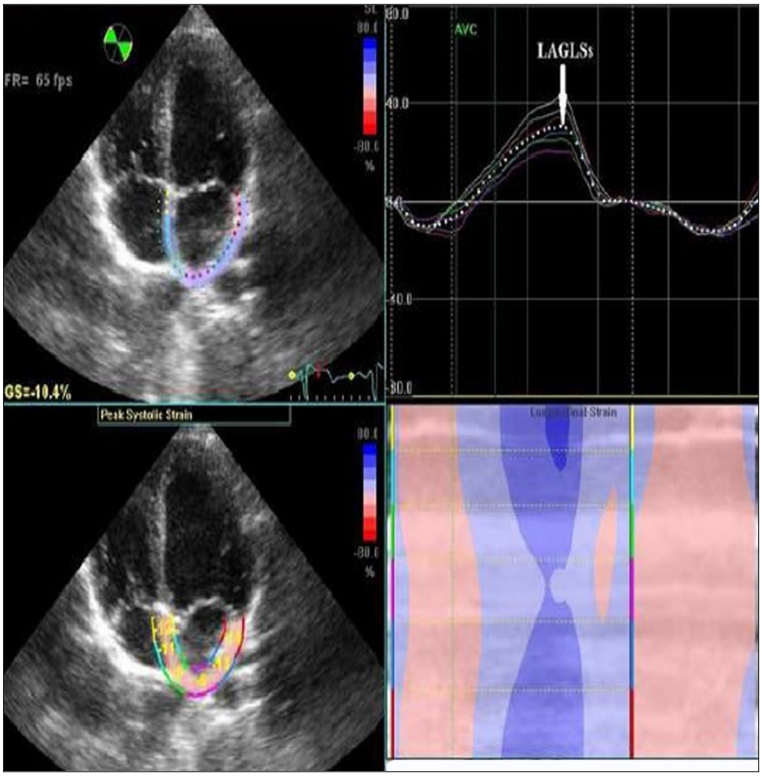


**Figure 1.** Measurements of LAGLSs on an image obtained from apical 4-chamber view (LAGLSs: peak left atrial strain during left ventricular systole).

Cardiac dimensions were measured in accordance with recommendations of the American Society of Echocardiography [12].

### Two-dimensional speckle tracking imaging analysis of the left atrium

Two-dimensional echocardiography views for the LA were attained from the apical 4-chamber image. All views were attained with patients holding their breath at end-expiration and the views were stored in a cineloop format from 3 sequential beats. The frame rate for views was set at 60–90 frames/second. After determining the endocardial border manually, the software system was automatically improved for each frame. If the automatically attained tracking segments were sufficient for analysis, the software system was allowed to read the data, and analytically insufficient tracking segments were either corrected manually or excluded from the analysis. The view-tracking algorithm automatically divided the LA wall into 6 segments. The typical LA strain graph was attained for each patient. Mean peak LA strain valuations during LV systole (LAGLSs) for 6 segments were evaluated (Figure 1).

### BNP measurement

Blood samples were obtained from NSTEMI patients and control subjects during the echocardiographic study. The blood samples were immediately centrifuged at 1500 rpm for 5 minutes and plasma was stored at –80°C until the time of evaluation. The quantitative definition of BNP in plasma was performed using the immune fluorescence method.

### Reproducibility

Measurements were performed by a single person. Intraobserver reproducibility for the LAGLSs was assessed. For intraobserver evaluation, views from 25 randomly selected patients were reassessed after 1 week. The Bland-Altman analyses and intraclass correlation coefficient (ICC) demonstrated good intraobserver compromise; for intraobserver compromise, the mean difference was 1.3 (–2.1, 3.2) and ICC 0.91. To assess the intraobserver variability, selected images were analyzed at a different time by an observer blinded to the results of the previous measurements [13].

### Statistical analysis

Results are reported as the mean ±SD and statistical analysis of clinical data between the 2 groups consisted of unpaired t-tests for parametric data, Mann-Whitney U test analysis for nonparametric data, and analysis of variance for repeated measures for parametric data. To analyze correlation between variables, the Pearson correlation coefficient was used. Statistical analysis was performed using PASW 18 (SPSS/IBM, Chicago, IL, USA). The level of significance was established at 0.05 (2-sided).





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**Table 1.** Demographic characteristics of NSTEMI patients.

| Parameters | Value |
|---|---|
| Gender (%), male | 88.7 |
| Age, years (mean ±SD) | 56.4±9.2 |
| Family history (%) | 14 |
| Hypertension (%) | 22 |
| Diabetes mellitus (%) | 11 |
| Hyperlipidemia (%) | 32 |
| Smoking (%) | 78 |
| Revascularized vessels (RCA,CX,LAD) (n: 74) | Respectively; 18, 24, 32 |
| Peak CK (mg/dl) (mean ±SD) | 1400.1±966.4 |
| Peak CK-MB (mg/dl) (mean ±SD) | 202.5±128.8 |
| Peak Troponin I (ng/dl) (mean ±SD) | 33.7±21.4 |

CX – circumflex coronary artery; LAD – left anterior descending coronary artery; RCA – right coronary artery.

## Results

There was a male dominancy in both Group 1 (88.7%) and Group 2 (83%); the mean ages of subjects were 56.4±9.2 years in Group 1 and 54.7±8.4 years in Group 2. Demographic characteristics of Group 1 patients are shown in Table 1. Table 2 shows a comparison of some clinical and echocardiographic characteristics of Group 1 patients and Group 2 individuals. Average time spent for offline analysis of LAGLSs for each patient was 4 min and 94% of LA segments were tracked appropriately by the software and included in our analysis. BNP values were significantly higher in Group 1 patients compared to Group 2 (114 [12.0–1249.5] *vs.* 6.0 [3.0–23.1]; pg/ml p=0.001). The differences between the measurements of transmitral flow velocities (E, A), and E/Em and E/A ratios of the groups were also significant (Table 2). Maximum and minimum left atrial volumes were increased in Group 1 patients (Table 3). Mean LAGLSs in Group 2 was higher than Group 1 (30.2±5.4% *vs.* 21.0±6.4% p=0.001). LAGLSs had significant correlation with LVEF (r=0.51, p=0.001), also there was a significant inverse correlation between LAGLSs and BNP level (Figure 2) (r=–0.44, p=0.001), E/Em (r=–0.34, p=0.001), LAVmax (r=–0.43, p=0.001), LAVmin (r=–0.48, p=0.001), LAEF (r=0.36 p=0.001) and LVESV (r=–0.37, p=0.001).

## Discussion

We demonstrated that LAGLSs was significantly reduced after NSTEMI compared to controls, and it was closely related with LVEF and BNP levels. LA size and function is an important determinant of cardiovascular morbidity and mortality. LAGLSs provides additional prognostic value. Assessment of LAGLSs using 2-dimensional speckle tracking imaging has recently been introduced for the quantification of regional and global LA deformation. LAGLSs measurement has been proposed as an alternative method for the estimation of LV filling pressure.

**Table 2.** Comparison of some clinical and echocardiographic characteristics of NSTEMI patients and control individuals.

| Parameters | Group 1 | Group 2 | P value |
|---|---|---|---|
| Age, years | 56.4±9.2 | 54.7±8.4 | 0.32 |
| Gender, %, male | 88.7 | 83 | 0.56 |
| BNP, pg/ml* | 114 [12–1249] | 6 [3–23] | 0.001 |
| A, m/s | 0.69±0.1 | 0.79±0.1 | 0.001 |
| E, m/s | 0.60±0.1 | 0.78±0.1 | 0.001 |
| E/A | 0.87±0.3 | 0.99±0.3 | 0.001 |
| Em septal, cm/s | 5.6±1.7 | 7.2±1.8 | 0.001 |
| Em lateral, cm/s | 6.3±1.7 | 8.0±1.8 | 0.001 |
| E/Em septal | 13.5±3.1 | 10.9±1.9 | 0.001 |
| E/Em lateral | 13.2±2.7 | 10.8±1.4 | 0.001 |
| LVEDV, ml | 109.1±18.4 | 106.0±18.6 | 0.5 |
| LVESV, ml | 55.4±15.2 | 42.7±9.1 | 0.006 |
| LVEF, (%) | 55.6±15.3 | 60.0±5.2 | 0.003 |

A – mitral inflow velocity during atrial contraction; BNP – indicates brain natriuretic peptide; E – early mitral inflow velocity; Em – early mitral annular tissue Doppler diastolic velocity; LVEDV – left ventricular end diastolic volume; LVEF – left ventricular ejection fraction; LVESV – left ventricular end systolic volume; * median values and range are given in the table for BNP.





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**Table 3.** Echocardiographic assessment of left atrium.

| Parameters | Group 1 | Group 2 | P value |
|---|---|---|---|
| LAVmax (ml) | 47.6±12.5 | 41.1±10.4 | 0.001 |
| LAVmin (ml) | 23.2±16.2 | 16.2±5.8 | 0.001 |
| LAVr (ml) | 24.3±8.9 | 24.8±9.1 | 0.01 |
| LAEF (%) | 51.6±8.2 | 60.1±10.1 | 0.001 |
| LAGLSs (%) | 21.0±6.4 | 30.2±5.4 | 0.001 |

LAVmax – maximum left atrial volume; LAVmin – minimum left atrial volume; LAVr – reservoir left atrial volume; LAEF – left atrium ejection fraction; LAGLSs – peak left atrial strain during left ventricular systole.

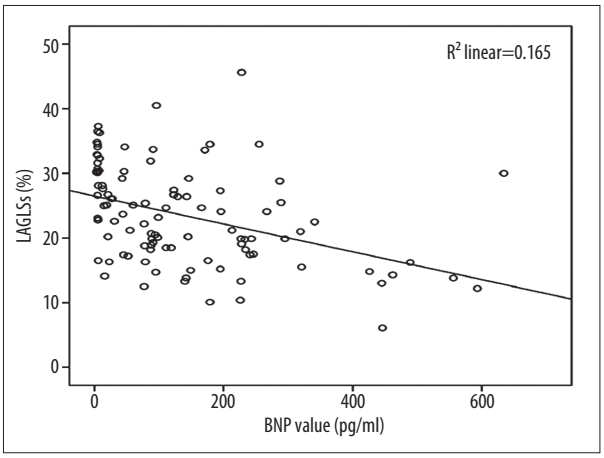


**Figure 2.** Correlation of LAGLSs with BNP (LAGLSs: Left atrium global peak systolic strain, BNP: Brain natriuretic peptide).

Decreased LA strain has been correlated with increased left ventricular end-diastolic pressure. Cameli et al. [10] demonstrated that in a group of patients with advanced systolic heart failure, E/Em ratio correlates poorly with invasively obtained LV filling pressures. Nevertheless, LAGLSs analysis by speckle tracking imaging correlates well with pulmonary capillary wedge pressure, providing a better estimation of LV filling pressure in this particular clinical setting. E/Em ratio, LA volumes, and BNP were also significantly increased in NSTEMI patients, reflecting increased diastolic filling pressures and diastolic dysfunction. Although experimental studies demonstrated rapid BNP release in response to cardiac ischemia, it is unlikely that BNP will be used to diagnose cardiac ischemia because many other conditions are also associated with modest BNP elevation. In contrast, BNP holds tremendous promise as a prognostic marker in patients with NSTEMI. Studies to date have consistently shown that higher BNP levels are associated with worse clinical outcomes, and that BNP provides unique information about clinical variables, other biomarkers, and left ventricular ejection fraction. Neurohumoral activation as evidenced by BNP appears as a unifying feature that is independent of other biochemical markers (e.g., myocardial necrosis) and is a powerful and independent determinant of the short-term cardiac risk in patients with NSTEMI. Whether serial measurements of BNP in patients with NSTEMI may be used to more rapidly identify patients suitable for early discharge or more intensive therapy deserves future prospective studies. Future studies are needed to identify the therapeutic implications of BNP elevation in patients with NSTEMI. Patients who have elevated LV filling pressures after MI are more likely to have chronic heart failure and increased mortality. After several decades of investigation, current consensus recommendations state that LA function plays an important role in optimizing overall cardiac function, and the changes in LA size and function are associated with cardiovascular disease and are risk factors for atrial fibrillation, stroke, and death. The left atrium serves as a blood reservoir during ventricular systole and a conduit for the passage of blood from the pulmonary veins into the left ventricle during early and middle ventricular diastole, as well as acting as a booster pump, increasing LV filling during late diastole. Using the E/Em ratio, an accurate forecast of LV filling pressures can be attained in a extensive spectrum of patients [14,15]. The E/Em ratio is superior to other echocardiographic parameters in this regard and after MI, a high ratio predicts higher mortality and enhanced risk of reverse remodeling [16,17]. However, Ommen et al. [18] reported that an E/Em ratio of 8–15 was associated with a very large range of average LV diastolic pressures. Because most of our patients had E/Em ratios of 8–15, forward echocardiography evaluating LA volumes and LA function was performed. E/Em ratios were substantially higher in our NSTEMI patients. Once it is indexed to body surface area, LA volume is independently related with enhanced cardiovascular risk and disease burden [19] and is a strong predictor of middle-term outcome in patients with suspected heart failure [20], as well as in patients with NSTEMI [21,22]. We hypothesized that enhanced LA volumes evaluated by the area length method in our NSTEMI patients was a result of LA dilation as an adaptation to LV pressure and volume overburden. At first, LA dilatation contributes to advance cardiac output as an adaptable mechanism; but when the ideal Frank Starling relationship is surpassed, this dilatation results in diminished LA compliance





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and enhanced risk of atrial arrhythmias [23]. Two-dimensional speckle tracking imaging was demonstrated in many studies to be useful in quantification of atrial myocardial deformation. LA myocardial deformation curves attained with 2-dimensional STI are similar to LA volume graphs. LA volume and function graphs contain 3 phases, known as reservoir, conduit, and booster pump [24]. LAGLSs is closely related to the LA reservoir function (LARF), and the LA strain during atrial systole is associated with booster pump function [12]. The LARF is evaluated in 2 sequential phases: early and late. Although the early LARF depends on LA relaxation, the late LARF depends on LV contraction through the descent of the base during systole. Thus, both LA relaxation and LV systolic function might influence the LARF and, subsequently, LAGLSs. Wakami et al. investigated the impact of LVEDP on LAGLSs during LV systole [12], reporting that enhanced LVEDP is related to a decrease of LAGLSs. Furthermore, several studies showed the superiority of peak systolic atrial deformation parameters over diastolic atrial myocardial deformation parameters as a predictor of atrial fibrillation and cardiovascular events. Therefore, in our research we evaluated LAGLSs to assess diastolic dysfunction after NSTEMI. Additionally, the LAGLSs, being an index of LARF, is further associated with LV systolic function [25]. Cameli et al. found a good correlation between LAGLSs and PCWP in patients with advanced heart failure [26] – our results agreed; in our NSTEMI patients, average LAGLSs was substantially lower than in controls, and LAGLSs was correlated with LVEF. Our NSTEMI population showed a substantial decrease in systolic and diastolic LV function. Parameters such as BNP may also be used to predict increased LV filling pressures [27]. Levels of BNP were correlated with elevated PCWP and LVEDP [28]. We observed that LAGLSs was inversely correlated with BNP level, as well as with echocardiographic parameters of diastolic function such as E/Em, LAVmax, LAV min, and LV end-systolic volume.

### Study limitation

This study has several limitations. Strain and strain rate have been demonstrated to be affected by preload change, and assessment of LA function by 2-dimensional STI is relatively time consuming and difficult. To attain suitable LA views for strain analysis in patients with inadequate echocardiographic views is difficult and sometimes impossible. The most important limitation of our research was that instead of evaluating LVEDP invasively, it was anticipated using BNP and echocardiographic measurements. The patients were not followed to evaluate the prognostic influence of diminished LAGLSs after NSTEMI.

## Conclusions

We demonstrated that 2-dimensional STI is a non-invasive, reproducible, and relatively simple technique for evaluating LA myocardial function in patients with NSTEMI. We observed that LAGLSs values decreased consistently with deteriorating systolic and diastolic function. Our results suggest that LAGLSs measurements may be helpful as a complimentary method to evaluate diastolic function when inconclusive results are obtained by conventional echocardiographic parameters.

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