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Assessment of Left Atrial Function Using Speckle Tracking Imaging in Patients with Heart Failure Receiving Sacubitril Valsartan

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ABSTRACT

Background: Speckle-tracking echocardiography (STE) is a non-invasive ultrasound imaging method that enables an objective and quantitative assessment of both global and localised myocardial function. Sacubitril-Valsartan represents a breakthrough class of medications added to the arsenal of drugs used in Heart Failure therapy.

Objective: To study the function of the left atrium (LA) using two-dimensional (2-D) speckle tracking echocardiography (STE) among individuals with heart failure and reduced ejection fraction (HFrEF) who were undergoing treatment with Sacubitril/ Valsartan, also known as angiotensin receptor blocker -neprilysin inhibitor (ARNI). **Methods:** This randomised clinical study was performed on 123 HFrEF patients of both sexes and aged above 18 years. Only 100 HFrEF patients agreed to complete the study follow-up period. They were randomized into two equal groups according to the treatment plan: Group I (study group) received the traditional treatment for HF plus ARNI (Sacubitril/Valsartan replacing ACE inhibitors / ARBs). Group II (control group) received traditional treatment for HF without ARNI (ACE inhibitors / ARBs were given). Conventional echocardiography and 2D STE were performed to assess LA and LV strain functions at baseline and after 12 months using GE vivid 9 echo machine equipped with a M5S (1.7-4MHz) phased array transducer.

Results: Speckle tracking echocardiography strain findings after 12 months follow up revealed statistically significant enhancements of the LA conduit, LA reservoir, and LA contractile strain values in addition to improved global LV longitudinal strain (LS) and LV EF in ARNI group in comparison with non-ARNI group ($p < 0.001$).

Conclusions: STE showed that Sacubitril/Valsartan for a period of 12 months led to significant improvements in LA and LV strain parameters when added to standard Heart Failure therapy.

Keywords: Speckle tracking imaging, Left atrial strain, Heart failure, ARNI.

INTRODUCTION

Heart failure (HF) is a clinical condition characterised by a combination of fundamental symptoms, such as dyspnea, swelling of the ankles, and fatigue, together with accompanying signs, such as raised jugular venous pressure (JVP), pulmonary crackling, and peripheral edoema. It should be noted that HF is not considered a singular pathological diagnosis. The presence of a structural and/or functional anomaly in the heart leads to increased pressures inside the heart along with insufficient cardiac output throughout periods of rest and/or physical activity. Left ventricular ejection fraction (LVEF) ≤ 40% is designed as HFrEF [1].

The function of the atria, which is closely interconnected with the function of the LV, has a significant impact on preserving an optimum performance of the heart. The LA plays a role in regulating LV filling by performing three functions: Reservoir, conduit, and booster pump. On the other hand, the functioning of the LV affects the performance of the LA during the whole cardiac cycle. The LA has the ability to actively respond to increasing LV filling pressure, particularly in cases of substantial myocardial stiffness. In addition, the left atrial remodelling (LAR) is also associated with LV remodelling, and the function of the LA plays a crucial role in preserving an adequate cardiac output even in the presence of poor LV relaxation and decreased left ventricular compliance **[2]**. STE is a non-invasive imaging approach that utilizes ultrasonography to objectively and quantitatively assess global and localised myocardial function. This assessment is conducted independently from the angle of insonation and heart translational motions [3-6]. The technique known as STE depends upon an examination of spatial displacement, sometimes referred to as tracking of speckles. Speckles are characterised as spots that arise from the interaction between the ultrasonic beam and myocardial fibers and are seen on standard 2-D sonograms **[7]**. While the STE approach was first developed for the specific purpose of analysing LV functioning, a number of subsequent investigations have expanded its potential applications to include additional cardiac chambers, which include the LA **[8]**. The atrial longitudinal strain, which is obtained by utilising the technique of cardiac deformation analysis employing STE in the atrial chambers, is recognised as the first parameter that is valuable for assessing the functional characteristics of the LA. Furthermore, it exhibits a high level of practicality and repeatability [9]. In our study, we tried to evaluate LA function using STE imaging in patients with HFrEF receiving Sacubitril/Valsartan.

PATIENTS AND METHODS

This randomised clinical study was performed on 123 patients aged above 18 years of both sexes suffering from heart failure with reduced EF. The study was done in The Cardiology Outpatient Clinics,

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Menoufia University Hospitals through the period from July 2021 to August 2022.

Inclusion criteria: 1. Prior to conducting any examination, it was essential to get written informed permission. 2. Individuals who are at least 18 years old, regardless of gender. 3. Individuals had a LVEF of 40% or less already receiving HF guidelines approved medical therapy, who met the criteria for receiving sacubitril/valsartan medication according to the established standard of care. 4. NYHA functional classification ranges from II to IV.

Exclusion criteria: 1. Women who are pregnant or breastfeeding. 2. The individual's medical history included a documented hypersensitivity to any of the pharmaceutical agents used in the research. 3. The historical development of angioedema treatments, whether drug-related or otherwise. 4. Participants who have had the implantation of a cardio resynchronization treatment device (referred to as cardiac resynchronization therapy [CRT] or CRT Defibrillator) during a period of 6 months prior to the screening visit. 5. Participants who were now receiving inotropic drugs. 6. Any hospitalization linked to HF occurring during the two-week period previous to the baseline assessment. 7. Potassium >5.2 mEq/L at screening. 8. Patients with atrial fibrillation. 9. Poor Echogenic window. 10. Patients receiving ACE inhibitors within 48 hours before the start of ARNI

All participants had been exposed to the following at baseline and after 12 months: Full history taking, clinical assessment, resting 12-lead ECG, and echocardiography.

Randomization and blindness: Randomization was performed using closed envelop technique. Randomization was single-blinded. After exclusion of 23 patients who did not complete the study follow up the remaining 100 cases were allocated into 2 equal groups: Group I (study group) received the traditional treatment for HF plus ARNI (Sacubitril/Valsartan replaced ACE inhibitors / ARBs). Group II (control group) received traditional treatment for HF without ARNI (ACE inhibitors / ARBs were given).

Echocardiography

All subjects underwent conventional and two-dimensional speckle tracking echocardiography examination with vivid E9, general electric health care (GE Vingemed, Norway) equipped with a harmonic M5S variable frequency (1.7-4MHz) phased array transducer. Examinations were done during breath hold while the patients were in the left lateral position with stable electrocardiographic tracing. 2-D images and cine frames of 3 consecutive cardiac cycles were acquired in apical four, two and three chamber views along with parasternal long-axis and short-axis at the levels of aortic valve using frame rates from 70–100 frames/s. All images were digitally stored on the hard disk of the machine. Raw data was transferred on compact disks (CD) to be used for off-line analysis using EchoPac software version 113.

Assessment of LV dimensions: Measures were obtained at end diastole with a preference to utilize the maximum LV cavity diameter. Additionally, measures were performed during end systole, utilising the minimum LV cavity diameter. The diastolic measures acquired included the thickness of the inter-ventricular septal wall, the left ventricular internal diameter at end diastole, and the thickness of the posterior wall.

Systolic function assessment: The ejection fraction (EF) was determined by calculating the percentage change in left ventricular chamber volumes between diastole and systole, utilising the apical four and two chamber views and applying the modified biplane Simpson's method. EF 40% or below was considered as reduced ejection fraction

Diastolic function assessment: The pulsed-wave Doppler echocardiography was utilised to assess the diastolic function of the left ventricle. Doppler experiments were conducted from the apical 4-chamber view, with a sample volume placed inside the inflow region of the left ventricle, specifically positioned halfway between the annular borders of the mitral valve. The velocity profiles of the mitral valve were digitised by extracting data from the Doppler tracings.

Waves measured by pulsed conventional doppler:

1. The velocity of the peak E (early fast ventricular filling) wave.
2. The velocity of the Peak A wave during the late ventricular filling phase.
3. The E/A ratio, which represents the ratio between the early and late filling waves.

Tissue Doppler imaging: Three significant velocities were measured at the septal annular locations. The maximum positive systolic velocity seen during the annulus movement to the apex (S). There were two prominent instances of significant negative velocities seen throughout the annulus' retrograde motion towards the base in the early (e') and late (a') phases of diastole. The E/e' ratio was also computed. Diastolic dysfunction is classified when the ratio of TDI (e'/a') is less than 1, or when the ratio of E/e' exceeds 10.

Assessment of LA volume index (LAVI):

Clear apical 4-chamber and 2-chamber views of the left atrium were used to measure LA volume at End-Systole just before the mitral valve opens. After tracing the LA endocardial border, the biplane method of disks (modified Simpson's rule) was used to calculate the LA volume. The result was then divided by the patient's surface area to estimate the LA volume index (LAVI) mL/m^2.

2D Speckle tracking imaging: The acquisition of 3 apical views (apical 4,2 and 3 chambers views) was performed. Throughout a breath hold, three successive cardiac cycles were captured for each view followed by tracing of the endocardial border. The measurement of

longitudinal strain (LS) was conducted offline via the specialised software. Subsequently, the program used a selection process to identify and monitor stable speckles located inside the myocardium. These speckles were then tracked on a frame-by-frame basis for the whole of the cardiac cycle. The time of aortic valve closure was determined automatically with the ability of manual readjustment.

Assessment of LA strain: 2-D grayscale pictures were obtained using conventional apical 4- and 2-chamber views. LA strain is typically analysed in terms of reservoir strain (during ventricular systole), conduit strain (during early ventricular diastole), and contractile strain (during late ventricular diastole). In order to identify the timing, the of reservoir function of the LA was linked to beginning of QRS in the ECG as a point of reference. Global peak atrial LS was determined by averaging the recorded peak LS values in all LA segments obtained.

Assessment of LV Global Longitudinal strain (LV GLS): 2-D grayscale pictures were obtained using apical 4, 2 and 3 chamber views. After identifying the endocardial border, the program then identified region of interest and partitioned the left ventricular myocardium into three segments for each of the 6 walls, resulting in a total of 18 segments. Global LVGLS was determined by averaging the observed peak LS values of all LV segments.

Ethical approval: **Ethical approval for this investigation was obtained from The Ethical Committee of Menoufia University Hospitals, Egypt. Written informed permissions were obtained from the participants or their relatives. The study adhered to the Helsinki Declaration throughout its execution.**

Statistical analysis

The data were organised and recorded in the SPSS software edition 29. Categorical data were presented as number and percent. Continuous data were presented as either mean ± standard deviation if parametric or media, minimum and maximum if non- parametric. Chi- square test was utilized to contrast categorical data. Student t- test was utilized to contrast parametric continuous data and Man Whitney test was utilized to contrast parametric continuous data. Spearman correlation was utilized to test the association between data. Level of significance was adjusted to be ≤ 0.05.

RESULTS

This research included the assessment of 123 individuals to determine whether they were eligible. Out of these individuals, 15 individuals did not match the predetermined criteria, while eight individuals declined to take part in the trial. The remainder of the 100 individuals were assigned randomly into two groups with 50 participants in each group. The participants who were assigned to certain groups were thereafter monitored and subjected to statistical analysis. No statistically substantial variations were existed between the two groups as regards age, gender (Table 1).

Table (1): Demographics and baseline characteristics between both groups

	Group I (n= 50)	**Group II (n= 50)**	**P value**
Age (years)	68.2±10.9	67.5±8.4	0.1
Sex - Male - Female	 31 (62%) 19 (38%)	 36 (72%) 14 (28%)	0.28

As regards to conventional echocardiography parameters at baseline, no statistically substantial variations existed among participants of both groups. Speckle tracking findings at baseline including LVGLS, LA reservoir strain, LA conduit stain and LA contractile strain also showed no statistically significant differences between group I and group II (Table 2).

Table (2): Baseline echocardiography findings between both groups

	Group I	**Group II**	**P value**
Conventional Echocardiography			
LVEDV (mL)	156.5 ± 30.26	156.2 ± 21.07	0.95
LVESV (mL)	102.98 ± 18.76	105.04 ± 17.48	0.57
Ejection fraction (%)	34.88 ± 3.66	34.08 ± 4.5	0.33
E/e` ratio	10.5 ± 1.6	10.1 ± 1.5	0.09
LAVI (mL/ m^2)	38.7±9.1	40.2±5.8	0.34
MR grade 2 3 4	 28 (56%) 8 (16%) 14 (28%)	 30 (60%) 12 (24%) 8 (16%)	0.28
Diastolic dysfunction grade: 1 2 3	 2 (4%) 39 (78%) 9 (18%)	 0 (0%) 40 (80%) 10 (20%)	0.356
TR grade 1 2 3 4	 7 (14%) 19 (38%) 17 (35%) 7 (14%)	 2 (4%) 23 (46%) 21 (42%) 4 (8%)	0.22
TR velocity (m/s)	2.7±0.3	2.8±0.3	0.058
Speckle tracking			
Average left ventricle GLS (%)	-9.95 ± 1.7	-9.7 ± 1.95	0.07
LA reservoir strain	31.3±5.65	31.7±4.9	0.67
LA conduit strain	-22.07±1.04	-22.08±1	0.95
LA contractile strain	-13.5±3.6	-13.8±2.6	0.61

Data are presented as Mean ±SD or frequency (%). Level of significance< 0.05; **LVEDV:** Left ventricular end diastolic volume; **LVESV:** Left ventricular systolic volume; **GLS:** Global longitudinal strain; **LA:** Left atrium; **LAVI:** Left atrium volume index.

Regarding conventional echocardiography findings after 12 months, LVEDV, LVEESV, E/e` ratio and left atrium volume index had lower mean values among group I compared to group II with statistically substantial differences (p= 0.04, 0.024, 0.002 & < 0.001 respectively). A statistically substantial variations existed among both groups as regards TR and MR grades with higher percent of low grades among group I and higher percent of high grades among conventional group (p < 0.001 & 0.001 respectively). As regards speckle tracking findings after 12 months, LVGLS, ejection fraction, LA reservoir strain, LA conduit and LA contractile strain were higher with statistically significant differences among group 1 (p < 0.001) (Table 3).

Table (3): Comparison of echocardiography findings between both groups after 12 months of treatment

		Group I (n=50)	Group II (n=50)	P value
Conventional Echocardiography	**LVEDV** (mL)	152.2 ± 29.75	163.52 ± 26.5	***0.04***
	LVESV (mL)	97.058 ± 22.25	107.15 ± 22.09	**0.024**
	Ejection fraction (%)	39.2 ± 2.9	34.3 ± 4.3	**<0.001**
	E/e` ratio	9.2 ± 1.8	10.96 ± 2.48	**0.002**
	LAVI (mL/ m^2)	34.59 ± 8.5	42.5 ± 5.9	**<0.001**
	MR grade 2 3 4	 40 (80%) 5 (10%) 5 (10%)	 33 (66%) 11 (22%) 6 (12%)	**<0.001**
	TR grade 1 2 3 4	 17 (34%) 22 (44%) 9 (18%) 2 (4%)	 2 (4%) 27 (54%) 18 (36%) 3 (6%)	**<0.001**
Speckle tracking	**Average left ventricle GLS** (%)	-11.2 ± 1.2	-9.6 ± 1.6	***<0.001***
	LA reservoir strain	34.3 ± 4.3	30.6 ± 4.9	***<0.001***
	LA conduit strain	-26.23 ± 2.13	-22.04 ± 0.88	***<0.001***
	LA contractile strain	-15.6 ± 2.7	-13.2 ± 2.55	***<0.001***

Data are presented as Mean ±SD or frequency (%). Level of significance< 0.05; **LVEDV:** Left ventricular end diastolic volume; **LVESV:** Left ventricular systolic volume**; GLS:** Global longitudinal strain; **LA:** Left atrium; **LAVI:** Left atrium volume index.

In group I, conventional echocardiography showed that mean values of LVEDV, LVESV and E/e` were decreased after 12 months with statistically significant differences (p= 0.038, 0.04 & 0.002 respectively). EF was increased significantly after 12 months (p< 0.001). Left atrial volume index (LAVI) was decreased after 12 months with statistically substantial variation when contrasted to baseline (p < 0.001). There were statistically substantial differences among baseline and 12-months follow up as regards TR and MR grades (p= 0.02; 0.03 resp.). In group II, LAVI increased after 12 months when contrasted to baseline (p< 0.001). E/e` ratio increased after 12 months with statistically significant difference (p= 0.039). There were no statistically substantial variations among baseline and after 12 months regarding LVEDV, LVESV, TR, MR grades, GLS, EF and LA conduit strain. Regarding speckle tracking parameters in group I, mean values of LVGLS, LA reservoir strain, conduit strain and contractile strain were increased after using sacubitril/valsartan with statistically significant differences. While in group II, LA reservoir strain and left atrial contractile strain were decreased when compared to baseline (p< 0.001) (**Error! Reference source not found.**).

Table (4): Comparison of echocardiography findings between baseline and 12 months in both groups

		Group I (n=50)			Group II (n=50)		
		Baseline	**12- month**	**P value**	**Baseline**	**12-month**	**P value**
Conventional echocardiography	**LVEDV** (mL)	156.5 ± 30.26	152.2 ± 29.75	**0.038**	156.2 ± 21.07	163.52 ± 26.5	0.13
	LVESV (mL)	102.98 ± 18.76	97.058 ± 22.25	**0.04**	105.04 ± 17.48	107.15 ± 22.09	0.6
	Ejection fraction (%)	34.88 ± 3.66	39.2 ± 2.9	**<0.001**	34.08 ± 4.5	34.3 ± 4.3	0.17
	E/e` ratio	10.5 ± 1.6	9.2 ± 1.8	**0.002**	10.1 ± 1.5	10.96 ± 2.48	**0.039**
	LAVI (mL/ m^2)	38.7±9.1	34.59 ± 8.5	**<0.001**	40.2±5.8	42.5 ± 5.9	**<0.001**
	MR grade 2 3 4	 28 (56%) 8 (16%) 14 (28%)	 40 (80%) 5 (10%) 5 (10%)	**0.03**	 30 (60%) 12 (24%) 8 (16%)	 33 (66%) 11 (22%) 6 (12%)	0.78
	TR grade 1 2 3 4	 7 (14%) 19 (38%) 17 (35%) 7 (14%)	 17 (34%) 22 (44%) 9 (18%) 2 (4%)	**0.02**	 2 (4%) 23 (46%) 21 (42%) 4 (8%)	 2 (4%) 27 (54%) 18 (36%) 3 (6%)	0.87
Speckle tracking echocardiography	**Average left ventricle GLS** (%)	-9.95 ± 1.7	-11.2 ± 1.2	**<0.001**	-9.7 ± 1.95	-9.6 ± 1.6	0.08
	LA reservoir strain	31.3±5.65	34.3 ± 4.3	**<0.001**	31.7±4.9	30.6 ± 4.9	**<0.001**
	LA conduit strain	-22.07±1.04	-26.23 ± 2.13	**0.004**	-22.08±1	-22.04 ± 0.88	0.83
	LA contractile strain	-13.5±3.6	-15.6 ± 2.7	**<0.001**	-13.8±2.6	-13.2 ± 2.55	**<0.001**

Data are presented as Mean ±SD or frequency (%). Level of significance< 0.05; **LVEDV:** Left ventricular end diastolic volume; **LVESV:** Left ventricular systolic volume; **GLS:** Global longitudinal strain; **LA:** Left atrium**; LAVI:** Left atrium volume index.

At baseline, all patients started sacubitril at dose of 50 mg Bid, which was titrated every 2 weeks up to 200 mg Bid. Out of 50 patients, 17 patients could not tolerate titration (34%), 26 patients could not tolerate more than 100 mg/day (52%) and only 7 patients tolerated 200 mg/day (14%) (Table 5).

Table (5): Doses of sacubitril over 12 months

Dose of Sacubitril - Valsartan	Number of patients at baseline	Number of patients at 12 months
50 mg Bid	50 (100%)	17 (34%)
100 mg Bid	-	26 (52%)
200 mg Bid	-	7 (14%)

Bid: twice daily, mg: milligram

DISCUSSION

STE is a technique that enables the automated monitoring of myocardial movements trajectory in a frame-by-frame manner all through the cardiac cycle. This is achieved through determining the position as well as movement of speckles in 2-D images. Subsequently, various parameters such as myocardial velocity, strain, strain rate, rotation, and torsion are gathered through post-processing [10].

In the present study, at baseline, all patients started sacubitril at dose of 50 mg Bid, which was planned to be titrated up to 200 mg Bid. Out of 50 patients, 17 patients could not tolerate titration (34%), 26 patients could not tolerate more than 100 mg/ day (52%) and only 7 patients tolerated 200 mg/ day (14%) due to occurrence of low blood pressure. In agreement with the current study, **Bras *et al.*** [4] showed that not all patients in his study could maintain full dose of the drug after 2- 4 weeks. In **Bayard *et al.*** [11], 11 patients (21%) did not tolerate full dose of sacubitril/valsartan therapy.

As regard left atrium strain by STE, statistically substantial enhancements in LA strains existed in group I in our study. On the other hand, there was statistically significant worsening of LA strain phases in group II. In agreement with the current study, **Bras *et al.*** [4] reported significant improvement of all phases of strain in sacubitril/valsartan group. Also, **Moon *et al.*** [12] demonstrated that enhanced LA reservoir strain within 6-months period of sacubitril/valsartan treatment. **Mandoli *et al.*** [13] reported significant improvement in LA strain phases after sacubitril/valsartan and he correlated baseline LA strain to the outcome and considered it as significant

predictor for improvement. However, **Correale *et al.*** [6] were unable to exhibit substantial impact of sacubitril/valsartan on atrial contractile.

The present study showed that LAVI was improved significantly after 1 year of sacubitril/valsartan use in group I (38.7±9.1 vs. 34.59 ± 8.5; p< 0.001). In contrary, LAVI increased significantly (worsened) in group II (40.2±5.8 vs. 42.5 ± 5.9; p< 0.001). **Mandoli *et al.*** [13] showed significant improvement in LAVI after sacubitril/valsartan in 13 HFrEF patients. **Bras *et al.*** [4] showed substantial enhancement in left atrium volume after 6 months of sacubitril/valsartan. **Pericas *et al.*** [14] demonstrated similar findings with improving LAV after treatment. In contrary, **Monosilio *et al.*** [15] did not show significant improvement of LAV following 6-month period of sacubitril/valsartan. **Mazzetti *et al.*** [16] did not find significant impact of sacubitril/valsartan on LAV.

In the current work there were statistically significant improvement in LVEDV, LVESV and EF% among the ARNI group, in comparison with non-ARNI group along the 12 month follow up (0.04, 0.03 and 0.001 respectively). **Bras *et al.*** [4] showed significant improvement in LVEDV and LVESV among 35 patients received sacubitril/valsartan over 6 months. He also found increased mean EF with statistically substantial variation (p< 0.001). **Monosilio *et al.*** [15] also showed that the administration of sacubitril/valsartan for a duration of a six-month period resulted in a noteworthy decrease in left ventricular end-diastolic and end-systolic volumes, as well as an enhancement in left ventricular ejection fraction, as seen in a cohort of 36 participants. **Abumayyaleh *et al.*** [2] found that The LVEF showed a statistically significant improvement after the administration of sacubitril/valsartan. Prior to the commencement of sacubitril/valsartan, the median LVEF was 28% (with a range of 3% to 65%). However, at the 24-month follow-up, the median LVEF increased to 34% (with a range of 13% to 64%) (p <0.001).

The present study also showed that LV strain (global longitudinal strain) improved significantly after 1- year in group I (-9.95 ± 1.7 vs. -11.2 ± 1.2; p< 0.001). This finding was not present in group II. In concordance to the current study, **Bras *et al.*** [4] reported significant improvement in variable LV strain phases after 6- month of sacubitril/valsartan. **Moon *et al.*** [12] demonstrated that LV GLS improved from 10.2% to 13.9% in 409 patients received 6- month sacubitril/valsartan. Also, **Miric *et al.*** [17] reported better LV GLS in study group than in control group after 3 months of follow up. **Monosilio *et al.*** [15] showed following 6-months period of treatment that GLS substantially enhanced. Similar results were reported by **Castrichini *et al.*** [5] showing improvement in GLS and peak atrial longitudinal strain.

In group I, the present work demonstrated that a statistically substantial improvement existed as regards E/e` ratio (10.5 ± 1.6 vs. 9.2 ± 1.8; P< 0.001), while in group II, a statistically substantial deterioration of E/e` ratio (10.1 ± 1.5 vs. 10.96 ± 2.48; p= 0.039) was existed. In agreement with the current work, **Pericas *et al.*** [14] found that E/e` improved with statistically substantial variation (p= 0.004). In contrary, **Bras *et al.*** [4] did not find significant improvement of E/e` ratio following 6-months period of sacubitril/ valsartan. Another study by **Miric *et al.*** [17] who did not report significant improvement in E/e ratio after only 3-months period of sacubitril/valsartan with no substantial variation among study and control group 3 months post-treatment. **Landolfo *et al.*** [18] also did not find significant difference as regards E/e` ratio after 3 months and after 12 months. **Castrichini *et al.*** [5] similarly did not show significant changes in E/e' ratio.

From all of the above-mentioned data, it appears that the effects of the ARNI surpass the LV myocardial mechanics to the mechanics of left atrium where the reverse remodelling of the LV could affect or be reflected to the left atrium, also the hypothesis of chronic unloading [19] could also lead to restoration of atrial remodelling and contractility.

CONCLUSION

STE showed that Sacubitril/Valsartan for a period of 12 months led to significant improvements in LA and LV strain parameters when added to standard Heart Failure therapy.

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Conflict of Interest: Nil.

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