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Assessment of effect of irbesartan and nebivolol on the left atrium volume and deformation in the patients with mild-moderate hypertension

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Abstract. – BACKGROUND: We aimed to assess the effects of irbesartan and nebivolol on the left atrium (LA) volume and deformation in the patients with mild-moderate hypertension.

PATIENTS AND METHODS: The study comprised of 160 patients (mean age: 55.6±9.6 years), who had Stage 1 or 2 hypertension according to the European Society of Cardiology (ESC) and have not been receiving antihypertensive therapy. The patients were assigned to treatment groups; irbesartan (n=80) and nebivolol (n=80). The patients were clinically and echocardiographically reevaluated on the 6th and 12th months after the onset of treatment.

RESULTS: There was no difference between the two treatment groups in terms of baseline demographic, clinical and echocardiographic characteristics. Moreover, no difference was observed between the treatment groups on the 6th and 12th months. Intragroup analyses revealed that systolic blood pressure (SBP) and diastolic blood pressure (DBP) significantly decreased in time and diastolic function parameters were improved. However, whilst significant increase was observed in conduit volume, decrease was observed in other volumes of the LA in the irbesartan and nebivolol groups. This significant change was observed on the 6th month in both treatment groups. LA global peak systolic strain (LAGLSs), LA global peak systolic strain rate (LAGLSRs), LA global peak strain rate during early ventricular diastole (LAGLSRe) and LA global peak strain rate (LAGLSRa) during late ventricular diastole (LAGLSRa) values began to be significantly increased after 6 months of treatment in both treatment groups.

CONCLUSIONS: We found that nebivolol, which is a new generation beta blocker, is effective as irbesartan with proven efficacy in improving LA volume and LA myocardial performance in patients with mild-moderate hypertension. Moreover, we determined that strain and strain rate, which are the new echocardiographic parameters, are effective as LA volumes in assessing LA functions.

Key Words:
Irbesartan, Nebivolol, Left atrial function.

Introduction

Left atrium (LA) enlargement is seen in the patients with moderate-severe hypertension (HT)[1,2]. LA enlargement enhances the risk of atrial fibrillation and diastolic dysfunction[3,4]. It is known that LA volume is a sensitive marker for severe diastolic dysfunction[5]. LA enlargement is associated with left ventricle remodeling and diastolic dysfunction, which reflect cardiac target organ injury[6-8]. New echocardiographic techniques such as strain and strain rate are frequently used in left ventricle mechanics and myocardial performance, whereas they are less frequently used in LA mechanics and myocardial performance[9]. Irbesartan, which is renin angiotensin system (RAS) blocker and prevents LA remodeling by lowering atrial fibrosis, is commonly used in HT. There is no study about the effect of new generation beta blocker nebivolol on LA volume and deformation. In the present report, we tried to investigate effects of antihypertensive agents, as monotherapy, on LA volume and myocardial

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deformation. For this purpose, we compared irbesartan, which is frequently used for the treatment of hypertension with proven efficacy, and nebivolol with no study about its effect on LA volume and myocardial deformation.

Patients and Methods

Study Population

The research was conducted in the Cardiology Clinic in accordance with Helsinki Declaration after the approval of hospital Ethical Committee. All patients were informed before the study and they gave consent. The study comprised of 174 patients aged between 18 and 80 years, who had in Stage 1 or Stage 2 hypertension (HT) according to the European Society of Cardiology (ESC) and have not been receiving antihypertensive therapy. Patients with Stage 3 hypertension and had received or have been receiving antihypertensive therapy or receiving any medical therapy were not included in the study. Causes of secondary hypertension were excluded. Patients with comorbid conditions (diabetes mellitus (DM), coronary artery disease (CAD), presence or history of stroke, congestive heart failure (CHF), any cardiac valve disease, hepatic insufficiency, renal insufficiency, chronic obstructive pulmonary disease, malignancies, connective tissue disease, etc.) were also excluded.

Study Design

This is a clinical prospective cohort study. The patients were assigned to two groups as Irbesartan monotherapy and Nebivolol monotherapy. The patients began receiving irbesartan 150 mg 1x1 or nebivolol 5 mg 1x1 on their first visits. On the polyclinic visit performed one month later, drug dose was increased in the patients with high blood pressure (300 mg for Irbesartan and 10 mg for Nebivolol). Patients receiving additional medical therapy were excluded. Effects of these two antihypertensive agents on LA volumes, LA global strain, LA global strain rate and diastolic parameters were examined using standard echocardiography and 2-dimension speckle tracking echocardiography at baseline (Month 0) before treatment and on the 6th and 12th months after the onset of treatment.

Arterial Blood Pressure Measurement

Blood pressure was measured while the patients were in sitting position after at least 5 minutes of resting using blood pressure measuring device in accordance with standard criteria for blood pressure measurement. Patients with a mean blood pressure ≥140/90 mm Hg (mean of three consecutive measurements) on the first visit were included. Subsequent information about the blood pressures of patients was obtained via phone call. Blood pressure was re-measured in the clinic on the 6th and 12th months after the onset of treatment.

Definition of hypertension was done according to the European Society of Cardiology, 2007 Guidelines for the Management of Arterial Hypertension[10]. According to this guideline, HT is defined as a systolic blood pressure (SBP) of 140 mmHg or higher and a diastolic blood pressure (DBP) of 90 mmHg or higher without receiving antihypertensive drug, or if the patients have been receiving antihypertensive drug. Whilst a SBP between 140 and 159 mmHg and a DBP between 90 and 99 mmHg is defined as Stage 1 HT, a SBP between 160 and 179 mmHg and a DBP between 100 and 109 mmHg is defined as Stage 2 HT. BMI is formulized as body weight (kg)/height (m^2).

Conventional Echocardiographic Study

This was performed by Vivid 7 (GE Healthcare, Horten, Norway) echocardiography device using 2.5 Mhz transducer. It was performed in the left lateral decubitis position in all subjects and echocardiograms were recorded in standard parasternal and apical views. Measurements were done at the end of normal inspirium and expirium. M-mode, B-mode, colored flow map and pulse wave Doppler records were obtained for each subject. LA volumes were measured using biplane ''area-length'' method from apical 4- and 2- chamber views and their mean was measured. LA maximum volume (LAV_{max}) was measured when mitral valve was completely opened, LA minimum volume (LAV_{min}) was measured when mitral valve was completely closed, and LA presystolic volume (LAVp) was measured at the beginning of p wave on electrocardiogram and following parameters were calculated using these measurements: LA passive emptying volume (LAPEV): LAV_{max}-LAVp, Conduit volume (CV): Left ventricular systolic volume- (LAVp-LAV_{min}) LA active emptying volume (LAAEV): LAVp-LAV_{min} LA total emptying volume (LATEV): LAV_{max}-LAV_{min}. All measurements were repeated during three consecutive heart beats and their mean was calcu-

lated. All measurements were obtained based on the American Society of Echocardiography standards[11].

2-D Speckle Tracking Echocardiography

Apical 4-chamber and 2-chamber grey scale views were digitally stored. Records were then processed by acoustic tracking software (EchoPAC version 7.0, GE Vingmed, Horten, Norway). Global strain and strain rate were calculated by averaging the values measured in 15 atrial segments. Frame rate was 50-80 frame/sec. Global peak systolic LA myocardium strain during left ventricular systole (LAGLSs), global peak systolic positive LA myocardial strain rate during left ventricular systole (LAGLSRs), global peak negative LA myocardial strain rate during early ventricular diastole (LAGLSRe), and global peak negative LA myocardial strain rate (LAGLSRa) during late ventricular diastole were obtained (Figure 1).

Statistical Analysis

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

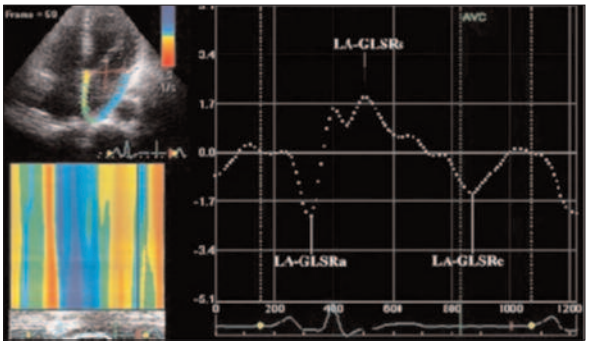

Figure 1. Measurement of global longitudinal left atrial strain rate from an apical four-chamber view. The dashed curve represents the global longitudinal atrial strain along the cardiac cycle. LAGLSRa: left atrial global longitudinal peak negative strain rate during late ventricular diastole. LAGLSRs: left atrial global longitudinal peak positive strain rate during late ventricular systole. LAGLSRe: left atrial global longitudinal peak negative strain rate during early ventricular diastole. AVC: aortic valve closure.

Results

A total of 292 patients, who had recently been diagnosed with HT, were evaluated among the patients admitted to the Cardiology Polyclinic of our hospital. Of these patients, 52 with Stage 3 HT, 6 with aortic stenosis/aortic insufficiency and hypertrophic cardiomyopathy, 8 with CHF, 24 with DM, and 28 with CAD were not included in the study. Thus, there were 174 patients that met the baseline inclusion criteria. A total of 14 patients, 6 from irbesartan group and 8 from nebivolol group, were dropped out of the study since they have not come for at least one of the 6th month or subsequent visits. Finally, the study was completed with 160 patients and the study groups was formed.

Baseline (Before Treatment) Demographic, Clinical and Echocardiographic Characteristics of the Groups

The mean age of the patients in the irbesartan group was 56.75±11.75 years. The mean age of the patients in the nebivolol group was 54.12±10.78 years. There was no statistically significant difference between the two groups in terms of age. Eighty one (51%) of the patients were male and 79 (49%) were female. Baseline demographic, clinical and echocardiographic characteristics of the groups are demonstrated in Tables I to III. There was no statistically significant difference between two groups in terms of baseline demographic, clinical and echocardiographic characteristics (Tables I to III).

Intragroup and Intergroup Demographic, Clinical and Echocardiographic Changes After Treatment

The difference between the groups in terms of demographic, clinical and echocardiographic values on the 6th and 12th months of treatment was not statistically significant (I to III). Intragroup demographic, clinical and echocardiographic changes of each group are demonstrated in Tables I to III. Intragroup and intergroup comparisons of BMI, SBP, DBP, HR, E, A, EE', and DT values are demonstrated in Table I. BMI in nebivolol group was significantly higher on the 12th month as compared to the 6th month. Decrease in intragroup SBP and DBP after treatment was statistically significant in both groups ($p < 0.001$). Whilst there was statistically significant increase in heart rate on the 6th

Table I. Change in intragroup and intergroup clinical and echocardiographic parameters in time.

Parameter	Measurement time (month)	Irbesartan n = 80 mean ± SD	Nebivolol n = 80 mean ± SD	95% CI of the difference Lower/Upper	*p* value (between groups)
BMI (kg/m^2)	Baseline	24.6 ± 1.02	24.9 ± 0.82	-0.3-0.26	0.6
	6	24.3 ± 0.73	24.6 ± 0.76	-0.36-0.10	0.3
	12	24.8 ± 0.61	25.0 ± 0.53[a]	-.33-0.02	0.09
SBP (mmHg)	Baseline	156.6 ± 7.28	157.2 ± 8.18	-2.9-1.8	0.6
	6	127.5 ± 4.05*	126.5 ± 4.92*	-0.4-0.2.4	0.2
	12	123 ± 4.61**[1]	122.5 ± 4.77**[1]	-1.0-1.9	0.6
DBP (mmHg)	Baseline	93.7 ± 4.49	93.0 ± 4.05	-1.3-1.3	0.65
	6	83.7 ± 3.25*	82.5 ± 3.12*	-0.8-1.1	0.5
	12	81.6 ± 2.33**[1]	80.4 ± 2.37**[1]	-.86-0.6	0.3
HR (beat/min)	Baseline	86.1 ± 8.25	80.2 ± 8.78	-1.7-3.6	0.09
	6	90.6 ± 8.72*	79.6 ± 9.72*	8.1-13.9	.000*
	12	91.5 ± 7.39**	77.5 ± 11.11[a]	11.0-17.0	.000*
E (m/s)	Baseline	0.82 ± 0.05	0.81 ± 0.05	-.02-0.01	0.69
	6	0.84 ± 0.03*	0.85 ± 0.04*	-0.01-0.1	0.43
	12	0.81 ± 0.04[a]	0.82 ± 0.04**[1]	-0.01-0.01	0.66
A (m/s)	Baseline	0.87 ± 0.04	0.88 ± 0.04	-0.01-0.01	0.72
	6	0.83 ± 0.04*	0.81 ± 0.05*	-.01-0.014	0.5
	12	0.79 ± 0.07[1]	0.80 ± 0.06**[1]	-.019-0.02	0.83
EE'	Baseline	8.8 ± 0.87	9.2 ± 0.89	-0.29-0.28	0.4
	6	8.4 ± 1.01	8.5 ± 0.96	-0.33-0.28	0.8
	12	7.15 ± 0.96**[,a]	7.62 ± 0.91**[,a]	-0.22-0.25	0.6
DT (ms)	Baseline	213.6 ± 10.38	206 ± 10.55	-4.6-1.8	0.1
	6	203.3 ± 7.4*	197.55 ± 7.51*	-2.5-2.1	0.08
	12	191.7 ± 7.61**[,1]	195.8 ± 7.72**[1]	-2.4-2.3	0.24

BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, peak E: peak mitral velocity of early diastolic filling from transmitral flow, Peak A indicates peak mitral inflow contraction velocity, E': early diastolic filling using DTI. DTI, Doppler tissue imaging. DT: Deceleration time. *$p < 0.001$, intragroup 6th month versus baseline, **$p < 0.001$, intragroup 12th month versus baseline, [1]$p < 0.001$, intragroup 12th month versus 6th month 6, [a]$p < 0.01$ intragroup 12th month versus 6th month.

and 12th months of treatment in the irbesartan group, there was significant decrease in the nebivolol group. Intragroup E and A waves were statistically significantly different in both groups on the 6th month of treatment ($p < 0.001$), whereas there was no significant difference between the 6th and 12th months. Intragroup DT and EE values showed significant decrease in both groups on the 6th and 12th months of treatment ($p < 0.001$).

Intragroup and Intergroup Changes in LA Volumes After Treatment

There was no statistically significant difference between the groups in terms of LA volumes after treatment ($p > 0.05$) (Table II). Intragroup changes in LA volumes are demonstrated in Table II. Whilst no significant decrease was observed in LAV_{max} value in the Irbesartan group on the 6th month, there was significant decrease on the 12th month of treatment (baseline 45.1±2.54 ml; 12th month 39.9±3.6 ml, $p < 0.001$). Moreover, significant decrease was determined on the 12th month versus 6th month of treatment ($p < 0.001$). Significant decrease was observed in LAV_{max} value both on the 6th and 12th months in the Nebivolol group ($p < 0.001$) with significant decrease on the 12th month versus 6th month. Significant decrease was observed in LAV_{min} and LAVp values on the 6th and 12th months of treatment in both groups with significantly lower values on the 12th month versus 6th month in both groups ($p < 0.001$). Statistically nosignificant decrease was observed in LAPEV value on the 6th and 12th months in the irbesartan group. In Nebivolol group, however, significant decrease was observed in LAPEV value on the 6th month ($p < 0.001$). CV value significantly increased in both groups on the 6th and 12th months with significantly higher values on the 12th month versus 6th month ($p < 0.001$). Significant decrease was observed in LAAEV and LATEV values in both groups on the 6th and 12th months ($p < 0.001$).

Table II. Intragroup and intergroup changes in left atrial volumes in time.

Parameter	Measurement time (month)	Irbesartan n = 80 mean ± SD	Nebivolol n = 80 mean ± SD	95% CI of the difference Lower/Upper	*p* value (between groups)
LAV_{max} (ml)	Baseline	45.1 ± 2.54	47.0 ± 2.54	–1.1-0.5	0.51
	6	43.0 ± 1.79	42.9 ± 2.59*	–1.1-0.48	0.2
	12	39.9 ± 3.6**,1	40.0 ± 3.6**,1	–1.49-0.67	0.18
LAV_{min} (ml)	Baseline	11.1 ± 1.94	11.9 ± 1.94	–0.55-0.63	0.7
	6	10.7 ± 1.34*	11.5 ± 1.37*	–0.44-0.4	0.4
	12	9.2 ± 1.91**,1	9.4 ± 1.85**,1	–0.75-0.43	0.68
LAVp (ml)	Baseline	20.4 ± 2.68	21.0 ± 2.43	–1.07-0.65	0.63
	6	18.7 ± 2.5*	19.4 ± 2.5*	–0.95-0.65	0.41
	12	17.4 ± 2.34**,1	17.1 ± 2.42**,1	–0.99-0.51	0.54
LAPEV (ml)	Baseline	24.7 ± 3.0	25.9 ± 3.69	–1.2-1.0	0.59
	6	24.3 ± 3.14	23.3 ± 3.14*	–1.1-0.77	0.68
	12	23.6 ± 3.61**,1	22.8 ± 3.33**,1	–1.26-0.9	0.65
CV (ml)	Baseline	65.3 ± 2.71	66.0 ± 3.23	–1.6-0.24	0.14
	6	69.5 ± 3.64*	67.5 ± 3.64*	–1.61-0.68	0.12
	12	68.0 ± 3.61**,1	69.1 ± 3.59**,1	–1.67-0.57	0.23
LAAEV (ml)	Baseline	9.3 ± 1.89	9.1 ± 2.24	–0.89-0.39	0.7
	6	8.0 ± 2.28*	7.9 ± 2.28*	–0.87-0.60	0.71
	12	8.2 ± 1.7**	7.7 ± 1.81**	–0.730.36	0.5
LATEV (ml)	Baseline	34.0 ± 3.35	35.1 ± 3.35	–1.35-0.70	0.26
	6	32.3 ± 2.71*	33.1 ± 2.64*	–1.19-0.47	0.34
	12	30.7 ± 3.54**	30.6 ± 3.21**	–1.25-0.85	0.3

*$p < 0.001$, intragroup 6th month versus baseline, **$p < 0.001$, intragroup 12th month versus baseline, $^1p < 0.001$, intragroup 12th month versus 6th month.

Intragroup and Intergroup Changes in Strain and Strain Rate After Treatment

There was no statistically significant difference between the groups in terms of LAGLSs, LAGLSRs, LAGLSRe and LAGLSRa values after treatment ($p > 0.05$) (Table III). Intragroup LAGLSs value was significantly increased in both groups on the 6th month versus baseline (irbesartan group: baseline, 37.1±6.32, 6th month, 38.83±5.8, $p < 0.001$; nebivolol group: baseline,

Table III. Intragroup and intergroup changes in the left atrium global strain and strain rate in time.

Parameter	Measurement time (month)	Irbesartan n = 80 mean ± SD	Nebivolol n = 80 mean ± SD	95% CI of the difference Lower/Upper	*p* value (between groups)
LAGLSs (%)	Baseline	37.1 ± 4.32	36.4 ± 4.28	–2.8-1.18	0.23
	6	38.83 ± 5.8*	39.6 ± 5.9*	–2.9-0.79	0.26
	12	40.45 ± 5.6**,1	41.52 ± 5.9**,1	–2.8-0.75	0.25
LAGLSRs	Baseline	2.03 ± 0.35	2.0 ± 0.32	–0.12-0.89	0.7
(s^{-1})	6	2.09 ± 0.27*	2.11 ± 0.27*	–0.10-0.67	0.68
	12	2.15 ± 0.24**,1	2.18 ± 0.23**,1	–0.09-0.62	0.6
LAGLSRe	Baseline	-1.24 ± 0.15	-1.28 ± 0.13	–0.05-0.04	0.6
(s^{-1})	6	-1.22 ± 0.15*	-1.19 ± 0.13*	–0.05-0.03	0.7
	12	1.11 ± 0.16**,1	1.15 ± 0.14**,1	–0.06-0.03	0.3
LAGLSRa	Baseline	-1.37 ± 0.09	-1.42 ± 0.08	–0.04-0.04	0.5
(s^{-1})	6	-1.35 ± 0.08*	-1.37 ± 0.08*	–0.02-0.03	0.4
	12	-1.31 ± 0.09**,1	-1.34 ± 0.09**,1	–0.02-0.03	0.6

*$p < 0.001$, intragroup 6th month versus baseline, **$p < 0.001$, intragroup 12th month versus baseline, $^1p < 0.001$, intragroup 12th month versus 6th month. LAGLSs: Left atrium global peak systolic strain, LAGLSRs: Left atrium global peak systolic strain rate, LAGLSRe: Left atrium global early diastolic strain rate, LAGLSRa: Left atrium global late diastolic strain rate.

36.4±4.28, 6th month, 39.6±5.9, $p < 0.001$). In addition, significant increase was observed in intragroup LAGLSs values in both groups on the 12th month versus baseline with significantly higher increment on the 12th month versus 6th month in both groups (irbesartan group: 12th month, 40.45±5.6, nebivolol group: 12th month, 41.52±5.9, $p < 0.001$). Significant increase was observed in intragroup LAGLSRs, LAGLSRe and LAGLSRa values in both groups on the 6th and 12th months of treatment ($p < 0.001$) with significantly higher increment on the 12th month versus 6th month in both groups ($p < 0.001$).

Correlation Between LA Strain, LA Volume and Blood Pressure

Correlation between LAV_{max}, LAAEV, LA strain, SBP and DBP was analyzed in the treatment groups. In the Irbesartan group, there was significant positive correlation between LAV_{max} and SBP (r: 0.35, $p < 0.001$) and between DBP and LAV_{max} (r: 0.33, $p < 0.001$) measured on the 6th month. In addition, significant negative correlation was observed between LAGLSs and SBP measured on the 6th month (r: –0.61, $p < 0.001$) (Figure 2). There was significant negative correlation between LAAEV and SBP (r: –0.43, $p < 0.001$), between SBP and LAGLSs (r: –0.56, $p < 0.001$), and between LAV_{max} and LAGLSs (r: –0.38, $p < 0.001$) measured on the 12th month.

In the Nebivolol group, there was significant positive correlation between SBP and LAV_{max} (r: 0.67, $p < 0.001$) and between DBP and LAV_{max} (r: 0.25, $p < 0.001$) measured on the 6th month. Additionally, significant negative correlation was determined between SBP and LAGLSs (r: –0.39, $p < 0.001$) measured on the 6th month. There was significant negative correlation between SBP and LAGLSs (r: –0.54, $p < 0.001$) (Figure 2), between SBP and LAAEV (r: –0.43, $p < 0.001$), and between LAV_{max} and LAGLSs (r: –0.33, $p < 0.01$) measured on the 12th month.

Discussion

Despite the numerous animal researches investigating effect of RAS inhibitors on LA myocardium and LA function, the number of clinical studies investigating effect of RAS inhibitors on LA function is quite limited. However, as far as we know, there is no clinical study investigating effect of nebivolol, a new generation beta blocker, on LA function and myocardium. For this reason, we compared irbesartan, a RAS inhibitor, and nebivolol in terms of LA volume and myocardial deformation.

Numerous researches have been conducted on blood pressure lowering effect of irbesartan, a RAS inhibitor, and nebivolol, a new generation beta blocker. One of these was a randomized prospective study conducted by Latea et al[12] in 108 patients (55 in valsartan group and 53 in nebivolol group) with mild-moderate hypertension, whose blood pressures were monitored for 6 months. This study found 6-month valsartan therapy as effective as nebivolol in 24-hour SBP values. Nebivolol therapy was found superior to valsartan therapy in reducing DBP. In the present work, although SBP and DBP showed significant decrease in both treatment groups, no significant difference was observed between the groups.

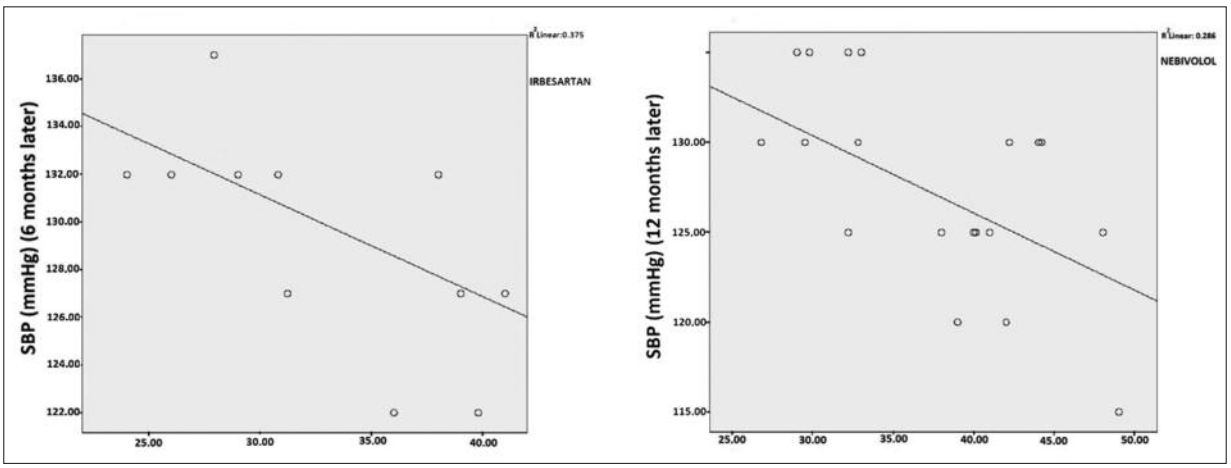

Figure 2. Correlations of peak left atrial strain during left ventricular systole with SBP (6 and 12 months).

Again, in this investigation, there was no significant difference between the treatment groups in terms of diastolic function despite significant intragroup improvement. In addition, there was a significant difference between the groups in terms of heart rate on the 6th month and 12th month. Intragroup analyses revealed that heart rate was significantly decreased on the 6th and 12th months in the nebivolol group, but heart rate was significantly higher on the 6th and 12th months versus baseline in the irbesartan group (Table I). In a randomized, double-blind report[13], nebivolol was compared with placebo in terms of SBP, DBP and heart rate. The study determined a decrease by 12.4 mmHg in SBP, 11.1 mmHg in DBP and 9.2 beat/min in heart rate after 3 months. In this investigation, we observed that heart rate and blood pressure were decreased in the nebivolol group. Decrease in heart rate might contribute to decrease in blood pressure. With regard to the decrease in blood pressure and significant intragroup improvement in diastolic function, Vitale et al[14] conducted a randomized double-blind study in 65 patients and compared nebivolol + hydrochlorothiazide (5 mg/12.5 mg) with irbesartan + hydrochlorothiazide (150 mg/12.5 mg) for 8 weeks in terms of endothelial function, augmentation index corrected according to heart rate, pulse wave velocity, and central and brachial blood pressures. They observed decrease in pulse wave velocity, systolic and diastolic central pressures and brachial pressure and improvement in arterial stiffness. Again, in another double-blind, randomized, parallel group report, nebivolol was compared with losartan, an angiotensin receptor blocker, in terms of quality of life and antihypertensive efficacy[15]. The patients received nebivolol 5 mg/day and losartan 50 mg/day for 12 months. It was observed that both agents decreased systolic blood pressure, made no difference in terms of quality of life, but decrease in diastolic blood pressure was in favor of nebivolol. In the present work, both SBP and DBP were similarly decreased in both groups.

Population-based studies determined LA enlargement in 22% of hypertensive patients. In the recent times, despite increased interest in LA volumes, many researches assessed only LAV_{max}[1,2]. It was demonstrated that CV and LAPEV is decreased along with the increase in active emptying volume in untreated severe hypertension[16]. In the present study, LAPEV was significantly lower on the 6th and 12th months versus baseline in both groups. In addition, in the nebivolol group, LAPEV value was significantly lower on the 12th month versus 6th month. CV value was significantly higher on the 6th and 12th months versus baseline in both groups with significantly higher CV on the 12th month versus 6th month. In this paper, we determined decrease in LAPEV and increase in CV with treatment. Difference in LAPEV as compared to above-mentioned study might have resulted from mild-moderate hypertensive patients in the present study. However, increase was observed in CV. Moreover, active volume's being high at baseline and decreased in time is consistent with the above-mentioned study. This result indicates that need for atrial contraction is decreased with treatment. LAV_{max} value was significantly lower on the 12th month versus baseline and 6th month in the irbesartan group, whereas it was lower both on the 6th and 12th months versus baseline in the nebivolol group with significantly lower values on the 12th month versus 6th month. Both LAV_{min} and LAVp were significantly lower on the 6th and 12th months versus baseline in both groups with significantly lower values on the 12th month versus 6th month. LAAEV and LATEV values were significantly lower on the 6th and 12th months versus baseline in both groups. Cioffi et al[17] observed an increase also in LATEV in addition to LAAEV. In this report, LATEV was increased at baseline but decreased with treatment. Eshoo et al[18] compared 112 mild hypertensive patients with placebo and demonstrated increase in overall LA volumes in relation with active volume. Mattioli et al[19] demonstrated that LA volumes were decreased with intensive treatment in the patients with severe hypertension. We observed also that LA volumes were high at baseline and significantly decreased with treatment. However, no difference was observed between treatment groups. In addition, significant positive correlation was determined between SBP, DBP and LAV_{max} on the 6th month in both treatment groups, which is an expected result.

Kokubu et al[20] compared 80 hypertensive patients with 50 normotensive patients and determined that LA volume was increased but LAGLSRs was decreased in the hypertensive group. Moreover, they determined that RAS inhibitors increases LAGLSRs. In this work, LAGLSRs, LAGLSRe and LAGLSRa values were significantly increased on the 6th and 12th months versus baseline in both groups (Table III). There was no significant difference between the groups in terms of these parameters.

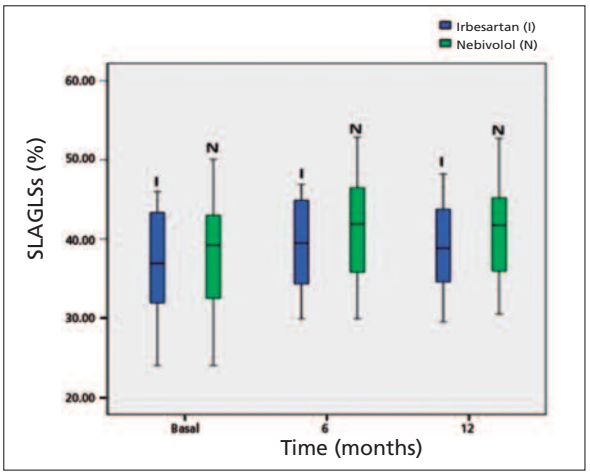

Figure 3. Change of LAGLSs in the treatment groups.

Intragroup LAGLSs values were significantly higher on the 6th and 12th months versus baseline in both groups with significantly higher LAGLSs on the 12th month versus 6th month in both groups (Figure 4). Based on current data, we can say that atrial deformation is improved with treatment in the patients with mild-moderate hypertension. Correlation analysis revealed significantly negative correlation between SBP and LAGLSs on the 6th and 12th months in the irbesartan group (r: -0.61, and r: -0.56 respectively, $p < 0.001$; Figure 2). Mottram et al[21] compared aldosterone antagonists and placebo in 30 hypertensive patients with diastolic dysfunction and observed that aldosterone antagonists (spironolactone) improved LA strain and strain rate 6 months after treatment. We observed also that irbesartan, which blockades aldosterone, showed similar effect. In the nebivolol group, there was significantly negative correlation between SBP and LAGLSs on the 6th and 12th months (r: -0.39 and r: -0.54 respectively, $p < 0.001$; Figure 3). Inaba et al[22] demonstrated that LAGLSRs is decreased due to increase in LA volume. Likewise, this paper, significant negative correlation was observed between LAV_{max} and LAGLSs on the 12th month in both treatment groups (r: -0.38 and r: -0.33 respectively, $p < 0.001$). Based on these data, we can say that improvement in LA function can be demonstrated not only by decrease in LA volume but also by LA global strain and LA global strain rate. Current information indicates that LAGLSs might be a new parameter that would indicate SBP regulation and decrease in LA volume.

Conclusions

We found that nebivolol, a new generation beta blocker, improves LA volume and LA myocardial performance as good as irbesartan with proven efficacy in the patients with mild-moderate hypertension. In addition, we determined that strain and strain rate, which are new echocardiographic parameters, are as effective as LA volumes in demonstrating LA functions. Moreover, we demonstrated that LA enlargement was reduced and LA myocardial performance was improved along with controlled SBP and DBP. We determined that myocardial deformation was improved with decrease in LA enlargement. Nevertheless, further investigations are needed.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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