Effects of myocardial function in geriatric hypertension at 1 year of follow-up in the single-center SPRINT

Running Head：Myocardial function in geriatric hypertension

Xiaoyan Chen[1], Qingmei Yang[1], Jianxiu Fang[1], Haifeng Guo[2]

1. Department of Ultrasound, Shanxi Academy of Medical Sciences & Shanxi Bethune Hospital, Taiyuan, Shanxi Province, P. R. China

2. Department of Medical Imaging, Shanxi Armed Police Force Hospital, Taiyuan, Shanxi Province, P. R. China

Corresponding Author：Xiaoyan Chen

Address: No. 99 Longcheng Street, Department of Ultrasound, Shanxi Academy of Medical Sciences & Shanxi Bethune Hospital, Taiyuan, Shanxi Province, P. R. China

Email: xiaoguoguo119@163.com

Phone: +8613934200119

CRediT authorship contribution statement

Xiaoyan Chen: Conceptualization, data analysis, methodology, writing the original draft, and reviewing and editing the manuscript; **Qingmei Yang:** data analysis; **Jianxiu Fang:** data analysis; and **Haifeng Guo:** data analysis.

Declaration of competing interest

The authors report no relationships that could be construed as a conflict of interest.

Grant supporting this paper

This work was supported by Shanxi Province Key Research and Development Plan (Grant Numbers: 201903D321199).

Abstract

Background

A lower systolic blood pressure (SBP) target reduces major cardiovascular events and mortality from any cause in geriatric hypertension. However, the effect of different SBP targets on left ventricular (LV) function remains unclear. This study aimed to determine changes in LV strain in older hypertensive patients after 1 year of different SBP goals, and to evaluate its effects on LV function in this population.

Methods

We studied 313 hypertensive adults aged 60 years or older after 1 year of the Systolic Blood Pressure Intervention Trial. They were divided into the intensive group (target SBP: 110–130 mmHg) and the standard group (target SBP: 130–150 mmHg). All participants underwent echocardiography within 1 week after enrollment and 1 year after participating in the study. Global longitudinal strain (GLS) of the LV (endocardial, middle, and epicardial layer: GLS-end, GLS-mid, and GLS-epi, respectively) and improvement of GLS at 1 year (ΔGLS-end, ΔGLS-mid, and ΔGLS-epi) were measured.

Results

At 1 year, GLS-end in the intensive group was decreased compared with that before the trial (−23.78%±3.10% vs −22.58%±3.11%, $P<0.05$). The ΔGLS-end and ΔGLS-mid in the intensive group were higher than those in the standard group (both $P<0.05$). Moreover, SBP at 1 year and an angiotensin II type 1 receptor antagonist were independent factors that affected ΔGLS-end.

Conclusions

These trial results suggest that a lower SBP target is beneficial for LV myocardial

function of older hypertensive patients at 1 year.

Keywords

Hypertension; Blood pressure target; Older population; Echocardiography; Strain; Left ventricular function

1. Introduction

Hypertension is defined as a persistently elevated blood pressure ≥140/90 mmHg. Hypertension affects more than 1.2 billion individuals worldwide and has become the most critical public health problem[1]. This condition is a major risk factor for cardiovascular events worldwide, especially in older patients with hypertension[2]. Treating high blood pressure can significantly reduce the risk of cardiovascular disease, including stroke, myocardial infarction, and heart failure[3,4].

However, at present, there is no unified international blood pressure control target for older hypertensive patients. The European Society of Hypertension and the European Society of Cardiology target a systolic blood pressure (SBP) of <140–150 mmHg with lower goals in fit and healthy patients [5]. The 2017 American College of Cardiology/American Heart Association guidelines for hypertension suggest that for a general healthy age ≥65 years, the blood pressure control target should be <130 mmHg[6]. The 2019 Chinese Hypertension Guidelines consider that blood pressure of older patients should be reduced to <150/90 mmHg[7]. Guidelines for hypertension vary and which blood pressure target is better for heart function is unknown. Findings from the Systolic Blood Pressure Intervention Trial (SPRINT) showed that intensive

lowering of blood pressure (SBP <120 mmHg) was associated with lower rates of cardiovascular events and mortality in hypertensive fit and frail older subjects compared with standard treatment[8]. These findings suggested that lowering of blood pressure was beneficial for cardiac function[9]. However, there is a high incidence of adverse events, such as hypotension, syncope, electrolyte disturbance, and acute renal failure, in the short term of intensive hypotension, and these can impair cardiac function[10,11].

Whether a lower or higher SBP target is associated with better LV myocardial function in older adults is currently unknown. Myocardial strain obtained using speckle-tracking echocardiography can quantify left ventricular (LV) function[12]. The best evaluated strain parameter is longitudinal strain (LS), which is more sensitive than the LV ejection fraction in adult hypertension[12,13]. In this study, we used speckle-tracking echocardiography to evaluate myocardial LS in older hypertensive patients who were enrolled in the SPRINT for 1 year. We aimed to assess the effects of different antihypertensive targets on cardiac function in geriatric hypertension.

2. Methods

2.1. Study participants

In this prospective study, we recruited older hypertensive patients who were treated in our hospital from July 2019 to October 2019. Inclusion criteria were as follows: (1) patients with primary hypertension, including newly diagnosed hypertension, with an average follow-up (3 times) of outpatient SBP ≥140 mmHg, and patients undergoing

antihypertensive treatment; (2) patients of Han ethnicity, aged 60–80 years; and (3) patients signed an informed consent form. Exclusion criteria were as follows: (1) SBP ≥190 mmHg or diastolic blood pressure <60 mmHg; (2) confirmed secondary hypertension; (3) a history of stroke or acute myocardial infarction in the past 6 months, those who had revascularization surgery performed or planned within the next 6 months, or those with persistent atrial fibrillation or arrhythmia that affected blood pressure measurement with heart failure; (4) severe valve disease, cardiomyopathy, rheumatic heart disease, or congenital heart disease; (5) poor diabetes control, severe liver and kidney disease, or a history of malignant tumors; (6) patients with cognitive dysfunction or inability to take care of themselves; (7) participation in other clinical trials; (8) poor image quality that affected analysis; and (9) not participating in the study with incomplete data.

Using blood pressure control goals, the patients were divided into the intensive group (target SBP: 110–130 mmHg) and the standard group (target SBP: 130–150 mmHg) if achievable without undue burden. All participants' daily blood pressure was reported, monitored, and managed by a cardiologist. Under the condition that the patient could tolerate the procedure, blood pressure was gradually adjusted within 3 months to reach the corresponding target in each group.

Informed consent was provided by the patients and the study protocol was approved by the medical ethics committee. Finally, the study included 374 older hypertensive patients (age, 60–81 years), including 187 in the intensive group and 187 in the standard group. After 1 year of follow-up, there were 159 patients in the intensive

group and 154 patients in the standard group. Reasons for loss to follow-up were as follows: 3 patients had acute cardiovascular events, 2 had breast cancer requiring chemotherapy, 6 had arrhythmia, and 50 could not be contacted or voluntarily left the study.

2.2. Laboratory analysis

Biochemical analyses, including measurement of total cholesterol, triglyceride, low-density lipoprotein, and high-density lipoprotein levels, were performed in all patients.

2.3. Echocardiography

Echocardiographic imaging was performed using the Vivid E9 GE Medical Systems commercial scanner (GE Vingmed Ultrasound AS, Norway), which was equipped with a 5S probe (1–5 MHz). All patients underwent echocardiography within 1 week after enrollment and after 12 months of participation in the study in accordance with the recommendations of the American Society of Echocardiography[14]. LV end-diastolic diameter, LV end-systolic diameter, and end-diastolic inter-ventricular septal and LV posterior wall thickness were measured with M-mode echocardiography. The LV mass was calculated according to a previously published methodology[14]. The LV mass index was calculated as follows: LV mass index=LV mass/body surface area[14]. Early and late mitral valvular blood flow velocity peak (E and A, respectively) were measured by pulsed-wave Doppler, and LV sidewall mitral annular early and late peak velocity (Em and Am, respectively) were measured by tissue Doppler. E/A and E/Em were then calculated. The LV ejection fraction was measured by the Simpson biplane method.

After acquiring the apical long axis and four- and two-chamber views of three consecutive cardiac cycles, the different views were analyzed using Echo PAC analysis software (version: 201). We sketched the subendocardial area of each view.

The software was used to automatically create a region of interest, which contained subendocardial, middle, and subepicardical areas, and we adjusted the region of interest to include the complete LV myocardium. The software performed speckle tracking analysis on the LV myocardium in each view. Upon delineating the region of interest, the software automatically generated time–domain strain curves in six segments with which end-systolic strain was subsequently calculated. Global longitudinal strain (GLS) was defined as the average longitudinal strain at end-systole in 18 segments.

After this analysis, we obtained GLS of the LV endocardial layer, middle layer, and epicardial layer (GLS-end, GLS-mid, and GLS-epi, respectively) (Fig. 1). Fig. 2 shown that we calculated improvement of the strain value after 1 year of treatment in all patients (ΔGLS: ΔGLS-end, ΔGLS-mid, and ΔGLS-epi, respectively): ΔGLS=|GLS(1 year after joining this trial)–GLS(before joining the trial)|.

2.4. Statistical analysis

All statistical analyses were performed with SPSS 17.0 (SPSS Inc., Chicago, IL). Continuous data are presented as mean ± SD. Frequencies are expressed as percentages. The Student's t-test was used as appropriate for comparison of continuous data between the two groups. The chi-square test was used for comparing the variables of sex and medication between the two groups. The paired t-test was used as appropriate for comparison of continuous data before and after participating in this trial. Pearson's correlation was chosen to test correlations among the clinical dates, LV structure, LV function parameters, and strain parameters. Independent

determinants of LV myocardial strain parameters were examined using multivariate stepwise linear regression. P values <0.05 were considered statistically significant.

For reliability of the GLS-end, GLS-mid, and GLS-epi results, the intra-class correlation coefficient (ICC) was used to evaluate inter- and intra-observer variability. Twenty patients were randomly chosen for this analysis. Clinical significance was categorized as follows: good, ICC ≥0.75; moderate, ICC ≥0.4 and <0.75; and poor, ICC <0.4.

3. Results

3.1. Baseline characteristics of the two groups of participants

The clinical characteristics of the two groups of participants are shown in Table 1. No significant difference was found in sex distribution, age, body mass index, body surface area, blood pressure, heart rate, duration of hypertension, proportion of diabetes, and glucose, triglyceride, cholesterol, high-density lipoprotein, or low-density lipoprotein levels between the intensive and standard groups.

General parameters of echocardiography between the two groups are shown in Table 3. There were no significant differences regarding structural and conventional functional parameters of the LV between the two groups. The left ventricular ejection fraction and E/Em were in the normal range in the groups.

There were also no significant differences in GLS-end, GLS-mid, and GLS-epi between the two groups (Table 4).

3.2. Comparison of antihypertensive medication between the two groups of patients after enrolling in the trial

To achieve the target blood pressure of each group, we adjusted the medication

regimen according to the patient's individual situation. Comparison of the distribution of an angiotensin II type 1 receptor antagonist (olmesartan medoxomil tablets), calcium antagonist (amlodiping besylate tablets), and diuretic (hydrochlorothiazide) in the two groups is shown in Table 2. The rate and dosage of angiotensin II type 1 receptor antagonists and diuretics in the intensive group were significantly higher than those in the standard group (all $P<0.05$). There was no significant difference in the distribution of a calcium antagonist between the two groups.

3.3. Changes in the two groups of patients at 1 year

We found that SBP was significantly reduced at 1 year ($P<0.05$). Additionally, SBP in the intensive group was significantly lower than that in the standard group at 1 year ($P<0.05$) (Table 4).

After 1 year of starting the trial, GLS-end in the intensive group was significantly decreased compared with that before the trial ($P<0.05$) (Table 4, Fig. 3) . Furthermore, improvement of the strain value (ΔGLS-end and ΔGLS-mid) in the intensive group was significantly higher than that in the standard group (both $P<0.05$) (Table 4, Fig. 4). There was no change in other strain parameters in older hypertensive patients within the groups after 1 year. Additionally, there were no differences in LV structure and functional parameters between the two groups after 1 year (Table 3).

3.4. Factors affecting the degree of improvement of GLS

To examine the factors affecting ΔGLS-end, ΔGLS-mid, and ΔGLS-epi, the medication regimen and current blood pressure were tested using multivariate

backward stepwise linear regression analysis (Table 5). SBP at 1 year and an angiotensin II type 1 receptor antagonist were independent factors that affected ΔGLS-end (β=−0.004, P=0.007; β=0.083, P<0.001, respectively).

3.5. Intra-observer and inter-observer variability

Table 6 shows intra- and inter-observer variability for GLS-end, GLS-mid and GLS-epi. The ICCs for intra- and inter-observer variability were 0.970–0.982 and 0.875–0.958, respectively, which suggested that GLS in each layer of the LV was consistent.

4. Discussion

The main findings of our study were as follows. (1) One year after enrolling in the single-center SPRINT, GLS-end in the intensive group was slightly decreased compared with that before the trial. (2) The degree of improvement in myocardial strain (ΔGLS-end and ΔGLS-mid) in the intensive group was higher than that in the standard group. (3) SBP at 1 year and the dosage of olmesartan were independently associated with ΔGLS-end.

After enrolling in the SPRINT, the patient's adherence to antihypertensive drugs increased. Therefore, blood pressure control in older hypertensive patients in this study was more stable compared with previously. Doctors adjusted the treatment plan on the basis of the patient's daily change in blood pressure, which was generally controlled at the target level (i.e., intensive group: target SBP of 110–130 mmHg and standard group: target SBP of 130–150 mmHg). However, owing to the white-coat effect, SBP measured in the office is higher than the usual level[15]. In patients with hypertension without complications, the LVEF is generally normal at rest[16].

Therefore, the LVEF of older hypertensive patients in this study was in the normal range and remained unchanged after 1 year.

A previous study showed that changes in LV strain were accompanied by myocardial fibrosis and hypertrophy of cardiomyocytes [17]. In our study, the intensive group had lower SBP compared with the standard group. This finding suggested that patients in the intensive group had lower cardiac after-load, less cardiac work, less myocardial oxygen consumption, milder myocardial fibrosis, less hypertrophy of cardiomyocytes, and better myocardial compliance, which resulted in lower GLS[18]. Patients with lower GLS may have a lower risk of incident heart failure, acute myocardial infarction, or cardiovascular death[19]. Patients in the intensive group may have a lower risk of cardiovascular events in the future[20], as suggested by the results of a large number of SPRINT studies in recent years[8]. However, follow-up of our patients should be conducted in the future.

Longitudinal strain of LV could be a surrogate of subendocardial fibrotic changes[17]. Investigators have found that the endocardium is vulnerable to the effect of LV filling pressure, and its function is easily impaired in patients with hypertension[21]. Conversely, when afterload of the LV is reduced, endocardial myocardial function should be restored earlier[22, 23]. Our study showed that the degree of improvement of myocardial strain (ΔGLS-end and ΔGLS-mid) in the intensive group was higher than that in the standard group.

Olmesartan is a selective angiotensin II type 1 receptor antagonist. Angiotensin receptor blockers have been effectively used in hypertension, cardiac remodeling, and

heart failure[24]. These antagonists affect systemic and coronary hemodynamics, heart pump function, and development of cardiac hypertrophy[25, 26]. Additionally, with knockdown of angiotensin II, olmesartan can effectively inhibit heart remodeling caused by pressure overload[27]. Therefore, olmesartan can reverse LV remodeling and LV hypertrophy, and improve LV myocardial function [28, 29]. In our study, the dose of olmesartan in the intensive group was higher than that in the standard group. This resulted in a lower SBP at 1 year in the intensive group than in the standard group. Additionally, the degree of improvement of myocardial strain in the intensive group was higher than that in the standard group. Therefore, in this trial, SBP at 1 year and the dosage of olmesartan were independent predictors of the degree of recovery of myocardial strain. We also found that ΔGLS-end was reduced by 0.004% for a 1-mmHg increase in the SBP at 1 year and ΔGLS-end was increased by 0.083% for each increase of 5 mg of olmesartan.

5. **Limitations**

The main limitation of this study is that it was a single-center study with a limited population. Additionally, there were no obvious complications in this group of older patients with hypertension. Therefore, the sample was biased. Future research should address this issue. Moreover, the follow-up time for this study was short. A longer follow-up is required to better understand the effect of blood pressure targets on myocardial function in older patients with hypertension.

6. Conclusion

In this single-center SPRINT for older hypertensive patients, a lower systolic blood pressure target (110–130 mmHg) was beneficial for myocardial strain and

improvement in myocardial strain in the short term. This lowering of blood pressure has a certain protective effect on LV myocardial function.

CRediT authorship contribution statement

Xiaoyan Chen: Conceptualization, data analysis, methodology, writing the original draft, and reviewing and editing the manuscript; **Qingmei Yang:** data analysis; **Jianxiu Fang:** data analysis; and **Haifeng Guo:** data analysis.

Declaration of competing interest

The authors report no relationships that could be construed as a conflict of interest.

Grant supporting this paper

This work was supported by Shanxi Province Key Research and Development Plan (Grant Numbers: 201903D321199).

Data Availability Statement

All data generated or analyzed during this study are included in this article.

References

[1]Rahimi K, Emdin CA, MacMahon S. The epidemiology of blood pressure and its worldwide management. Circ Res. 2015 Mar 13;116(6):925-36. doi: 10.1161/CIRCRESAHA.116.304723.

[2]Gianpaolo Reboldi, Giorgio Gentile, Fabio Angeli, Giuseppe Ambrosio, Giuseppe Mancia, Paolo Verdecchia. Effects of intensive blood pressure reduction on myocardial infarction and stroke in diabetes: a meta-analysis in 73913 patients. J Hypertens. 2011 Jul;29(7):1253-69. doi: 10.1097/HJH.0b013e3283469976.

[3]Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report

of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report.JAMA. 2003 May 21;289(19):2560-72. doi: 10.1001/jama.289.19.2560.

[4]B Neal, S MacMahon, N Chapman. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. Blood Pressure Lowering Treatment Trialists' Collaboration Lancet. 2000 Dec 9;356(9246):1955-64. doi: 10.1016/s0140-6736(00)03307-9.

[5]Bryan Williams, Giuseppe Mancia, Wilko Spiering, Enrico Agabiti Rosei, Michel Azizi, Michel Burnier, Denis L Clement, Antonio Coca, Giovanni de Simone, Anna Dominiczak , et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension.Eur Heart J. 2018 Sep 11;39(33):3021-3104. doi: 10.1093/eurheartj/ehy339.

[6]David M Reboussin, Norrina B Allen, Michael E Griswold, Eliseo Guallar, Yuling Hong, Daniel T Lackland, Edgar Pete R Miller 3rd, Tamar Polonsky, Angela M Thompson-Paul, Suma Vupputuri.Systematic Review for the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.J Am Coll Cardiol. 2018 May 15;71(19):2176-2198. doi: 10.1016/j.jacc.2017.11.004. Epub 2017 Nov 13.

[7]Qi Hua, Li Fan, Jing Li, Joint Committee for Guideline Revision. 2019 Chinese guideline for the management of hypertension in the elderly.J Geriatr Cardiol. 2019 Feb;16(2):67-99. doi: 10.11909/j.issn.1671-5411.2019.02.001.

[8]SPRINT Research Group; Jackson T Wright Jr, Jeff D Williamson, Paul K Whelton, Joni K Snyder, Kaycee M Sink, Michael V Rocco, David M Reboussin, Mahboob Rahman, Suzanne Oparil ，et al. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med. 2015 Nov 26;373(22):2103-16. doi: 10.1056/NEJMoa1511939. Epub 2015 Nov 9.

[9]Mark A. Supiano, MD Jeff D. Williamson, MD, T MHS. New Guidelines and SPRINT Results Implications for Geriatric Hypertension.Circulation. 2019;140:976–978. DOI: 10.1161/CIRCULATIONAHA.119.037872.

[10]Rocco MV, Sink KM, Lovato LC, Wolfgram DF, Wiegmann TB, Wall BM, Umanath K, Rahbari-Oskoui F, Porter AC, Pisoni R ，et al. Effects of Intensive Blood Pressure Treatment on Acute Kidney Injury Events in the Systolic Blood Pressure Intervention Trial (SPRINT).Am J Kidney Dis. 2018 Mar;71(3):352-361. doi: 10.1053/j.ajkd.2017.08.021. Epub 2017 Nov 20.

[11]Christine D Jones, Laura Loehr, Nora Franceschini, Wayne D Rosamond, Patricia P Chang, Eyal Shahar, David J Couper, Kathryn M Rose. Orthostatic hypotension as a risk factor for incident heart failure: the atherosclerosis risk in communities study. Hypertension. 2012 May; 59(5):913-8. doi: 10.1161/HYPERTENSIONAHA.111.188151. Epub 2012 Mar 19.

[12]Smiseth OA, Torp H, Opdahl A, Haugaa KH, Urheim S. Myocardial strain imaging: how useful is it in clinical decision making? Eur Heart J. 2016 Apr 14;37(15):1196-207. doi: 10.1093/eurheartj/ehv529. Epub 2015 Oct 27.

[13]Marwick TH, Gillebert TC, Aurigemma G, Chirinos J, Derumeaux G, Galderisi M, Gottdiener J, Haluska B, Ofili E, Segers P ，et al. Recommendations on the Use of Echocardiography in

Adult Hypertension: A Report from the European Association of Cardiovascular Imaging (EACVI) and the American Society of Echocardiography (ASE). J Am Soc Echocardiogr. 2015 Jul;28(7):727-54. doi: 10.1016/j.echo.2015.05.002.

[14]Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise J , et al; American Society of Echocardiography's Nomenclature and Standards Committee; Task Force on Chamber Quantification; American College of Cardiology Echocardiography Committee; American Heart Association; European Association of Echocardiography, European Society of Cardiology. Recommendations for chamber quantification. Eur J Echocardiogr. 2006 Mar;7(2):79-108. doi: 10.1016/j.euje.2005.12.014. Epub 2006 Feb 2.

[15]Jan Filipovský. White-coat hypertension and masked hypertension.Vnitr Lek. 2015 May;61(5):401-5.PMID: 26075847.

[16]Fouad FM. Cardiac function and dysfunction in hypertension. Cleve Clin J Med. 1994 Sep-Oct;61(5):351-5. doi: 10.3949/ccjm.61.5.351.

[17]Tomoko Ishizu, Yoshihiro Seo, Yuri Kameda, Ryo Kawamura, Taizou Kimura, Nobutake Shimojo, Dongzhu Xu, Nobuyuki Murakoshi, Kazutaka Aonuma. Left ventricular strain and transmural distribution of structural remodeling in hypertensive heart disease. Hypertension. 2014, Mar;63(3):500-6. doi: 10.1161/HYPERTENSIONAHA.113.02149. Epub 2014 Jan 6.

[18]Murai D, Yamada S, Hayashi T, Okada K, Nishino H, Nakabachi M, Yokoyama S, Abe A, Ichikawa A, Ono K , et al. Relationships of left ventricular strain and strain rate to wall stress

and their afterload dependency. Heart Vessels. 2017 May;32(5):574-583. doi: 10.1007/s00380-016-0900-4. Epub 2016 Oct 12.

[19]Biering-Sorensen T, Biering-Sorensen SR, Olsen FJ, Sengelov M, Jorgensen PG, Mogelvang R, Shah AM, Jensen JS. Global longitudinal strain by echocardiography predicts long-term risk of cardiovascular morbidity and mortality in a low-risk general population: the Copenhagen city heart study. Circ Cardiovasc Imaging. 2017;10:e005521. doi: 10.1161/CIRCIMAGING.116.005521.

[20]Biering-Sorensen T, Biering-Sorensen SR, Olsen FJ, Sengelov M, Jorgensen PG, Mogelvang R, Shah AM, Jensen JS. Global longitudinal strain by echocardiography predicts long-term risk of cardiovascular morbidity and mortality in a low-risk general population: the Copenhagen city heart study. Circ Cardiovasc Imaging. 2017;10:e005521. doi: 10.1161/CIRCIMAGING.116.005521.

[21]Nakamura N, Hirata K, Imanishi T, Kuroi A, Arita Y, Ikejima H, Tsujioka H, Takemoto K, Tanimoto T, Kitabata H ， et al. Electrocardiographic strain and endomyocardial radial strain in hypertensive patients. Int J Cardiol. 2011 Aug 4;150(3):319-24. doi: 10.1016/j.ijcard.2010.04.049.

[22]Duan F, Xie M, Wang X, Li Y, He L, Jiang L, Fu Q. Preliminary clinical study of left ventricular myocardial strain in patients with non-ischemic dilated cardiomyopathy by three-dimensional speckle tracking imaging. Cardiovasc Ultrasound. 2012 Mar 7;10:8. doi: 10.1186/1476-7120-10-8.

[23]Marcia M Barbosa, Manoel O Costa Rocha, Daniel Furtado Vidigal, Renata de Carvalho Bicalho Carneiro, Rafaela Drumond Araújo, Mariana Campos Palma, Marcio Vinicius Lins de Barros, Maria Carmo P Nunes. Early detection of left ventricular contractility abnormalities by two-dimensional speckle tracking strain in Chagas'disease. Echocardiography. 2014 May;

386 31(5):623-30. doi: 10.1111/echo.12426..

387 [24]Martin C Michel , Carolyn Foster, Hans R Brunner, Lisheng Liu. A systematic comparison of

388 the properties of clinically used angiotensin II type 1 receptor antagonists. Pharmacol Rev. 2013

389 Mar 13;65(2):809-48. PMID: 23487168. DOI: 10.1124/pr.112.007278

390 [25]Richer C, Fornes P, Cazaubon C, Domergue V, Nisato D, Giudicelli JF. Effects of long-term

391 angiotensin II AT1 receptor blockade on survival, hemodynamics and cardiac remodeling in

392 chronic heart failure in rats. Cardiovasc Res. 1999 Jan;41(1):100-8. doi: 10.1016/s0008-

393 6363(98)00227-2.

394 [26] Anand Ramalingam, Siti Balkis Budin, Norsyahida Mohd Fauzi, Rebecca H Ritchie, Satirah

395 Zainalabidin. Angiotensin II Type I Receptor Antagonism Attenuates Nicotine-Induced Cardiac

396 Remodeling, Dysfunction, and Aggravation of Myocardial Ischemia-Reperfusion Injury in

397 Rats.Front Pharmacol. 2019 Dec 12;10:1493. doi: 10.3389/fphar.2019.01493. eCollection 2019.

398 [27]Xingxu Wang , Yong Ye, Hui Gong, Jian Wu, Jie Yuan , Shijun Wang , Peipei Yin, Zhiwen

399 Ding, Le Kang, Qiu Jiang ，et al. . The effects of different angiotensin II type 1 receptor blockers

400 on the regulation of the ACE-AngII-AT1 and ACE2-Ang(1-7)-Mas axes in pressure overload-

401 induced cardiac remodeling in male mice. J Mol Cell Cardiol. 2016 Aug;97:180-90.

402 PMID: 27210827. DOI: 10.1016/j.yjmcc.2016.05.012.

403 [28]V Regitz-Zagrosek, M Neuss, J Holzmeister, E Fleck. Use of Angiotensin II Antagonists in

404 Human Heart Failure: Function of the Subtype 1 Receptor. J Hypertens Suppl. 1995

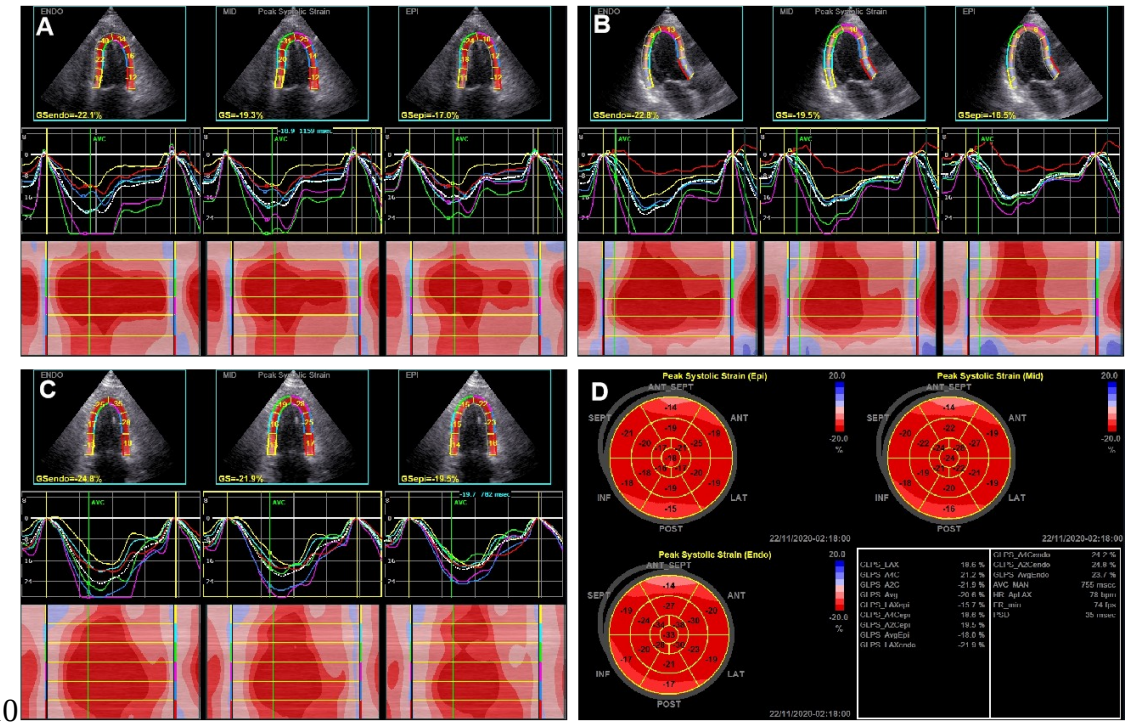
405 Jul;13(1):S63-71. doi: 10.1097/00004872-199507001-00010.

406 [29]O D Ostroumova, A I Kochetkov. Effects of Amlodipine/Lisinopril Fixed-Dose Combination

407 on Severity of Left Ventricular Hypertrophy and Parameters of Myocardial Stiffness in Patients

408 With Hypertension. Kardiologiia. 2016 Dec;56(11):27-37. doi: 10.18565/cardio.2016.11.27-37.

409



410

411Figure. 1 Strain analysis image of a subject, A Left ventricular longitudinal strain curve of apical
412four-chamber view, B Left ventricular longitudinal strain curve of apical long axis view, C Left
413ventricular longitudinal strain curve of apical two-chamber view, D Bull's eye diagram of
414longitudinal strain of left ventricular endocardium, middle and epicardial layers

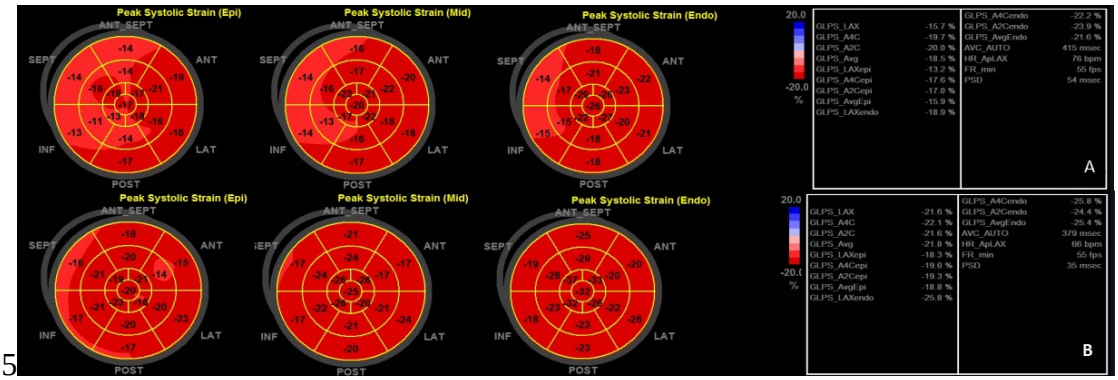


Figure. 2 Left ventricular strain images of a patient before and after one year，A Before participating in this trail, B After participating in this trail for one year

Calculation improvement of the strain value after 1 year of treatment：ΔGLS-end=|-25.4- -21.6|=3.8(%), GLS-mid=|-21.8- -18.5|=3.3(%),ΔGLS-epi=|-18.8- -15.9|=2.7(%)

GLS, global longitudinal strain; GLS-end, GLS-mid and GLS-epi global longitudinal strain of left ventricular endocardial layer, middle layer and epicardial layer

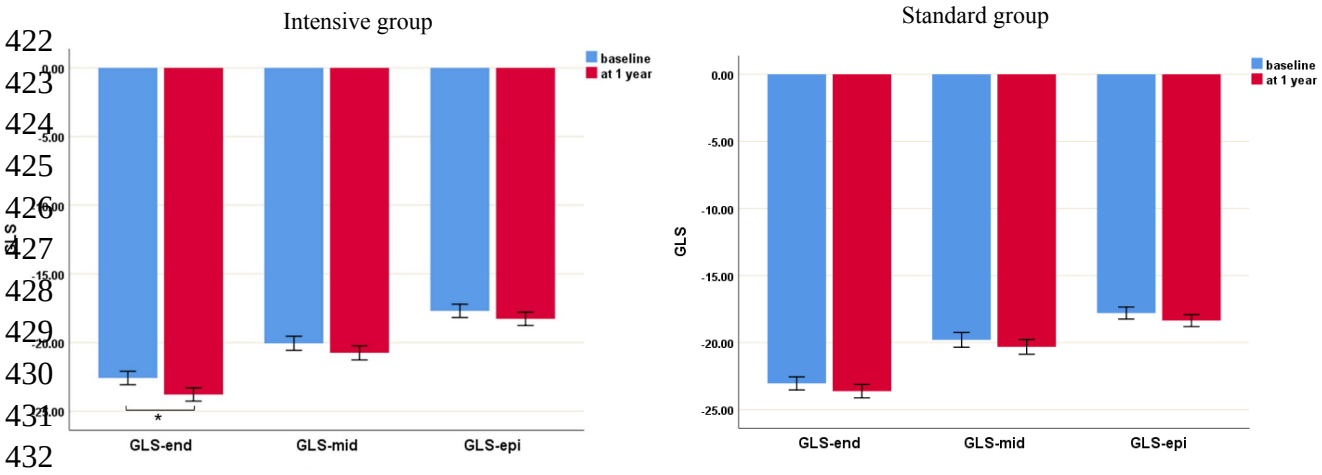


Figure. 3 Changes of strain parameters in the two groups of patients after participating in this trail for one year

GLS, global longitudinal strain; GLS-end, GLS-mid and GLS-epi global longitudinal strain of left ventricular endocardial layer, middle layer and epicardial layer.

* p Value ≤ 0.05 versus Before participating in this trail.

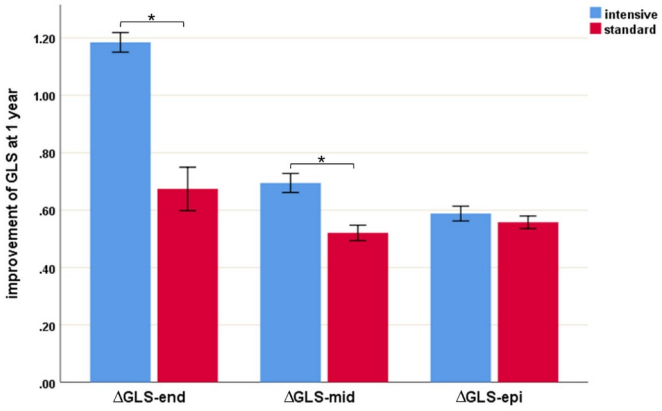


Figure. 4 Comparison of GLS improvement in A and B groups after one year

GLS, global longitudinal strain; ΔGLS-end ΔGLS-mid and ΔGLS-epid improvement value after one year of global longitudinal strain of left ventricle layers.

* p Value ≤ 0.05 versus Standard group.

Table 1 Before participating in this trail characteristics of the participants

Parameter	Intensive group n=159	Standard group n=154	t/χ2	*P* value
Age (years)	66.23±4.98	66.23±4.76	-0.002	0.999
Male gender, n (%)	69(43.4%)	72(46.8)	0.356	0.571
High（cm）	162.89±7.28	163.23±7.78	-0.404	0.687
Weight（Kg）	67.82±9.89	69.78±11.51	-1.614	0.108
Body mass index(Kg/m^2)	25.54±3.09	26.10±3.31	-1.553	0.121
Body surface area(m^2)	1.73±0.15	1.73±0.18	-0.223	0.824
Waistline(cm)	88.73±9.75	90.64±9.74	-1.739	0.083
Heart rate (beats/min)	74.43±11.43	73.73±12.49	0.518	0.605
Office SBP (mm Hg)	143.70±20.65	143.43±14.42	0.134	0.893
Office DBP (mm Hg)	80.83±9.92	82.43±9.65	-1.445	0.150
SBP - max (mm Hg)	167.94±13.91	165.63±12.03	1.568	0.118
DBP - max (mm Hg)	99.46±11.65	99.91±12.41	-0.334	0.739
Plasma triglycerides (mmol/l)	2.01±1.14	1.86±1.06	1.203	0.230
Total cholesterol (mmol/l)	4.50±0.90	4.44±1.01	0.585	0.559
Low-density lipoprotein (mmol/l)	1.63±1.10	1.52±0.82	1.021	0.308
High-density lipoprotein (mmol/l)	2.68±0.75	2.61±0.83	0.767	0.444
Hypertension duration (years)	16.95±8.86	15.55±7.64	1.503	0.134

Data presented as mean ± standard deviation or n (%) ; SBP systolic blood pressure , DBP Diastolic blood pressure.

448**Table 2 Antihypertensive medication after joining this trail of the two groups**

Parameter	**Intensive group n=159**	**Standard group n=154**	χ^2	*P* value
Angiotensin II type 1 receptor antagonists （Olmesartan Medoxomil Tablets）			20.805	0.000
0mg	62(39.0%)	99(64.3%)		
5mg	2(1.3%)	2(1.3%)		
10mg	41(25.7%)	25(16.2%)		
20mg	54(34.0%)	28(18.2%)		
Calcium antagonists （Amlodiping Besylate Tablets）			6.868	0.082
0mg	16(10.0%)	10(6.5%)		
1-2mg	2(1.3%)	6(3.9%)		
2.5-5mg	130(81.8%)	134(87.0%)		
5.5-10mg	11(6.9%)	4(2.6%)		
Diuretics （Hydrochlorothiazide）			10.855	0.017
0mg	135(84.9%)	144(93.5%)		
10mg	2(1.3%)	1(0.6%)		
12.5mg	6(3.8%)	0(0.0%)		
25mg	16(10.0%)	9(5.9%)		

449Data presented as n (%).

Table 3 Left ventricular structure and function before and after joining this trail of the two groups

Parameter	Intensive group n=159	Standard group n=154	*t*	*P* value
Before participating in this trail				
IVSd(mm)	10.16±0.81	10.00±0.78	1.781	0.076
PWTd(mm)	10.11±0.97	10.04±0.82	0.716	0.475
LVDd(mm)	46.37±3.24	46.87±3.47	-1.339	0.182
LVDs(mm)	30.18±2.72	29.80±3.06	1.151	0.251
LVEF(%)	66.77±3.71	66.81±4.60	-0.101	0.920
LVMI(g/m2)	91.68±9.60	92.28±9.76	-0.540	0.589
E(m/s)	58.62±18.77	59.47±22.58	-0.360	0.719
A(m/s)	70.65±28.42	79.38±54.71	-1.763	0.079
Em(m/s)	6.93±3.91	6.55±3.43	0.909	0.364
E/A	0.87±0.20	0.85±0.25	0.861	0.390
E/Em	9.39±2.69	9.78±2.21	-1.374	0.170
After participating in this trail for one year				
IVSd(mm)	10.24±0.82	10.15±0.81	1.047	0.296
PWTd(mm)	10.20±0.87	10.30±0.85	-0.975	0.330
LVDd(mm)	47.14±3.01	47.54±3.22	-1.141	0.255
LVDs(mm)	30.45±2.67	30.13±3.04	1.012	0.312
LVEF (%)	65.68±3.86	64.97±4.39	1.514	0.131
LVMI(g/m2)	91.64±10.82	91.99±9.13	-0.309	0.758
E(m/s)	56.56±19.34	59.83±20.71	-1.443	0.150
A(m/s)	84.88±109.88	84.12±54.65	0.077	0.939
Em(m/s)	8.26±18.36	7.15±4.80	0.729	0.467
E/A ratio	0.84±0.29	0.85±0.29	-0.260	0.795
E/Em	9.31±3.22	9.47±2.61	-0.493	0.622

Data presented as mean ± standard. IVSd end-diastolic inter-ventricular septum thickness, LVPWTd left ventricular posterior wall thickness, LVDd left ventricular end-diastolic diameter, LVDs left ventricular end-systolic diameter, LVEF left ventricular ejection fraction, LVMI left ventricular mass index.

* *p* Value ≤ 0.05 versus **Before participating in this trail.**

Table 4 Changes of blood pressure and strain parameters in the two groups of patients after participating in this trail for one year

Parameter	Intensive group n=159	Standard group n=154	*t*	*P* value
Before participating in this trail				
Office SBP (mm Hg)	143.70±20.65	143.43±14.42	0.134	0.893
Office DBP (mm Hg)	80.83±9.92	82.43±9.65	-1.445	0.150
GLS-end(%)	-22.58±3.11	-23.04±3.07	1.310	0.191
GLS-mid(%)	-20.06±3.27	-19.80±3.45	-0.686	0.493
GLS-epi(%)	-17.69±3.09	-17.80±2.82	0.316	0.752
After participating in this trail for one year				
Office SBP (mm Hg)	130.87±14.87*	135.52±16.31*	-2.636	0.009
Office DBP (mm Hg)	79.95±8.57	80.33±9.97	-0.358	0.720
GLS-end(%)	-23.78±3.10*	-23.62±3.14	-0.453	0.651
GLS-mid(%)	-20.75±3.28	-20.32±3.46	-1.144	0.254
GLS-epi(%)	-18.28±3.08	-18.36±2.81	0.233	0.816
GLS improvement value after one year				
ΔGLS-end(%)	1.20±0.23	0.67±0.48	12.415	0.000
ΔGLS-mid(%)	0.70±0.21	0.52±0.17	8.229	0.000
ΔGLS-epid(%)	0.59±0.16	0.56±0.14	1.665	0.097

Data presented as mean ± standard deviation；SBP systolic blood pressure，DBP Diastolic blood pressure, GLS-end, GLS-mid and GLS-epi global longitudinal strain of left ventricular endocardial layer, middle layer and epicardial layer, ΔGLS-end ΔGLS-mid and ΔGLS-epid improvement value after one year of global longitudinal strain of left ventricle layers.

* *p* Value ≤ 0.05 versus **Before participating in this trail.**

Table 5 Multiple linear regression model

	ΔGLS-end(%)			ΔGLS-mid（%）			ΔGLS-end（%）		
	β	95%CI	*P* value	β	95%CI	*P* value	β	95%CI	*P* value
Angiotensin II type 1 receptor antagonists（Olmesartan Medoxomil Tablets）	0.083	0.046-0.120	0.000	0.017	0.000-0.035	0.057	0.002	-0.011-0.015	0.791
Calcium antagonists（Amlodiping Besylate Tablets）	0.044	-0.036-0.124	0.280	0.008	-0.030-0.046	0.692	0.006	-0.022-0.033	0.692
Diuretics（Hydrochlorothiazide）	0.017	-0.040-0.074	0.558	0.015	-0.012-0.042	0.280	-0.005	-0.025-0.015	0.646
Current office SBP	-0.004	-0.008- -0.001	0.007	-0.001	-0.003-0.000	0.095	0.000	-0.001-0.001	0.790
Current office DBP	-0.004	-0.009-0.002	0.177	0.001	-0.001-0.004	0.303	0.000	-0.001-0.002	0.672

CI confidence interval, SBP systolic blood pressure，DBP Diastolic blood pressure,ΔGLS-end ΔGLS-mid and ΔGLS-epid improvement value after one year of global longitudinal strain of left ventricle layers.

Table 6 Intar-observer and inter-observer variability of left ventricular strain parameters (n = 20)

Parameter	Intra-observer (n=10) ICC	95%CI	Inter-observer (n=10) ICC	95%CI
GLS-end (%)	0.981	0.950-0.998	0.904	0.669-0.979
GLS-mid (%)	0.982	0.957-0.998	0.875	0.672-0.963
GLS-epi (%)	0.970	0.914-0.995	0.958	0.903-0.990

ICC interclass coefficient; CI confidence interval; GLS-end, GLS-mid and GLS-epi global longitudinal strain of left ventricular endocardial layer, middle layer and epicardial layer.