



# Assessment value of 3-dimensional speckle tracking imaging for changes of early left ventricular longitudinal systolic function in patients with primary hypertension

Jing Yu<sup>✉</sup>, Yun-Jian Huang

VIP Department, the 98th Hospital of PLA in Huzhou City, Zhejiang Province, Huzhou City, Zhejiang Province, 313000

## ARTICLE INFO

### Article history:

Received 9 Jul 2016

Received in revised form 18 Jul 2016

Accepted 15 Jul 2016

Available online 24 Jul 2016

### Keywords:

Primary hypertension

3-dimensional speckle tracking imaging

Left ventricular hypertrophy

Angiotensin

## ABSTRACT

**Objective:** To study the assessment value of 3-dimensional speckle tracking imaging for changes of early left ventricular longitudinal systolic function in patients with primary hypertension. **Methods:** Patients with primary hypertension who were treated in our hospital from May 2012 to October 2015 were selected, and 40 patients with left ventricular normal (LVN) primary hypertension and 40 patients with left ventricular remodeling (LVR) primary hypertension were screened according to Ganau typing and enrolled in the LVN group and LVR group of the study respectively; 40 cases of healthy volunteers who received physical examination in our hospital during the same period were selected as control group. Ultrasonic testing was conducted to determine conventional ultrasonic indicators and 3D-STI parameters, and serum was collected to determine AngII, ALD, TGF- $\beta$  1 and Ang1-7 levels. **Results:** LVEDd, LVPWT and LVEF of LVN group were not significantly different from those of control group, LVEF of LVR group was not significantly different from those of LVN group and control group, and LVEDd and LVPWT of LVR group were significantly higher than those of LVN group and control group; absolute values of GLS, GCS, GRS and GAS as well as serum Ang1-7 level of LVN group was significantly lower than those of control group, serum AngII, ALD and TGF- $\beta$  1 levels were higher than those of control group, absolute values of GLS, GCS, GRS and GAS as well as serum Ang1-7 level of LVR group was significantly lower than those of LVN group and control group, and serum AngII, ALD and TGF- $\beta$  1 levels were higher than those of LVN group and control group; absolute values of GLS, GCS, GRS and GAS were negatively correlated with serum AngII, ALD and TGF- $\beta$  1 levels, and positively correlated with serum Ang1-7 level. **Conclusion:** 3-dimensional speckle tracking imaging can be used for early evaluation of left ventricular longitudinal systolic function in patients with primary hypertension, and it also has high sensitivity in judging neurohumoral change.

## 1. Introduction

Primary hypertension is the cardiovascular system disease with the highest incidence rate in our country, and long-term increase of blood pressure levels will increase cardiac load and cause left ventricular hypertrophy (LVH). LVH is a common complicated change in patients with hypertension, early stage of LVH has certain

compensatory effect and can maintain normal cardiac output, but long-term LVH can increase the risk of cardiovascular events[1–3]. Therefore, early assessment of left ventricular systolic function and whether there is hypertrophy can provide basis for clinical treatment. However, the left ventricular ejection fraction (LVEF) measured by conventional two-dimensional ultrasound is still in the normal range in the early stage of LVH, and can not accurately reflect the changes of left ventricular systolic function[4,5]. 3-dimensional speckle tracking imaging (3D-STI) can track under full-volume state and determine myocardial strain parameters, and its evaluation on myocardial contractility is more objective and comprehensive. In the following study, the assessment value of 3-dimensional speckle

<sup>✉</sup>Corresponding author: Yu Jing, VIP Department, the 98th Hospital of PLA in Huzhou City, Zhejiang Province, Huzhou City, Zhejiang Province, 313000.

Tel: 05723269954; 15606729878

Fund Project: Zhejiang Provincial Medical Science and Technology Plan Projects in 2014 No: 2014KYA269.

tracking imaging for changes of early left ventricular longitudinal systolic function in patients with primary hypertension was analyzed.

## 2. Subjects and methods

### 2.1. Research subjects

Patients with primary hypertension who were treated in our hospital from May 2012 to October 2015 were selected, 40 patients with left ventricular normal (LVN) primary hypertension and 40 patients with left ventricular remodeling (LVR) primary hypertension were screened according to Ganau typing and they were enrolled in the LVN group and LVR group of the study respectively. LVN group were with left ventricular mass index (LVMI) 116 g/m<sup>2</sup>(male)/109 g/m<sup>2</sup>(female) and relative wall thickness (RWT) 0.42, included 25 male cases and 15 female cases, and were (58.92±7.91) years old; LVR group were with LVMI>116 g/m<sup>2</sup>(male)/109 g/m<sup>2</sup>(female) and RWT>0.42, included 27 male cases and 13 female cases, and were (59.15±7.87) years old. 40 cases of healthy volunteers who received physical examination in our hospital during the same period were selected as control group, were with blood pressure<140/90 mmHg, were without abnormality through physical examination, electrocardiogram and echocardiography, included 24 male cases and 16 female cases, and were (58.41±7.46) years old. Comparison of general information among three groups showed no significant differences.

### 2.2. Ultrasonic testing

Color Doppler ultrasonic diagnostic apparatus was used for examination, two-dimensional ultrasound scanning was carried out at first, and the specific measured indicators included: left ventricular end-diastolic diameter (LVEDd), left ventricular ejection fraction (LVEF) and left ventricular posterior wall thickness (LVPWT). The left ventricular full-volume image was set as the "layout" mode, meanwhile the 3D-STI was started to capture left ventricular apical four-chamber and apical two-chamber view as well as basal level, papillary level and apical level short-axis view, and the following parameter values were calculated: left ventricular global circumferential strain (GCS), left ventricular global longitudinal strain (GLS), left ventricular global area strain (GAS) and left ventricular global radial strain (GRS).

### 2.3. Serum index determination

6-10 mL of peripheral blood was collected from LVN group and LVR group before ultrasonic examination, 6-10 mL of peripheral blood was collected from control group during physical examination, the blood was centrifuged to get serum specimens, and enzyme-linked immunosorbent kit was used to determine angiotensin II

(AngII), aldosterone (ALD), transforming growth factor  $\beta$  1 (TGF- $\beta$  1) and Ang1-7 levels.

### 2.4. Statistical methods

Target index values were obtained and input into SPSS20.0 software system, measurement data comparison among three groups was by variance analysis and pair-wise comparison was by LSD-t test; correlation between two measurement data was by Pearson test and  $P<0.05$  was set as the standard of statistical significance in differences.

## 3. Results

### 3.1. Conventional ultrasonic indicators

LVEDd, LVPWT and LVEF of LVN group were not significantly different from those of control group ( $P>0.05$ ). LVEF of LVR group was not significantly different from those of LVN group and control group ( $P>0.05$ ), LVEDd and LVPWT of LVR group were significantly higher than those of LVN group and control group, differences in pair-wise comparison were statistically significant ( $P<0.05$ ).

**Table 1.**

Conventional ultrasonic indicators of three groups.

Group	n	LVEDd (mm)	LVPWT (mm)	LVEF (%)
Control	40	44.29±4.13	7.88±0.92	60.49±7.83
LVN	40	45.52±4.92	8.41±1.04	59.52±7.15
LVR	40	48.73±5.62 <sup>#</sup>	11.73±1.42 <sup>*#</sup>	58.89±6.48

<sup>\*</sup>: compared with control group,  $P<0.05$ ; <sup>#</sup>: compared with LVN group,  $P<0.05$ .

### 3.2. 3D-STI strain images and parameters

3D-STI strain images of three groups were the strain images corresponding to GLS, GCS, GRS and GAS respectively, and analysis of specific parameters was as follows: (1) GLS, GCS, GRS and GAS of three groups were significantly different ( $P<0.05$ ); (2) absolute values of GLS, GCS, GRS and GAS of LVN group were significantly lower than those of control group, and differences between two groups were statistically significant ( $P<0.05$ ). Absolute values of GLS, GCS, GRS and GAS of LVR group was significantly lower than those of LVN group and control group, and differences between two groups were statistically significant ( $P<0.05$ ).

**Table 2.**

3D-STI strain parameters of three groups.

Group	n	GLS	GCS	GRS	GAS
Control	40	-19.38±2.29	-27.15±3.86	37.41±5.51	-25.93±3.13
LVN	40	-14.27±1.89 <sup>*</sup>	-23.94±3.16 <sup>*</sup>	32.15±4.59 <sup>*</sup>	-22.14±3.26 <sup>*</sup>
LVR	40	-9.28±1.05 <sup>*#</sup>	-15.93±2.25 <sup>*#</sup>	22.42±4.92 <sup>*#</sup>	-19.30±2.68 <sup>*#</sup>

<sup>\*</sup>: compared with control group,  $P<0.05$ ; <sup>#</sup>: compared with LVN group,  $P<0.05$ .

**Table 3.**

Serum myocardial remodeling-related molecules of three groups.

Group	Case No.	AngII(ng/ml)	ALD(pg/ml)	TGF- $\beta$ 1(ng/ml)	Ang1-7(ng/ml)
Control	40	21.59 $\pm$ 4.96	57.48 $\pm$ 7.92	103.59 $\pm$ 15.82	4.29 $\pm$ 0.81
LVN	40	37.22 $\pm$ 6.14*	89.33 $\pm$ 11.32*	162.84 $\pm$ 22.35*	2.79 $\pm$ 0.58*
LVR	40	62.49 $\pm$ 8.29**	135.62 $\pm$ 17.78**	284.59 $\pm$ 41.32**	1.83 $\pm$ 0.22**

\*: compared with control group,  $P < 0.05$ ; \*\*: compared with LVN group,  $P < 0.05$ .

### 3.3. Serum myocardial remodeling-related molecules

Serum AngII, ALD, TGF- $\beta$  1 and Ang1-7 levels of three groups were significantly different ( $P < 0.05$ ). Serum AngII, ALD and TGF- $\beta$  1 levels of LVN group and LVR group were significantly higher than those of control group, Ang1-7 levels were significantly lower than that of control group, and differences between two groups were statistically significant ( $P < 0.05$ ); serum AngII, ALD and TGF- $\beta$  1 levels of LVR group were significantly higher than those of LVN group, Ang1-7 level was significantly lower than that of LVN group, and differences between two groups were statistically significant ( $P < 0.05$ ).

### 3.4. Correlation between 3D-STI parameters and serum indexes

Pearson test showed that the absolute values of GLS, GCS, GRS and GAS were negatively correlated with serum AngII, ALD and TGF- $\beta$  1 levels, and positively correlated with serum Ang1-7 level.

## 4. Discussion

Left ventricular hypertrophy (LVH) is a common concurrent change of primary hypertension, early LVH is the compensatory mechanism to maintaining myocardial contractility, but long-term LVH can increase the risk of cardiovascular events[6,7]. Therefore, early assessment of myocardial contractility and judgment of LVH state has positive clinical significance. LVEF as well as LVEDd and LVPWT are the conventional indexes to evaluate global left ventricular systolic function, but because ultrasound images are limited to two-dimensional plane, regarding myocardial motion as simple two-dimensional-space vasomotor will ignore the real myocardial space motion, and what's more, the heart rate, afterload and other factors can cause impact, which will cause measured deviation of conventional ultrasonic indicators [8–9]. In the study, evaluation of conventional ultrasonic indicators showed that the LVEF of three groups were not significantly different, LVEDd and LVPWT of LVR group significantly changed, but LVEDd and LVPWT of LVN group were not significantly different from those of control group. Thus it was analyzed that conventional ultrasonic indicators could not be used to evaluate whether the ventricular systolic function was abnormal or not in patients with left ventricular normal hypertension, and was not conducive to the evaluation of

early myocardial contractility damage and complication of LVH.

3D-STI technology is the ultrasonic testing technology developed from the principles of three-dimensional ultrasound and speckle tracking, can accurately track myocardial motion trail in three-dimensional volume and is not limited by myocardial motion direction, and the myocardial strain parameters determined by it can directly, objectively and comprehensively reflect myocardial contractility[10–12]. With reference to the studies of domestic scholars LI Chun-yan[13] and GAO Lei[14], four 3D-STI parameters GLS, GCS, GRS and GAS were chosen in the study to evaluate left ventricular systolic function in patients with essential hypertension, and the results showed that absolute values of GLS, GCS, GRS and GAS of LVN group were significantly lower than those of control group, and absolute values of GLS, GCS, GRS and GAS of LVR group were significantly lower than those of LVN group and control group. It indicated that that the 3D-STI parameters GLS, GCS, GRS and GAS significantly changed in the LVN group of patients, and the above four indicators could early reflect the changes in left ventricular systolic function in patients with essential hypertension. Various neurohumoral factors are involved in the development of primary hypertension to LVH, and play a very important regulating role. Angiotensin II (AngII) is an important hormone causing myocardial remodeling and ventricular hypertrophy[15], and AngII can combine with its type 1 receptor AT1R to activate aldosterone system and transforming growth factor  $\beta$  1 (TGF- $\beta$  1) expression, thereby promoting myocardial remodeling and ventricular hypertrophy through aldosterone (ALD) and TGF- $\beta$  1[16,17]. Angiotensin-converting enzyme 2 (ACE2)/Ang1-7/Mas is a newly discovered RAS axis in recent years, ACE2 can degrade AngII into Ang1-7, and the latter can combine with receptor Mas to improve the myocardial systolic function and inhibit the effect of AngII on promoting myocardial remodeling through NFAT way and NO/cGMP way[18,19]. In the study, the analysis of serum levels of myocardial remodeling-related molecules confirmed that serum AngII, ALD and TGF- $\beta$  1 levels of LVN group and LVR group were significantly higher than those of control group, and Ang1-7 levels were significantly lower than that of control group; serum AngII, ALD and TGF- $\beta$  1 levels of LVR group were significantly higher than those of LVN group, and Ang1-7 level was significantly lower than that of LVN group. Further analysis of the correlation between 3D-STI parameters and serum indicators showed that the absolute values of GLS, GCS, GRS and GAS were negatively correlated with serum AngII, ALD and TGF- $\beta$  1 levels, and positively correlated with serum Ang1-7 level.

To sum up, 3-dimensional speckle tracking imaging is the ideal method to detect cardiac dysfunction in patients with hypertension, and can early evaluate the left ventricular longitudinal systolic function and neurohumoral level change in patients with primary hypertension.

## References

- [1] Carpinella G, Pagano G, Buono F, Petitto M, Guarino G, Orefice G, et al. Prognostic value of combined target-organ damage in patients with essential hypertension. *Am J Hypertens* 2015; **28**(1): 127-134.
- [2] Yucel C, Demir S, Demir M, Tufenk M, Nas K, Molnar F, et al. Left ventricular hypertrophy and arterial stiffness in essential hypertension. *Bratisl Lek Listy* 2015; **116**(12): 714-718.
- [3] Lee H, Kong YH, Kim KH, Huh J, Kang IS, Song J. Left ventricular hypertrophy and diastolic function in children and adolescents with essential hypertension. *Clin Hypertens* 2015; **22**(21): 21.
- [4] Ruan W, Lim SH, Ding ZP, Sim DK, Gao F, Gunasegaran K, et al. Prevalence, Presentation, and Outcome of Heart Failure with Preserved Ejection Fraction among Patients Presenting with Undifferentiated Dyspnoea to the Emergency Room: A 10-year Analysis from a Tertiary Centre. *Ann Acad Med Singapore* 2016; **45**(1): 18-26.
- [5] Yarbrough WM, Baicu C, Mukherjee R, Van Laer A, Rivers WT, McKinney RA, et al. Cardiac-restricted overexpression or deletion of tissue inhibitor of matrix metalloproteinase-4: differential effects on left ventricular structure and function following pressure overload-induced hypertrophy. *Am J Physiol Heart Circ Physiol* 2014; **307**(5): 752-761.
- [6] Fang X, Wang Z, Wang C, Wu J, Yang Y, Li F, et al. Cardiovascular and Cognitive Health Study in Middle-Aged and Elderly Residents of Beijing (CCHS-Beijing): Design and Rationale. *Neuroepidemiology* 2016; **46**(3): 182-190.
- [7] Artigao-Ródenas LM, Carbayo-Herencia JA, Palazón-Bru A, División-Garrote JA, Sanchis-Domènech C, Vigo-Aguiar I, et al. Construction and Validation of a 14-Year Cardiovascular Risk Score for Use in the General Population: The Puras-GEVA Chart. *Medicine (Baltimore)* 2015; **94**(47): e1980.
- [8] Zhou X, Thavendirathan P, Chen Y, Cheng L, Qian Z, Liu S, et al. Feasibility of Automated Three-Dimensional Rotational Mechanics by Real-Time Volume Transthoracic Echocardiography: Preliminary Accuracy and Reproducibility Data Compared with Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr* 2016; **29**(1): 62-73.
- [9] Celic V, Tadic M, Suzic-Lazic J, Andric A, Majstorovic A, Ivanovic B, et al. Two- and three-dimensional speckle tracking analysis of the relation between myocardial deformation and functional capacity in patients with systemic hypertension. *Am J Cardiol* 2014; **113**(5): 832-839.
- [10] Kawamura R, Seo Y, Ishizu T, Atsumi A, Yamamoto M, Machino-Ohtsuka T, et al. Feasibility of left ventricular volume measurements by three-dimensional speckle tracking echocardiography depends on image quality and degree of left ventricular enlargement: validation study with cardiac magnetic resonance imaging. *J Cardiol* 2014; **63**(3): 230-238.
- [11] Saeki M, Sato N, Kawasaki M, Tanaka R, Nagaya M, Watanabe T, et al. Left ventricular layer function in hypertension assessed by myocardial strain rate using novel one-beat real-time three-dimensional speckle tracking echocardiography with high volume rates. *Hypertens Res* 2015; **38**(8): 551-559.
- [12] Urbano-Moral JA, Rowin EJ, Maron MS, Crean A, Pandian NG. Investigation of global and regional myocardial mechanics with 3-dimensional speckle tracking echocardiography and relations to hypertrophy and fibrosis in hypertrophic cardiomyopathy. *Circ Cardiovasc Imaging* 2014; **7**(1): 11-19.
- [13] GAO Lei, LIU Xin, GUO Shuqin, LI Chunqing. Real-time Three-dimensional Speckle Tracking Imaging in Evaluating Global Left Ventricular Systolic Function in Patients with Type 2 Diabetes and Poor Blood Glucose Control. *Chin J Med Imaging* 2015; **6**(10): 439-444.
- [14] LI Chun-yan, ZHU Wen-hui, LIU Wen-gang. Assessment of Left Ventricular Systolic Function by Three-dimensional Speckle Tracking Imaging in Patients with Essential Hypertension. *Chin J Med Imaging* 2013; **3**(12): 197-200,205.
- [15] Tsuruda T, Sekita-Hatakeyama Y, Hao Y, Sakamoto S, Kurogi S, Nakamura M, et al. Angiotensin II Stimulation of Cardiac Hypertrophy and Functional Decompensation in Osteoprotegerin-Deficient Mice. *Hypertension* 2016; **67**(5): 848-856.
- [16] Borghi C; SIIA Task Force, Rossi F; SIF Task Force. Role of the Renin-Angiotensin-Aldosterone System and Its Pharmacological Inhibitors in Cardiovascular Diseases: Complex and Critical Issues. *High Blood Press Cardiovasc Prev* 2015; **22**(4): 429-444.
- [17] Catena C, Verheyen N, Pilz S, Kraigher-Krainer E, Tomaschitz A, Sechi LA, et al. Plasma aldosterone and left ventricular diastolic function in treatment-naïve patients with hypertension: tissue-Doppler imaging study. *Hypertension* 2015; **65**(6): 1231-1237.
- [18] de Almeida PW, Melo MB, Lima Rde F, Gavioli M, Santiago NM, Greco L, et al. Beneficial effects of angiotensin-(1-7) against deoxycorticosterone acetate-induced diastolic dysfunction occur independently of changes in blood pressure. *Hypertension* 2015; **66**(2): 389-395.
- [19] Mori J, Patel VB, Abo Alrob O, Basu R, Altamimi T, Desaulniers J, et al. Angiotensin 1-7 ameliorates diabetic cardiomyopathy and diastolic dysfunction in db/db mice by reducing lipotoxicity and inflammation. *Circ Heart Fail* 2014; **7**(2): 327-339.