BMC Cardiovascular Disorders

RESEARCH

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Early detection of left atrial dysfunction in young hypertensive patients with a normal left atrial size: a comprehensive analysis using four-dimensional auto left atrial quantification echocardiography

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Abstract

Background This study aimed to detect early left atrial (LA) function abnormalities in young hypertensive patients with a normal two-dimensional LA volume index (2D-LAVI) using four-dimensional auto LA quantification technology (4D Auto LAQ) and to analyse correlations between LA strain parameters and clinical metabolic indicators.

Methods This study enrolled 70 young patients who underwent standard hypertension treatment or diagnosis at the Second Affiliated Hospital, Jiangxi Medical College, Nanchang University, from October 2023 to July 2024 and 41 control volunteers enrolled during the same period. LA volume and strain parameters were evaluated with a 4D Auto LAQ. A correlation analysis was conducted between the clinical and strain parameters.

Results Compared with the control group, young hypertensive patients presented significantly greater LA minimum volume (LAVmin), LA minimum volume index (LAVImin) and LA pre-atrial volume (LAVpreA) values (all $p < 0.001$). The LA ejection fraction (LAEF) was reduced in young hypertensive patients (57.85%±4.47% vs. 50.44%±5.96%, $p < 0.001$), along with LA reservoir longitudinal strain (25.00% [20.50–29.50%] vs. 20.00% [16.00–24.25%], $p < 0.001$), LA conduit longitudinal strain (-16.32%±4.19% vs. -11.37%±4.65%, $p < 0.001$), LA contraction longitudinal strain (-12.27%±2.85% vs. -9.60 ± 4.12, $p < 0.001$), LA reservoir circumferential strain (34.32%±6.90% vs. 28.41%±6.95%, $p < 0.001$), LA conduit circumferential strain (-17.90%±4.84% vs. -11.46%±4.96%, $p < 0.001$), and LA contraction circumferential strain (-18.54%±4.85% vs. -16.23%±6.11%, $p < 0.05$). Multivariate linear regression analysis revealed that body mass index (BMI), triglyceride (TG), and uric acid (UA) were negatively and independently correlated with LA longitudinal strain.

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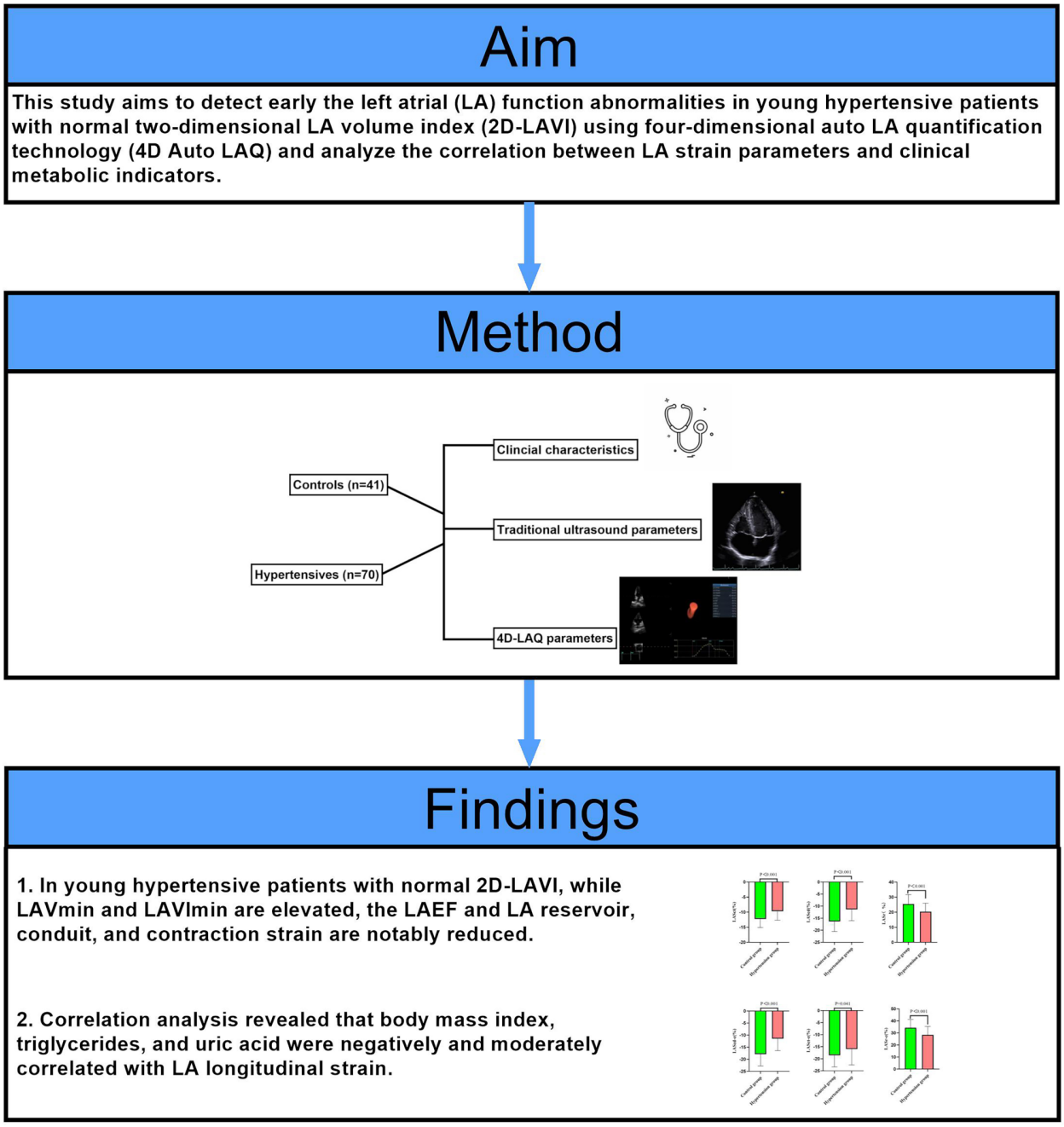
Conclusions In young hypertensive patients with normal 2D-LAVI, while LAVmin, LAVImin and LAVpreA are elevated, the LAEF and LA reservoir, conduit, and contraction strain are notably reduced. The application of 4D Auto LAQ technology may highlight altered values in young hypertensive patients with normal 2D-LAVI. 4D Auto LAQ may serve as a valuable tool for clinicians in the early detection and assessment of LA dysfunction in young hypertensive patients.

Graphical abstract



Keywords Four-dimensional auto left atrial quantification, Young hypertensive patients, Left atrial strain, Left atrial dysfunction, Correlation analysis

Background

Hypertension is a major global public health challenge, with its prevalence steadily rising in recent years and increasingly affecting younger populations at an alarming pace [1–3]. Traditionally considered a condition predominantly affecting older adults, emerging evidence indicates that hypertension is becoming a major risk factor in young adults, defined as individuals aged 18 to 45 years [4, 5]. As hypertension in young adults is often asymptomatic, it is typically only diagnosed once cardiovascular damage has already occurred. Prolonged exposure to hypertension significantly increases the risk of developing long-term cardiovascular conditions, including coronary artery disease, chronic renal failure, glucose metabolism disorders, and dyslipidaemia. Early-onset hypertension is of greater concern [6]. Research has indicated that early-stage hypertension can affect left atrial (LA) function; therefore, assessing LA function is essential in young hypertensive patients [7].

The traditional methods for assessing LA function include two-dimensional echocardiography (2DE) and two-dimensional speckle tracking imaging. Owing to the irregular geometry of the LA, accurately evaluating its structure and function using 2DE images is difficult [8]. Furthermore, most of these studies included patients irrespective of LA size [9, 10]. This raises the question of whether LA dysfunction in young hypertensive patients can be identified in the absence of LA enlargement. This question may be of clinical interest because LA size is frequently utilized in clinical practice as a surrogate marker of LA function [11]. Compared with patients included in prior research who had no constraint on the size of the LA, the hypertension patients included in this study did not have an enlarged LA as measured by 2DE. Therefore, we need an advanced and sensitive tool to analyse the LA from multiple dimensions and phases and assess whether LA dysfunction occurs before LA enlargement in young hypertensive patients.

Four-dimensional auto LA quantification (4D Auto LAQ) technology is a novel ultrasound tool developed specifically for LA. It can offer real-time, 4D cardiac imaging that comprehensively evaluates LA structure and function throughout the cardiac cycle, overcoming most of the limitations of 2DE techniques. The feasibility and reproducibility of 4D Auto LAQ for the study of LA function in cardiovascular diseases have been recently validated [12–14]. These studies also revealed that 4D Auto LAQ is a promising method for studying LA structure and functions. The purpose of this study was to use 4D Auto LAQ technology to detect early LA dysfunction in young hypertensive patients with a normal LA size and to analyse the associated factors.

Materials and methods

Study population

This single-centre prospective study received ethical approval from the Second Affiliated Hospital, Jiangxi Medical College, Nanchang University (No. IIT-O-2024-236) and conducted in compliance with Helsinki Declaration, all participants provided written informed consent. From October 2023 to July 2024, this study prospectively enrolled 80 young hypertensive patients, defined as individuals aged 18 to 45 years received basic hypertension treatment or diagnosis at the Second Affiliated Hospital, Jiangxi Medical College, Nanchang University. Forty-four healthy young volunteers (aged 18 to 45 years) were enrolled during the same period as the control group.

Hypertension was classified according to the European Society of Cardiology guidelines, with a blood pressure threshold of ≥ 140/90 mmHg on three or more occasions, or as antihypertensive treatment in the presence of a documented history of hypertension [15]. The inclusion criteria were as follows: (1) a definitive diagnosis of essential hypertension; (2) echocardiographic evidence of a normal 2D LA size, defined as a 2D LA volume index (2D-LAVI) < 34 mL/m² [16]; (3) young adults, defined as individuals aged 18 to 45 years [4, 5]; (4) with sinus rhythm. The exclusion criteria were as follows: (1) secondary hypertension; (2) left ventricular ejection fraction (LVEF) < 50%; (3) history of cardiovascular surgery or other interventions affecting LA function; (4) moderate or severe valvular stenosis or regurgitation; (5) congenital heart disease, cardiomyopathy or metabolic diseases such as hypertrophic cardiomyopathy, dilated cardiomyopathy, diabetes, thyroid disorders, chronic kidney disease, or other severe systemic diseases; (6) inadequate image quality. In the hypertension group, 3 patients with secondary hypertension (one patient with sleep apnoea syndrome, one patient with primary aldosteronism and one patient with pheochromocytoma), 3 patients with enlarged LA, 1 patient with congenital heart disease, and 3 patients with poor image quality were excluded. Three volunteers in the control group were excluded because of poor image quality (Fig. 1).

Image acquisition and analysis

Transthoracic echocardiography was performed using a GE Vivid E95 ultrasound diagnostic system (GE Healthcare, Vingmed Ultrasound, Horten, Norway) with the patient in the left lateral decubitus position at rest. An electrocardiogram (ECG) was connected before imaging, ensuring that the ECG signals were clear and complete.

Traditional 2DE image acquisition and analysis

Traditional 2D ultrasound was performed via an M5Sc transducer (frequency: 2.5–4.0 MHz). All measurements were conducted in accordance with the guidelines

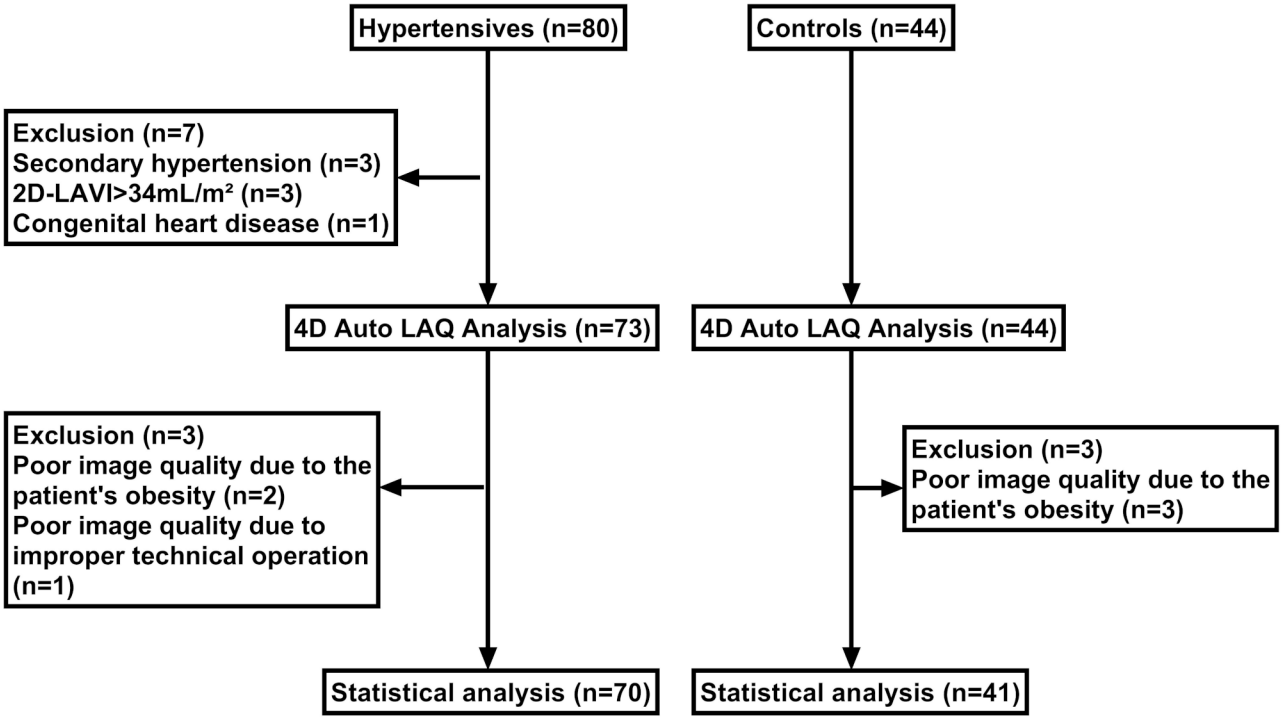


Fig. 1 Flow chart for participant inclusion in the hypertensive and control groups. 4D Auto LAQ, four-dimensional automated left atrial quantification; 2D-LAVI, two-dimensional left atrial volume index

of the American Society of Echocardiography [17]. The LA diameter (LAD), interventricular septal diameter (IVSD), LV posterior wall diameter (LVPWD), LV end-diastolic diameter (LVEDD) and LV end-systolic diameter (LVESD) were measured in the parasternal long-axis view. The LVEF was calculated using the modified Simpson's method. The peak early (E) and late (A) diastolic velocities of the mitral inflow were assessed with pulsed-wave Doppler ultrasound. The peak displacement velocities of early diastolic mitral annular motion (e') at the septal and lateral walls were obtained via tissue Doppler imaging, and the E/A and average E/e' ratios were computed. The 2D-LAVI was calculated using the biplane Simpson's method from the apical four-chamber and two-chamber views and then indexed to the body surface area (BSA) to obtain the LAVI.

4D auto LAQ image acquisition

The 4D Auto LAQ was performed using a 4 V transducer (frequency: 1.5–4.0 MHz). A 4D probe was used to collect apical four-chamber full-volume dynamic images, where the frame rate was adjusted to be >40% of the subject's heart rate (HR). With stable ECG monitoring, the sampling fan angle and depth were adjusted to display the entire view of LA, positioning the target point at the intersection of the mitral valve centre and the LA. The entire LA was visualized in the apical four-chamber view before switching to 4D mode. The subjects were instructed to hold their breath at the end of exhalation, and dynamic images were captured during 3 consecutive cardiac cycles [18].

4D auto LAQ image analysis

Images were imported into EchoPAC204 software, which activated the 4D volume auto measurement mode. Landmark points were set at end-systole for each plane, with further adjustments made to align the mitral valve centre, ensuring optimal visualization of the mitral annulus, walls, and apex. The software automatically identified and delineated the endocardial borders of the LA. In cases where the automatic identification is unsatisfactory, it can be manually adjusted [19]. In this study, no patient images required manual adjustment. The 4D parameters of the LA were obtained by selecting "Results" (Fig. 2). The 4D algorithm automatically calculates the LA volume and ejection fraction. Strain analysis was performed to assess the LA reservoir, conduit, and contractile functions during LV systole, early diastole, and late diastole, respectively. The volume parameters included the LA minimum volume (LAVmin), LA maximum volume (LAVmax), LA maximum volume index (LAVImax), and LA preatrial volume (LAVpreA). The LA minimum volume index (LAVImin) was calculated by dividing the LAVmin by the BSA. The strain parameters generated by the 4D Auto software included LA reservoir longitudinal strain (LASr), LA conduit longitudinal strain (LAScd),

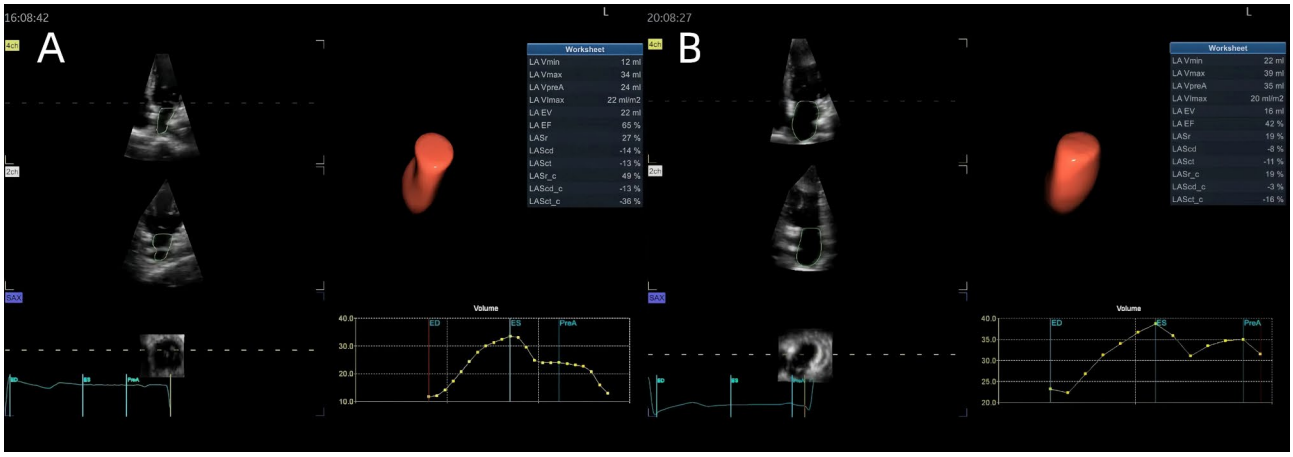


Fig. 2 4D left atrial parameters analysed by 4D Auto LAQ. **A**: a participant from the control group; **B**: a participant from the hypertensive group; 4D Auto LAQ, four-dimensional automated left atrial quantification

LA contractile longitudinal strain (LASct), LA reservoir circumferential strain (LASr-c), LA conduit circumferential strain (LAScd-c) and LA contraction circumferential strain (LASct-c).

Statistical analysis

All the statistical analyses were performed using SPSS version 27.0 (IBM, Chicago, IL, USA). Normality was assessed with the Shapiro–Wilk test, and homogeneity of variance was evaluated using Levene's test. Continuous variables following a normal distribution are presented as the mean ± standard deviation (SD). For continuous variables not conforming to a normal distribution, the 25–75% interquartile range (IQR) is presented. The comparisons between the two groups were performed via Student's t test or the Mann–Whitney U test. Categorical variables were compared between groups with the chi-square test or Fisher's exact test, with results expressed as percentages. The correlations between variables were evaluated using Spearman or Pearson correlation coefficients, as appropriate. Variables with p values < 0.1 in the correlation analysis were further analysed via multivariate regression adjusted for confounding factors, such as age and body mass index (BMI). To evaluate the repeatability and reproducibility of the 2DE and 4D Auto LAQ parameter measurements, 10 patients were randomly selected. Bland–Altman analysis was performed to assess intraobserver and interobserver agreement. The same observer repeated the analysis after one week, and a second independent observer also performed the analysis. A p value < 0.05 was considered statistically significant.

Results

Clinical characteristics

This study initially included 80 hypertensive patients, but 10 were subsequently excluded. The hypertension group consisted of the remaining 70 patients, of whom 2 had grade 1 hypertension, 32 had grade 2 hypertension, and 36 had grade 3 hypertension. Table 1 presents a summary of the clinical characteristics and medication usage between the hypertensive and control groups. No significant differences were observed between the groups in terms of age, sex, BSA, BMI, HR, smoking status, or drinking status. However, the systolic blood pressure (SBP), diastolic blood pressure (DBP), uric acid (UA), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) levels were notably greater in the hypertensive group than in the control group. Conversely, high-density lipoprotein cholesterol (HDL-C) levels were greater in the control group. The median duration of hypertension was 1.00 years (IQR 0.20–2.88 years) at the time of inclusion in this study.

2DE characteristics

The 2DE parameters for both the hypertensive and control groups are summarized in Table 2. There were no statistically significant differences between the hypertensive patients and the controls in terms of LAD, IVSD, LVPWD, LVEDD, LVESD, LVEF, E/A ratio, average E/e' ratio, or 2D-LAVI.

4D auto LAQ echocardiographic analysis

In our study, the control group had a significantly greater LAEF (57.85 ± 4.47% vs. 50.44 ± 5.96%, p < 0.001). The analysis of LA strain parameters revealed that the hypertensive group exhibited significantly lower strain values across multiple metrics than did the control group. Significant differences were observed in LASr, LAScd, LASct, LASr-c, LAScd-c, and LASct-c, with all p values < 0.05 as shown in Table 2; Fig. 3. LAScd/LAScd-c and LASct/LASct-c are negative values due to LA muscle fibre shortening during LV diastole. Given their negative values, absolute values are used to reflect the magnitude of contractile function.

Table 1 Baseline characteristics

Variables	Controls ($n=41$)	Hypertensives ($n=70$)	p value
Demographic characteristics			
Age (years)	39.07 ± 4.38	40.30 ± 4.70	0.177
Male *n* (%)	27 (66)	48 (69)	0.768
BSA (m^2)	1.73 ± 0.12	1.76 ± 0.16	0.298
BMI (Kg/m^2)	24.32 ± 0.93	25.06 ± 3.00	0.057
HR (bpm)	76.93 ± 9.61	78.41 ± 10.48	0.459
Lifestyle factors			
Smoking *n* (%)	5 (12.2)	10 (14.3)	0.148
Drinking *n* (%)	12 (29.2)	20 (28.6)	0.265
Blood pressure information			
HT duration (years)	/	1.00 (0.20–2.88)	/
SBP (mmHg)	120.78 ± 4.13	145.56 ± 19.33	< 0.001*
DBP (mmHg)	73.85 ± 4.58	91.7 ± 13.86	< 0.001*
Biochemical characteristics			
TG (mmol/L)	0.86 (0.75–1.07)	1.41 (1.00-2.22)	< 0.001*
HDL-C (mmol/L)	1.17 (0.93–1.37)	1.02 (0.90–1.10)	0.004*
LDL-C (mmol/L)	1.05 (0.95–1.10)	2.54 (1.95–3.10)	< 0.001*
UA (μmol/L)	150.63 ± 31.48	425.76 ± 53.24	< 0.001*
Medication use			
Beta-blockers *n* (%)	/	1 (1.4)	/
CCBs *n* (%)	/	25 (35.7)	/
ACEIs/ARBs *n* (%)	/	8 (11.4)	/
Diuretic *n* (%)	/	4 (5.7)	/
Alpha-blockers *n* (%)	/	1 (1.4)	/

BSA, body surface area; BMI, body mass index; HR, heart rate, HT, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; UA, uric acid; CCBs, calcium channel blockers; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; *, $p<0.05$

Moreover, the 4D Auto LAQ analysis revealed significant differences in some volume parameters. Compared with the control group, the hypertensive group presented significantly greater LAVmin (18.66 ± 3.53 mL vs. 15.46 ± 1.63 mL, $p<0.001$), LAVImin (10.66 ± 2.14 mL/m^2 vs. 9.04 ± 1.10 mL/m^2, $p<0.001$) and LAVpreA (27.20 ± 7.22 mL vs. 21.40 ± 0.44 mL, $p<0.001$) values. No significant differences in LAVmax or LAVImax were observed between the two groups.

Reproducibility of the 2DE and 4D Auto LAQ parameters

We randomly selected 10 patients to measure intraobserver and interobserver variability. The intraclass correlation coefficient (ICC) values and 95% confidence intervals (CIs) for each parameter are shown in Tables 3 and 4. The results demonstrated that all the 2DE and 4D Auto LAQ parameters had excellent intraobserver and interobserver reproducibility, as demonstrated by an ICC greater than 0.75.

Correlations between clinical variables and LA strain

In the univariate screening phase, BSA, BMI, TG, HDL-C, LDL-C and UA were associated with LA longitudinal strains at the predefined threshold of p value < 0.1. After that, a multivariate linear regression analysis was performed using these variables and the age factor. Multivariate linear regression revealed that BMI was independently inversely associated with LASct, TG was independently inversely associated with LASr, and UA was independently inversely associated with LAScd as shown in Table 5.

Discussion

Compared with 2DE technique, the 4D Auto LAQ technique revealed more subtle structural and functional differences between the two groups, providing clinicians with more comprehensive and detailed LA function information. The 4D Auto LAQ technique is more sensitive in detecting LA changes in young hypertensive patients. This conclusion has been validated by previous studies [20, 21].

Typically, LA function is divided into three key components: reservoir, conduit, and contractile functions. During LV systole, the LA serves as a reservoir by receiving blood from the pulmonary veins, acting as a conduit for pulmonary venous return during early ventricular diastole. Its contractile function involves active contraction of the LA at the end of LV diastole, facilitating additional blood flow into the LV [22].

Table 2 Comparison of two-dimensional echocardiography and four-dimensional left atrial auto quantification parameters

Variables	Controls ($n=41$)	Hypertensives ($n=70$)	Cohen d or Cliff's δ value (95% CI)	p value
two-dimensional echocardiographic parameters				
LAD (mm)	32.29 ± 1.95	33.09 ± 2.74	-0.319 (-0.706 ~ 0.069)	0.107
IVSD (mm)	10.15 ± 1.17	10.25 ± 1.31	-0.069 (-0.455 ~ 0.316)	0.678
LVPWD (mm)	9.37 ± 1.09	9.40 ± 1.14	-0.005 (-0.39 ~ 0.381)	0.962
LVEDD (mm)	45.90 ± 3.23	46.17 ± 3.47	-0.079 (-0.465 ~ 0.306)	0.687
LVESD (mm)	29.02 ± 3.00	28.97 ± 3.00	0.018 (-0.368 ~ 0.403)	0.929
LVEF (%)	65.76 ± 3.41	66.31 ± 3.74	-0.154 (-0.54 ~ 0.232)	0.435
E/A	1.06 ± 0.31	1.07 ± 0.31	-0.022 (-0.407 ~ 0.364)	0.906
Average E/e'	8.62 ± 1.84	8.26 ± 1.89	0.193 (-0.194 ~ 0.579)	0.328
LAVI (mL/m^2)	18.95 ± 2.57	19.86 ± 3.28	-0.297 (-1.007 ~ 0.413)	0.412
four-dimensional left atrial auto quantification parameters				
LAVmin (mL)	15.46 ± 1.63	18.66 ± 3.53	-1.073 (-1.482~-0.66)	< 0.001*
LAVmax (mL)	36.17 ± 3.57	37.43 ± 5.98	-0.241 (-0.627 ~ 0.147)	0.168
LAVImin (mL/m2)	9.04 ± 1.10	10.66 ± 2.14	-0.897 (-1.299~-0.492)	< 0.001*
LAVImax (mL/m2)	20.91 ± 2.91	21.40 ± 3.71	-0.142 (-0.527 ~ 0.244)	0.386
LAVpreA(mL)	21.40 ± 0.44	27.20 ± 7.22	-1.008 (-1.414~-0.598)	< 0.001*
LAEF (%)	57.85 ± 4.47	50.44 ± 5.96	1.357 (0.929 ~ 1.78)	< 0.001*
LASr (%)	25.00 (20.50–29.50)	20.00 (16.00-24.25)	0.499 (0.303 ~ 0.655)	< 0.001*
LAScd (%)	-16.32 ± 4.19	-11.37 ± 4.65	-1.103 (-1.513~-0.688)	< 0.001*
LASct (%)	-12.27 ± 2.85	-9.60 ± 4.12	-0.721 (-1.116~-0.322)	< 0.001*
LASr-c (%)	34.32 ± 6.90	28.41 ± 6.95	0.852 (0.448 ~ 1.252)	< 0.001*
LAScd-c (%)	-17.90 ± 4.84	-11.46 ± 4.96	-1.311 (-1.732~-0.886)	< 0.001*
LASct-c (%)	-18.54 ± 4.85	-16.23 ± 6.11	-0.406 (-0.794~-0.016)	0.041*

CI, Confidence interval; LAD, left atrial diameter; IVSD, inter ventricular septal diameter; LVPWD, left ventricular posterior wall diameter; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; E/A, the ratio of early peak diastolic velocity to late peak diastolic velocity of mitral valve orifice; Average E/e', the ratio of E to average e'; LAVI, left atrial volume index. LAVmin, left atrial minimum volume; LAVmax, left atrial maximum volume; LAVImin, left atrial minimum volume index; LAVImax, left atrial maximum volume index; LAVpreA, left atrial pre-atrial volume; LAEF, left atrial ejective fraction; LASr, left atrial reservoir longitudinal strain; LAScd, left atrial conduit longitudinal strain; LASct, left atrial contractile longitudinal strain; LASr-c, left atrial reservoir circumferential strain; LAScd-c, left atrial conduit circumferential strain; LASct-c, left atrial contraction circumferential strain; *, $p < 0.05$

Therefore, this study assessed LA function during the above phases via the 4D Auto LAQ technique. The analysis results revealed a significant reduction in LA strain parameters, indicating that the reservoir, conduit, and contractile functions of the LA are impaired in these individuals. Hypertension can cause aberrant cardiomyocyte arrangement, collagen deposition, and myocardial fibrosis. These conditions can contribute to LA remodelling, which diminishes LA systolic function and compliance and consequently lowers strain values. Even without a markedly increased LA, myocardial fibrosis and subtle microstructural changes can impair LA function, affecting strain values [23–25]. Previous studies have shown that LA function may be compromised in hypertensive patients, even those with a normal 2D LA size [26]. These findings are consistent with our results. It is worth mentioning that the myocardial fibrosis of hypertensive patients may cause atrial cardiomyopathy and increase the risk of atrial fibrillation (AF); some studies have shown that LA speckle-tracking echocardiography (i.e., strain analysis) may provide insight into the presence of atrial cardiomyopathy prior to AF [27, 28]. However, long-term follow-up investigations were not carried out in this study to verify that this population is susceptible to AF in the future.

Sustained elevated blood pressure increases the afterload on the LV. This increased systolic load leads to hypertrophy of cardiomyocytes, fibrosis, and the proliferation of interstitial cells, resulting in compensatory thickening of the LV wall. In this study, no significant differences in LV structure or function were detected between hypertensive patients and the control group, likely because the cohort consisted of young individuals with relatively short disease durations who were still in the early stages of hypertension. Although LV structure and function did not exhibit substantial changes, the 4D Auto LAQ technique revealed an increase in some 4D LA volume parameters, suggesting that structural abnormalities in the LA may already be present in hypertensive patients, even before LV hypertrophy or remodelling occurs [29, 30]. Hypertension can induce myocardial fibrosis, particularly in the LA, due to its thinner walls and shorter myocardial fibres, making it more susceptible to pressure and volume overload [31, 32].

Beyond that, our research conducted correlation analysis between the clinical and strain parameters. The results have shown that BMI, TG, and UA were independently

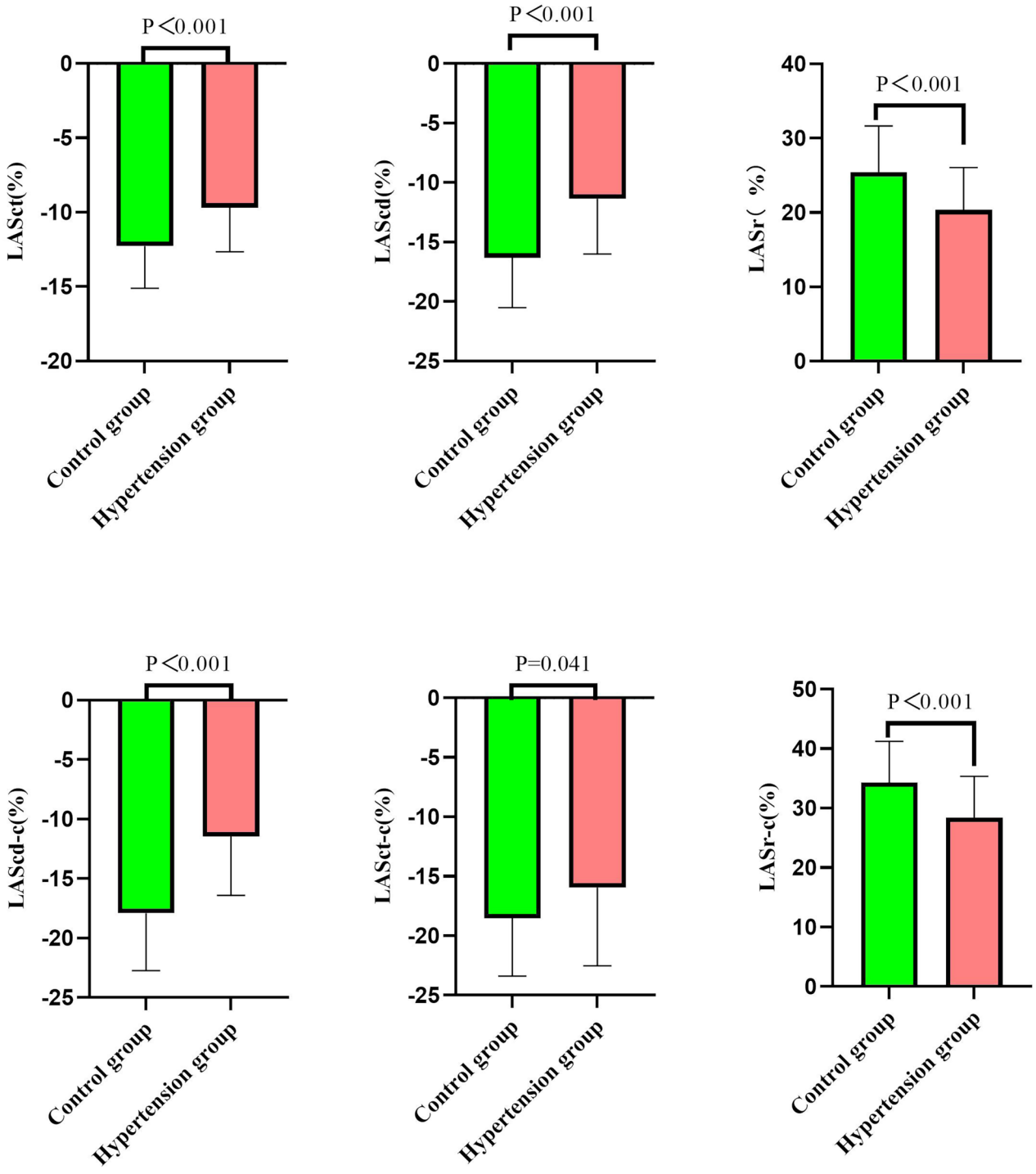


Fig. 3 Boxplots showing the comparison of left atrial strain. In comparison to the control group, the hypertension group's LA strain values were lower, and there was a statistically significant difference between the two groups. LASr, left atrial reservoir longitudinal strain, LAScd, left atrial conduit longitudinal strain; LASct, left atrial contractile longitudinal strain; LASr-c, left atrial reservoir circumferential strain; LAScd-c, left atrial conduit circumferential strain; LASct-c, left atrial contraction circumferential strain

Table 3 Intra- and Inter-observer variability of the four-dimensional automated left atrial quantification

Variables	Intra-observer		Inter-observer	
	ICC	95% CIs	ICC	95% CIs
LAVmin	0.881	0.595–0.969	0.903	0.658–0.975
LAVmax	0.966	0.869–0.991	0.962	0.856–0.990
LAVpreA	0.986	0.946–0.997	0.934	0.760–0.983
LAVImax	0.908	0.674–0.996	0.876	0.579–0.968
LAEF	0.926	0.731–0.981	0.892	0.626–0.972
LASr	0.977	0.909–0.994	0.928	0.738–0.982
LAScd	0.964	0.862–0.991	0.871	0.566–0.966
LASct	0.941	0.781–0.985	0.881	0.594–0.969
LASr-c	0.97	0.884–0.992	0.958	0.841–0.989
LAScd-c	0.955	0.831–0.989	0.922	0.719–0.980
LASct-c	0.988	0.954–0.997	0.921	0.716–0.980

LAVmin, left atrial minimum volume; LAVmax, left atrial maximum volume; LAVImin, left atrial minimum volume index; LAVImax, left atrial maximum volume index; LAVpreA, left atrial pre-atrial volume; LAEF, left atrial ejective fraction; LASr, left atrial reservoir longitudinal strain, LAScd, left atrial conduit longitudinal strain; LASct, left atrial contractile longitudinal strain; LASr-c, left atrial reservoir circumferential strain; LAScd-c, left atrial conduit circumferential strain; LASct-c, left atrial contraction circumferential strain; ICC, intra-class correlation coefficient; CIs, confidence intervals

Table 4 Intra- and Inter-observer variability of the two-dimensional echocardiography

Variables	Intra-observer		Inter-observer	
	ICC	95% CIs	ICC	95% CIs
LAD	0.842	0.436–0.952	0.863	0.528–0.958
IVSD	0.858	0.448–0.970	0.902	0.557–0.984
LVPWD	0.89	0.450–0.978	0.896	0.551–0.981
LVEDD	0.933	0.705–0.986	0.916	0.619–0.986
LVESD	0.921	0.657–0.984	0.872	0.543–0.964
LVEF	0.939	0.730–0.988	0.838	0.458–0.912
E/A	0.961	0.821–0.992	0.942	0.816–0.993
Average E/e'	0.921	0.658–0.984	0.912	0.572–0.973
LAVI	0.835	0.381–0.965	0.861	0.512–0.953

ICC, intra-class correlation coefficient; CIs, confidence intervals. LAD, left atrial diameter; IVSD, inter ventricular septal diameter; LVPWD, left ventricular posterior wall diameter; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; E/A, the ratio of early peak diastolic velocity to late peak diastolic velocity of mitral valve orifice; Average E/e', the ratio of E to average e'; LAVI, left atrial volume index

negatively correlated with LA longitudinal strain parameters. The observed associations between the above variables and LA longitudinal strain might be explained by the following mechanisms.

As the BMI increased, the LA longitudinal strain decreased significantly. The majority of hypertensive patients in this study were overweight or obese, and previous studies have shown that elevated BMI is independently associated with LV diastolic dysfunction and LA dysfunction [33, 34]. This association may be due to haemodynamic alterations and oxidative stress adversely affecting LA structure and function [35, 36]. TG is a predictor of cardiovascular disease risk in humans, and its impact on vascular damage is associated with the cholesterol carried by triglyceride-rich lipoproteins. These lipoproteins transport large amounts of triglycerides and cholesterol in the blood. When these lipoproteins are oxidized or degraded, high concentrations of cholesterol are retained within the subendothelial extracellular matrix [37, 38]. This process leads to vascular inflammation and myocardial ischaemia, subsequently leading to LV diastolic dysfunction and increased LA pressure. In parallel, elevated UA levels trigger cardiomyocyte apoptosis and fibrosis by releasing proinflammatory mediators, leading to a marked decrease in LA compliance. Chronic inflammation drives fibroblast proliferation, resulting in excessive collagen fibre deposition within the myocardial tissue, thereby impairing atrial contractile coordination. Furthermore, UA-induced endothelial dysfunction elevates systemic vascular resistance, subsequently increasing the LA pressure load and progressively diminishing the atrium's capacity for blood storage and transmission [39, 40]. These interrelated mechanisms may lead to the correlation of the above biomarkers with LA strain, even without significant structural abnormalities detectable by conventional 2DE.

In addition, a previous study has shown a significant association of beta-blocker use with impaired reservoir, conduit, and booster pump LA function compared with other antihypertensive agents [41]. In contrast, another study has shown that angiotensin-converting enzyme inhibitors produce significant benefits in terms of reversing remodelling of the LA [42]. These findings indicate that various classes of antihypertensive medications exert differential effects on LA function. Due to the varied medication regimens, this study could not evaluate drug-specific effects on LA function. Future controlled studies are warranted.

Limitations

Despite these significant findings, the current study has several limitations that must be acknowledged. First, as this was a single-centre study with a relatively small sample size, the generalizability and applicability of the results and statistical power may be limited. This limitation highlights the need for future studies with larger sample sizes and multiple centres to validate our preliminary findings and enhance their broader applicability. Second, most hypertensive patients in this study were receiving antihypertensive treatment, which can affect the cardiac structure and function through various mechanisms. Future research should control for this variable more rigorously or include hypertensive patients not on medication to better assess the impact of these drugs. This would facilitate a more precise evaluation of the independent effects of hypertension on myocardial function. Third, due to the insufficient number of hypertension grade 1 patients, subgroup analysis for the

Table 5 Correlation between clinical variables and LA strain

Univariate	**LASr**		**LAScd**		LASct	
	r (95% CIs)	***p***	**r (95% CIs)**	***p***	**r (95% CIs)**	***p***
HT duration	-0.019 (-0.243, 0.205)	0.875	-0.128 (-0.343, 0.087)	0.292	-0.046 (-0.267, 0.175)	0.705
HT grade	-0.100 (-0.317, 0.117)	0.411	-0.029 (-0.249, 0.191)	0.812	-0.109 (-0.328, 0.110)	0.370
Age	-0.050 (-0.269, 0.169)	0.681	-0.012 (-0.231, 0.207)	0.921	-0.058 (-0.277, 0.161)	0.631
BSA	-0.269 (-0.468, -0.040)	0.024$^{\#}$	-0.122 (-0.330, 0.086)	0.313	-0.208 (-0.415, 0.019)	0.083$^{\#}$
BMI	-0.325 (-0.513, -0.107)	0.006$^{\#}$	-0.171 (-0.380, 0.058)	0.156	-0.288 (-0.487, -0.059)	0.016
SBP	-0.137 (-0.356, 0.102)	0.259	-0.001 (-0.220, 0.218)	0.992	-0.112 (-0.331, 0.117)	0.354
DBP	-0.058 (-0.277, 0.161)	0.632	-0.044 (-0.263, 0.175)	0.715	-0.004 (-0.223, 0.215)	0.974
TG	-0.352 (-0.538, -0.124)	0.003$^{\#}$	-0.323(-0.514, -0.102)	0.006$^{\#}$	-0.112 (-0.331, 0.117)	0.354
HDL-C	0.149 (-0.087, 0.370)	0.218	0.235 (-0.010, 0.453)	0.050$^{\#}$	0.129 (-0.098, 0.347)	0.287
LDL-C	-0.063 (-0.282, 0.156)	0.063$^{\#}$	-0.033 (-0.252, 0.186)	0.786	-0.001 (-0.220, 0.218)	0.992
UA	-0.334 (-0.525, -0.113)	0.005$^{\#}$	-0.357 (-0.542, -0.136)	0.002$^{\#}$	-0.084 (-0.303, 0.135)	0.488
Multiple	**LASr**		**LAScd**		**LASct**	
	β (95% CIs)	***p***	**β (95% CIs)**	***p***	**β (95% CIs)**	***p***
Age	0.114 (-0.123, 0.351)	0.343	-0.032 (-0.273, 0.209)	0.795	0.010 (-0.239, 0.259)	0.938
BSA	-0.084 (-0.329, 0.161)	0.525	0.027 (-0.240, 0.294)	0.844	0.068 (-0.206, 0.342)	0.629
BMI	-0.231 (-0.480, 0.018)	0.067	0.105 (-0.146, 0.356)	0.414	-0.268 (-0.527, -0.009)	0.047*
TG	-0.294 (-0.551, -0.037)	0.041*	-0.155 (-0.441, 0.131)	0.293	0.135 (-0.161, 0.431)	0.375
HDL-C	-0.046 (-0.293, 0.201)	0.685	-0.066 (-0.294, 0.162)	0.573	-0.043 (-0.280, 0.194)	0.724
LDL-C	-0.040 (-0.287, 0.207)	0.740	0.083 (-0.158, 0.324)	0.504	-0.128 (-0.379, 0.123)	0.320
UA	-0.064 (-0.311, 0.183)	0.672	-0.325 (-0.631, -0.019)	0.04^{1*}	-0.072 (-0.390, 0.246)	0.659

HT, hypertension; BSA, body surface area; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; UA, uric acid; LASr, left atrial reservoir longitudinal strain, LAScd, left atrial conduit longitudinal strain; LASct, left atrial contraction longitudinal strain; CIs, confidence intervals; $^{\#}$, $p < 0.1$, *, $p < 0.05$

hypertension group was not conducted. Future studies will aim to include more patients with grade 1 hypertension and distributing the cases among the groups for subgroup analysis to increase the depth of the study. Fourth, the user-dependence of 4D Auto LAQ may limit its inter-institutional reproducibility. Finally, longitudinal follow-up studies to determine whether these lower LA strains in young patients with hypertension increase the risk of some clinical outcomes, such as AF, are lacking. We will continue to monitor whether hypertensive individuals with low strain are at increased risk of developing AF in subsequent research.

Conclusion

In young hypertensive patients with normal 2D-LAVI, while LAVmin, LAVImin and LAVpreA are elevated, the LAEF and LA reservoir, conduit, and contraction strain are notably reduced. The application of 4D Auto LAQ technology may highlight altered values in young hypertensive patients with normal 2D-LAVI. It is expected to be an essential technology for clinicians to assess LA dysfunction in young hypertension patients with normal LA size and offers new insights for timely diagnosis and clinical intervention.

Abbreviations

LA	Left atrial
2DE	Two-dimensional echocardiography
4D Auto LAQ	Four-dimensional auto left atrial quantification
LV	Left ventricle
LAVmin	Left atrial minimum volume
LAVmax	Left atrial maximum volume
LAVImin	Left atrial minimum volume index
LAVImax	Left atrial maximum volume index
LAVpreA	Left atrial preatrial volume
LAEF	Left atrial ejection fraction
LASr	Left atrial reservoir longitudinal strain
LAScd	Left atrial conduit longitudinal strain
LASct	Left atrial contractile longitudinal strain
LASr-c	Left atrial reservoir circumferential strain
LAScd-c	Left atrial conduit circumferential strain
LASct-c	Left atrial contraction circumferential strain

Acknowledgements

We thank the staff of the Department of Ultrasound at The Second Affiliated Hospital of Jiangxi Medical College, Nanchang University, for their support and cooperation in this study.

Author contributions

Jiwei Wang: Project Administration, Conceptualization, Methodology. Chunquan Zhang: Conceptualization, Supervision, Validation. Yulin Huang: Investigation, Data Collecting, Writing - Original Draft. Luyi Ping: Analysis and Interpretation of Data, Writing, Review. Gufeng Sun: Data Collecting. Lin Jin: Data Collecting. Xu Huang: Data Collecting. All authors have read, reviewed, revised, and approved the final manuscript.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article from the National Natural Science Foundation of China [Grant number 82160105].

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The studies involving humans were approved by the Human Ethics Committee of the Second Affiliated Hospital, Jiangxi Medical College, Nanchang University (No. IIT-O-2024-236) and conducted in compliance with Helsinki Declaration. The participants provided written informed consent to participate in this study.

Consent for publication

Not applicable.

Conflict of interest

The authors declare that they have no competing interests.

Clinical trial number

Not applicable.

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Received: 12 January 2025 / Accepted: 5 May 2025
Published online: 13 May 2025

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