Research Square

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Assessment of Left Atrial Function in Essential Hypertension Patients With Normal Left Ventricle Function by Volume-derived Values and Two-dimensional Strain

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Abstract

Background: To investigate left atrial(LA) function in essential hypertension(EHT) patients by using volume-derived values, two-dimensional strain.

Methods: 51 normal subjects and 95 EHT patients(without LVH: 50, and with LVH: 45) were enrolled for this research. LA Volume-derived index was measured in apical 4-, 2-chamber views by Simpson's method. LA strain(S-reservoir, S-conduit, S-booster pump) and strain rate (SR-reservoir, SR-conduit, SR-booster pump), representing the reservoir, conduit and booster pump functions, respectively, were measured by two-dimensional speckle tracking echocardiography(STE).

Results: Volume-derived values(contain Total LAEF, passive LAEF and active LAEF) and strain-derived values(S-reservoir, S-conduit, Sr-reservoir, Sr-conduit and Sr-booster pump) in EHT patients were significantly lower than normal subjects. Correlation test showed LA stiffness had a strong correlation with LA conduit function in EHT patients. The AUC values were higher for detection LA conduit function than LA reservoir and booster pump function in EHT patients. LA expansion index and LA stiffness also have the higher AUC with higher sensitivity and specificity values for detection the LA dysfunctions in EHT patients.

Conclusions: In this study, we concluded that LA functions were damaged in EHT patients, which could be detect by LA volume-derived values and two-dimensional strain sensitively and reproductively. LA stiffness maybe a predictor for LV remodelling in EHT patients.

Introduction

Essential hypertension (EHT) is a common risk factor for cardio-cerebrovascular disease, and its prevalence is increasing year by year. However, the pathophysiology of EHT is not completely found [1, 2]. Left atrial (LA) function plays an important role in cardiac cycle: as a reservoir during left ventricle (LV) systole, a conduit from pulmonary veins to LV during early diastole and a booster pump in late diastole[3, 4]. Earlier assessment of LA function in EHT patients is particularly crucial for its prognosis. An increasing LA size in EHT patients is a common finding in the clinical practice. LA function always evaluated by measuring LA volumes, pulmonary vein flow, and the strain of LA walls by tissue Doppler imaging (TDI) [2]. However, these approaches are limited by a number of shortcomings. Volume-derived values are limited by the irregular LA geometric[5, 6], pulmonary vein flow is limited by the image quality, and TDI is limited for its angle-dependence[7].

Speckle tracking echocardiography (STE) can detect LA function with its angle-independence and well reproducibility[8, 9]. Previous studies had proved that the technique could accurately detect LA function in hypertension, diabetes, hypertrophic cardiomyopathy, end-stage renal disease and atrial fibrillation patients[10–14].

In this research, we mainly study three functions of LA without and with left ventricle hypertrophy (LVH) in EHT patients with normal left ventricle ejection fraction (LVEF) using 2D strain and strain rate, and then compared these values with LA volume-derived values and LA stiffness. Furthermore, provide a simple and accurate technique to detect LA dysfunction in EHT patients without or with LV remodel in preserved LVEF.

Subjects And Methods

Study sample

55 normal subjects and 100 EHT patients were enrolled consecutively for the research. The inclusion criteria for EHT patients were: Meet the World Health Organization and International Society of Hypertension criteria[1]. LVEF > 50%, A LVEF > 50% was just considered that the EHT patients had a normal LV systolic function. All patients had no history of coronary heart disease, rheumatic heart disease, hyperlipidemia and diabetes mellitus. According to LV mass index, men with a LV mass index >115 g/m^2 and women with a LV mass index >95 g/m^2 were considered to have LV hypertrophy (LVH, 48 subjects). Patients without LVH were contained 52 subjects. EHT patients were then divided into two group: EHT patients without LVH and with LVH.

The normal subjects had no evidence of hypertension and any other cardiovascular diseases. All of the physical examination, electrocardiogram, and echocardiography were showed normal.

Two-dimensional Doppler echocardiography

All EHT patients and normal subjects underwent conventional 2D echocardiography (Vivid E9, GE Healthcare, Horten, Norway). The echocardiography was performed when the patient was in hospital. LA diameter (LAd), interventricular septal thickness at the end-diastolic period (IVSd) and LV posterior wall thickness at the end-diastolic period (LVPWd) were measured in the parasternal long-axis view of the LV using M-mode.

The peak early and late diastolic mitral valves velocities (E and A, respectively) were measured by pulsed-wave Doppler, and E/A was calculated. The peak early (e') and late (a') diastolic mitral annular velocities were obtained by averaging the values at the septum and lateral walls using pulsed wave TDI, and then E/e' was calculated.

LV end-diastole volume (LVEDV), LV end-systole volume (LVESV) and LVEF were measured by bi-plane Simpson's method.

The maximum LA volume (LAVmax), the precontraction LA volume (LAVpre) and the minimum LA volume (LAVmin) were measured in the 2D echocardiography images using Simpson's method in the apical 4- and 2- chamber views, then total LA stroke volume (LASV), passive LASV, active LASV, total LA ejection fraction (LAEF), passive LAEF, active LAEF and LA expansion index were calculated by using

methods in the following: Total LASV= LAVmax – LAVmin, Passive LASV= LAVmax – LAVpre, Active LASV= LAVpre – LAVmin, Total LAEF= LASV / LAVmax * 100, Passive LAEF= LASV / LAVmax * 100, Active LAEF= Active LASV / LAVpre * 100, LA expansion index= Total LASV / LAVmin * 100[11, 15, 16].

ECG leads were connected to all EHT patients and normal subjects. The standard high frame rate (>36 /s) of the apical 3-, 4- and 2-chamber views (all contained LA) of three consecutive cycles were stored for off-line analysis.

Data analysis for LA function

The apical 4-, 3- and 2-chamber views were analysed using the EchoPAC software (2D-Strain, EchoPAC PC version 203, GE Healthcare, Horten, Norway). Used the buttons LAX, A4C, and A2C to sketch the endomyocardial of LA, respectively. The software will automatically create a region of interest (ROI) that matched LA walls. Once the ROI was approved, the software divided LA walls into six segments. However, in the apical 3- chamber view, we included only the posterior wall of LA because the opposing wall included the ascending aorta [11]. LA strain (S-reservoir, S-conduit and S-booster pump) and strain rate (Sr-reservoir, Sr-conduit and Sr-booster pump) in the apical 4-, 3- and 2-chamber views were measured (Figure 1).

The ratio of E/e' to LA peak strain (S-reservoir) was used to estimate LA stiffness[14].

Reproducibility and repeatability

Intraobserver and interobserver variability for LA reservoir, conduit and booster pump strain and strain rate were determined by repeating measurements in random selected 30 patients among all enrolled patients. For the second intraobserver measurements, the observer was "blinded" to results of the initial measurements.

Statistical analysis

All data analyses were performed using SPSS 21.0 software (SPSS, Chicago, IL, USA). Shapiro-Wilk's test or Kolmogorov-Smirnov's test was used to detect the normality of all values. Differences between the EHT patients and normal subjects were compared with an independent Student's t-test for the data distribution was normal. For variables with a non-normal distribution, the nonparametric Mann-Whitney test was used. Differences among the EHT patients without LVH, with LVH and normal subjects about LA volume-derived values, two-dimensional strain and strain rate were compared with one-way analysis of variance (ANOVA). Comparisons of two samples were using the Student-Newman-Keuls (SNK) test. Correlations between variables were tested using Pearson or Spearman correlation tests as appropriate. The values for LA volume-derived values, LA strain, strain rate and LA stiffness of EHT patients were determined from receiver operating characteristic (ROC) curve analysis. Yoden's index was used to determine the cut-off point with the best composite of specificity and sensitivity. Data were presented as the mean ± standard deviation (SD). Difference was considered statistically significant in all tests when the P-value was <0.05.

Results

155 patients satisfied the baseline inclusion criteria. 9 patients were excluded from strain and LA volume analysis because of inadequate image quality (n = 5), tachycardia (n = 2) and irregular heartbeat (n = 2). A total of 146 patients (mean age, 51.55 ± 15.19 years, 82 men) were therefore evaluated in the study and were initially divided into two groups, normal controls (n = 51, mean age, 49.45 ± 17.56 years, 27 men) and EHT patients (n = 95, mean age, 52.68 ± 13.71 years, 55 men). EHT patients were then further subdivided into two groups, EHT without LVH (n = 50, mean age, 51.04 ± 14.50 years, 30 men) and EHT with LVH (n = 45, mean age, 54.51 ± 12.69 years, 25 men) (Table 1).

Table 1
Clinical characteristics of normal controls and EHT patients in the study groups

Variable	Normal controls (51)	Total EHT patients (95)	EHT without LVH (50)	EHT with LVH (45)
Age (y)	49.45 ± 17.56	52.68 ± 13.71	51.04 ± 14.50	54.51 ± 12.69
Male (%)	27(53)	55(58)	30(60)	25(56)
BSA (m^2)	1.61 ± 0.17	1.79 ± 0.32*	1.84 ± 0.28*	1.73 ± 0.35*^
HR (bpm)	71.65 ± 10.19	74.42 ± 11.63	74.72 ± 11.76	74.09 ± 11.60
SBP (mmHg)	117 ± 10	158 ± 14*	152 ± 10*	165 ± 14*#^
DBP (mmHg)	73 ± 8	99 ± 10*	98 ± 9*	100 ± 11*#^
NYHA Class				
I (%)	51(100)	95(100)	50(52)	45(48)
II (%)	0(0)	0(0)	0(0)	0(0)
III (%)	0(0)	0(0)	0(0)	0(0)
IV (%)	0(0)	0(0)	0(0)	0(0)
Medications				
ACEIs or ARBs (%)	0(0)	67(71)	32(48)	35(52)
Calcium antagonists (%)	0(0)	55(58)	25(45)	30(55)
β-blockers (%)	0(0)	18(19)	8(44)	10(46)
Diuretics (%)	0(0)	82(86)	40(49)	42(51)
EHT: essential hypertension, LVH: left ventricle hypertrophy, BSA: body surface area, HR: Heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure.				
*Significantly different ($p < 0.05$) when EHT patients compared with the normal controls.				
# Significantly different ($p < 0.05$) when EHT with LVH compared with EHT without LVH.				
^ Significantly different ($p < 0.05$) among Normal controls, EHT without LVH and EHT with LVH.				

Basic information in EHT patients and normal subjects (Table 1 and Table 2)

There were significant differences between EHT patients and normal subjects in BSA, SBP, SDP, LAD, IVSd, LVPWd, LVM, LVMI, A, E/A, e', E/e' and S/D ($p < 0.05$). However, there were no significant differences in LVEDV, LVESV, LVEF, E, a', S, D and Ar ($p > 0.05$).

Table 2
Conventional echocardiographic parameters in normal controls compared with all patients with EHT

Variable	Normal controls (51)	Total EHT patients (95)	EHT without LVH (50)	EHT with LVH (45)
LAd (mm)	34.10 ± 3.26	39.29 ± 4.79*	37.84 ± 4.44*	40.91 ± 4.69*#^
IVSd (mm)	9.08 ± 0.96	10.93 ± 1.33*	10.16 ± 0.79*	11.78 ± 1.30*#^
LVPWd (mm)	9.04 ± 1.01	10.67 ± 1.26*	9.86 ± 0.78*	11.58 ± 1.01*#^
LVM (g)	150.03 ± 40.67	191.64 ± 46.62*	170.07 ± 35.68*	215.61 ± 45.93*#^
LVMI(g/m^2)	92.85 ± 20.97	107.35 ± 21.99*	91.71 ± 14.45	124.73 ± 14.63*#^
LVEDV (mL)	78.10 ± 15.57	81.56 ± 17.75	79.84 ± 17.41	83.47 ± 18.13
LVESV (ml)	27.75 ± 8.54	30.02 ± 9.55	29.26 ± 9.57	30.87 ± 9.55
LVEF (%)	64.98 ± 5.60	63.62 ± 5.75	63.97 ± 5.83	63.24 ± 5.68
E(m/s)	0.82 ± 0.14	0.78 ± 0.18	0.80 ± 0.17	0.75 ± 0.18
A(m/s)	0.65 ± 0.18	0.83 ± 0.21*	0.81 ± 0.23*	0.85 ± 0.18*^
E/A	1.33 ± 0.36	0.99 ± 0.31*	1.06 ± 0.33*	0.92 ± 0.27*#^
e'-avg(cm/s)	0.11 ± 0.03	0.08 ± 0.03*	0.09 ± 0.03*	0.07 ± 0.02*#^
a'-avg(cm/s)	0.10 ± 0.02	0.10 ± 0.02	0.10 ± 0.02	0.10 ± 0.02
E/e'-avg	8.09 ± 2.48	10.47 ± 3.58*	9.89 ± 3.47*	11.11 ± 3.64*^
S(m/s)	0.57 ± 0.11	0.59 ± 0.14	0.60 ± 0.13	0.58 ± 0.15
D(m/s)	0.48 ± 0.11	0.45 ± 0.11	0.46 ± 0.10	0.44 ± 0.12
Ar(m/s)	0.33 ± 0.06	0.34 ± 0.07	0.35 ± 0.08	0.34 ± 0.05
S/D	1.22 ± 0.30	1.36 ± 0.36*	1.34 ± 0.36	1.37 ± 0.37
MR grade				
Absence/slight (%)	51(100)	91(96)	50(55)	41(45)
Mild (%)	0(0)	4(4)	0(0)	4(100)
Moderate (%)	0(0)	0(0)	0(0)	0(0)
Severe (%)	0(0)	0(0)	0(0)	0(0)

Variable	Normal controls (51)	Total EHT patients (95)	EHT without LVH (50)	EHT with LVH (45)
LAd: left atrial diameter, IVSd: interventricular septal thickness in end-diastolic period, LVPWd: left ventricular posterior wall thickness in end-diastolic period, LVM: left ventricle mass, LVMI: left ventricle mass index, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume, LVEF: left ventricular ejection fraction, E: the peak velocity during early diastole of anterior mitral leftlet, A: the peak velocity during late diastole of anterior mitral leftlet, e': peak early diastolic annular velocities obtained at septal positions, a': peak late diastolic annular velocities at septal positions, S: peak inflow velocity during ventricular systole at the right upper pulmonary vein, D: peak inflow velocity during the early phase of ventricular diastole at the right upper pulmonary vein, Ar: peak reversed atrial wave velocity during LA contraction at the right upper pulmonary vein, MR: mitral regurgitation.				
*Significantly different ($p < 0.05$) when EHT patients compared with the normal controls.				
# Significantly different ($p < 0.05$) when EHT with LVH compared with EHT without LVH.				
^ Significantly different ($p < 0.05$) among Normal controls, EHT without LVH and EHT with LVH.				

LA volume characteristics in EHT patients and normal subjects (Table 3, Fig. 2)

The values of LAVmax, LAVpre, LAVmin, total LASV and active LASV in EHT patients were significantly larger than normal subjects ($p < 0.05$). However, the values of total LAEF, passive LAEF, active LAEF and LA expansion index were significantly lower than normal subjects ($p < 0.05$). The values of passive LASV were larger than normal subjects, however, there were no significant difference between the two groups ($p > 0.05$).

Table 3
2D echocardiographic LA volume, function and LA reservoir, conduit and booster pump strain and strain rate in EHT patients and normal subjects (mean ± SD).

Variable		Normal controls (51)	Total EHT patients (95)	EHT without LVH (50)	EHT with LVH (45)
2D echocardiographic LA volume and function	LAVmax (ml)	37.78 ± 12.47	52.61 ± 13.60*	50.50 ± 13.72*	54.93 ± 13.21*^
	LAVpre (ml)	20.68 ± 7.75	33.70 ± 10.30*	31.51 ± 10.28*	36.13 ± 9.86*#^
	LAVmin (ml)	10.79 ± 5.16	18.60 ± 6.91*	17.04 ± 6.37*	20.33 ± 7.15*#^
	Total LASV (ml)	26.99 ± 8.23	34.01 ± 8.58*	33.46 ± 8.64*	34.61 ± 8.57*^
	Passive LASV (ml)	17.11 ± 6.19	18.89 ± 5.56	18.99 ± 5.44	18.79 ± 5.76
	Active LASV (ml)	9.88 ± 3.54	15.11 ± 4.95*	14.47 ± 5.22*	15.82 ± 4.58*^
	Total LAEF (%)	72.46 ± 7.52	65.20 ± 7.29*	66.77 ± 6.63*	63.44 ± 7.65*#^
	Passive LAEF (%)	45.83 ± 8.92	36.30 ± 7.58*	37.98 ± 7.06*	34.43 ± 7.77*#^
	Active LAEF (%)	49.52 ± 11.30	45.53 ± 8.30*	46.46 ± 8.43	44.51 ± 8.12*^
	LA expansion index (%)	3.13 ± 2.07	2.01 ± 0.72*	2.15 ± 0.77*	1.86 ± 0.64*^
LA reservoir, conduit and booster pump strain and strain rate	S-reservoir (%)	44.78 ± 9.48	35.15 ± 8.74*	37.59 ± 7.92*	32.45 ± 8.88*#^

LAVmax: maximum LA volume, LAVpre: precontraction LA volume, LAVmin: minimum LA volume, Total LASV: total LA stroke volume, Active LASV: active LA stroke volume, Passive LASV: passive LA stroke volume, Total LAEF: total LA ejection fraction, Active LAEF: active LA ejection fraction, Passive LAEF: passive LA ejection fraction, S-reservoir: LA strain corresponding to reservoir function, S-conduit: LA strain corresponding to conduit function, S-booster pump: LA strain corresponding to booster pump function, SR-reservoir: LA strain rate corresponding to reservoir function, SR-conduit: LA strain rate corresponding to conduit function, SR-booster pump: LA strain rate corresponding to booster pump function.

*Significantly different ($p < 0.05$) when EHT patients compared with the normal controls.

Significantly different ($p < 0.05$) when EHT with LVH compared with EHT without LVH.

^ Significantly different ($p < 0.05$) among Normal controls, EHT without LVH and EHT with LVH.

Variable		Normal controls (51)	Total EHT patients (95)	EHT without LVH (50)	EHT with LVH (45)
	S-conduit (%)	25.83 ± 7.40	17.39 ± 7.05*	19.51 ± 6.30*	15.04 ± 7.16*#^
	S-booster pump (%)	18.75 ± 5.15	17.63 ± 4.86	18.08 ± 4.64	17.12 ± 5.10
	Sr-reservoir (s^{-1})	2.01 ± 0.55	1.53 ± 0.35*	1.60 ± 0.32*	1.44 ± 0.37*^
	Sr-conduit (s^{-1})	-2.15 ± 0.62	-1.36 ± 0.56*	-1.52 ± 0.52*	-1.19 ± 0.55*#^
	Sr-booster pump (s^{-1})	-2.37 ± 0.54	-2.09 ± 0.51*	-2.20 ± 0.52	-1.97 ± 0.48*#^
	LA stiffness	0.19 ± 0.08	0.32 ± 0.16*	0.27 ± 0.11*	0.38 ± 0.20*#^
LAVmax: maximum LA volume, LAVpre: precontraction LA volume, LAVmin: minimum LA volume, Total LASV: total LA stroke volume, Active LASV: active LA stroke volume, Passive LASV: passive LA stroke volume, Total LAEF: total LA ejection fraction, Active LAEF: active LA ejection fraction, Passive LAEF: passive LA ejection fraction, S-reservoir: LA strain corresponding to reservoir function, S-conduit: LA strain corresponding to conduit function, S-booster pump: LA strain corresponding to booster pump function, SR-reservoir: LA strain rate corresponding to reservoir function, SR-conduit: LA strain rate corresponding to conduit function, SR-booster pump: LA strain rate corresponding to booster pump function.					
*Significantly different ($p < 0.05$) when EHT patients compared with the normal controls.					
# Significantly different ($p < 0.05$) when EHT with LVH compared with EHT without LVH.					
^ Significantly different ($p < 0.05$) among Normal controls, EHT without LVH and EHT with LVH.					

Subgroup analysis among EHT patients without LVH, with LVH and normal subjects. The values of LAVmax, LAVpre, LAVmin, total LASV and active LASV in EHT patients with LVH were larger than EHT patients without LVH, and larger than normal subjects. However, the values of total LAEF, passive LAEF, active LAEF and LA expansion index in EHT patients with LVH were lower than EHT patients without LVH, and lower than normal subjects. All above mentioned values had significant differences among normal controls, EHT patients without LVH and with LVH ($p < 0.05$).

LA strain, strain rate and LA stiffness in EHT patients and normal subjects (Table 3, Fig. 3)

The absolute values of S-reservoir, S-conduit, Sr-reservoir, Sr-conduit and Sr-booster pump in EHT patients were significantly lower than normal subjects ($p < 0.05$).

The values of LA stiffness in EHT patients were significantly larger than normal subjects ($p < 0.05$).

Subgroup analysis among EHT patients without LVH, with LVH and normal subjects. The absolute values of S-reservoir, S-conduit, S-booster pump, Sr-reservoir, Sr-conduit and Sr-booster pump in EHT patients with LVH were lower than EHT patients without LVH, and lower than normal subjects, however, the values of LA stiffness in EHT patients with LVH were larger than EHT patients without LVH, and larger than normal subjects. All above mentioned values exclude S-booster pump had significant differences among normal controls, EHT patients without LVH and with LVH ($p < 0.05$).

S-reservoir and Sr-reservoir versus 2D echocardiographic parameters in EHT patients (Table 4)

S-reservoir in EHT patients without LVH was negatively correlated with LAVmax index.

Sr-reservoir in EHT patients with LVH was negatively correlated with LAVmax.

Table 4
Correlations between LA reservoir strain, strain rate and 2D Doppler echocardiographic parameters in EHT patients

	NLVH(50)				LVH(45)			
	S-reservoir		SR-reservoir		S-reservoir		SR-reservoir	
	r	p	r	p	r	p	r	p
E/e'	-0.07	0.630	0.008	0.957	-0.087	0.570	-0.195	0.200
LAVmax	-0.305	**0.031**	-0.216	0.131	-0.251	0.096	-0.340	**0.022**
Total LASV	-0.208	0.146	-0.102	0.479	-0.126	0.409	-0.209	0.168
Total LAEF	0.197	0.171	0.270	0.058	0.154	0.314	-0.195	0.200
LA expansion index	-0.197	0.171	0.270	0.058	0.154	0.314	-0.195	0.200
S	-0.037	0.799	0.091	0.529	0.202	0.183	0.232	0.125
S/D	-0.093	0.519	0.010	0.947	0.144	0.346	-0.124	0.417

S-conduit and Sr-conduit versus 2D echocardiographic parameters and LA stiffness in EHT patients (Table 5, Fig. 4)

S-conduit in EHT patients without LVH was positively correlated with E, e', and negatively correlated with LA stiffness.

Sr-conduit in EHT patients without LVH was positively correlated with S/D, LA stiffness, and negatively correlated with E, e'.

S-conduit in EHT patients with LVH was positively correlated with E, e', Passive LAEF, LA Expansion Index, D, and negatively correlated with S/D, LA stiffness.

Sr-conduit in EHT patients with LVH was positively correlated with LA stiffness, and negatively correlated with e', E/e', passive LAEF, LA Expansion Index, D.

Table 5
Correlations between LA conduit strain, strain rate and 2D Doppler echocardiographic parameters in EHT patients

	NLVH(50)				LVH(45)			
	S-conduit		SR-conduit		S-conduit		SR-conduit	
	r	p	r	p	r	p	r	p
E	0.455	**0.001**	-0.419	**0.002**	0.295	**0.049**	-0.178	0.242
e'	0.403	**0.004**	-0.524	**< 0.001**	0.419	**0.004**	-0.531	**< 0.001**
E/e'	-0.055	0.705	0.176	0.222	-0.194	0.201	0.329	**0.027**
Passive LASV	-0.046	0.750	0.065	0.653	0.246	0.103	-0.184	0.227
Passive LAEF	0.215	0.133	-0.275	0.053	0.479	**0.001**	-0.442	**0.002**
LA expansion index	0.119	0.409	-0.157	0.275	0.345	**0.020**	-0.298	**0.047**
D	0.206	0.151	-0.194	0.178	0.513	**< 0.001**	-0.422	**0.004**
S/D	-0.270	0.058	0.310	**0.028**	-0.351	**0.018**	0.266	0.082
LA stiffness	-0.455	**0.001**	0.500	**< 0.001**	-0.495	**0.001**	0.603	**< 0.001**

S-booster pump and Sr-booster pump versus 2D echocardiographic parameters and LA stiffness in EHT patients (Table 6, Fig. 5)

S-booster pump in EHT patients without LVH was positively correlated with A, and negatively correlated with LA stiffness.

Sr-booster pump in EHT patients without LVH was negatively correlated with A and active LAEF.

S-booster pump in EHT patients with LVH was positively correlated with a'.

Sr-booster pump in EHT patients with LVH was positively correlated with Active LASV, LA stiffness, and negatively correlated with a'.

Table 6
Correlations between LA booster-pump strain, strain rate and 2D Doppler echocardiographic parameters in EHT patients

	NLVH(50)				LVH(45)			
	S-booster pump		SR-booster pump		S-booster pump		SR-booster pump	
	r	p	r	p	r	p	r	p
A	0.513	**< 0.001**	-0.584	**< 0.001**	0.273	0.069	-0.148	0.333
a'	0.253	0.076	-0.206	0.151	0.462	**0.001**	-0.450	**0.002**
E/e'	0.125	0.386	-0.111	0.441	0.014	0.927	0.092	0.546
Active LASV	-0.204	0.155	0.091	0.531	-0.074	0.631	0.321	**0.032**
Active LAEF	0.162	0.263	-0.281	**0.048**	0.059	0.700	-0.110	0.470
LA expansion index	0.228	0.112	-0.268	0.060	0.050	0.743	-0.176	0.249
Ar	0.124	0.389	-0.157	0.276	0.284	0.059	-0.205	0.176
S/D	0.170	0.237	-0.164	0.255	0.262	0.082	-0.199	0.190
LA stiffness	-0.289	**0.042**	0.250	0.080	-0.253	0.093	0.343	**0.021**

ROC curve analysis was presented in Table 7, Fig. 6.

ROC curve analysis was used to discriminate whether LA volume-derived values, LA strain and strain rate, LA stiffness were able to predict LA dysfunction.

Table 7
Receiver operating characteristic curve analysis for the detection LA dysfunction of EHT patients

Variable		AUC (SE)	AUC (95% CI)	Cut-off value	Sensitivity	Specificity	Youden index
LA reservoir function	Total LAEF	0.748	0.670–0.816	0.689	71.58	66.67	0.3825
	S-reservoir	0.774	0.698–0.839	40.24	73.68	70.59	0.4427
	Sr-reservoir	0.769	0.693–0.835	1.667	71.58	74.51	0.4609
LA conduit function	Passive LAEF	0.791	0.715–0.853	0.373	62.11	86.27	0.4838
	S-conduit	0.823	0.751–0.881	17.979	62.11	90.20	0.5230
	Sr-conduit	0.850	0.782–0.904	-1.414	64.21	92.16	0.5637
LA booster pump function	Active LAEF	0.593	0.509–0.674	0.583	98.95	17.65	0.1659
	S-booster pump	0.557	0.472–0.639	19.168	69.47	47.06	0.1653
	Sr-booster pump	0.667	0.580–0.739	-2.566	87.37	43.14	0.3051
LA function	LA Expansion Index	0.748	0.670–0.816	2.217	71.58	66.67	0.3825
	LA stiffness	0.797	0.722–0.859	70.232	72.63	78.43	0.5106

The areas under ROC curves (AUCs) were measured to determine the cut-off values, sensitivity, specificity, and accuracy for assessing LA dysfunction. The AUC values were higher for detection LA conduit function than LA reservoir and booster pump function in EHT patients. LA expansion index and LA stiffness also have the higher AUC values for detection the LA dysfunctions in EHT patients.

Intra- and Interobserver Variability was presented in Table 8.

30 patients were randomly selected and remeasured by two observers (experienced cardiac sonographer and cardiologist) blinded to patient clinical data and each other's results. Intra-observer variability was performed by the experienced cardiac sonographer on off-line data at different points in time. Interobserver variability was performed by the cardiologist repeating measurements from the same images. Intra- and interobserver variabilities were calculated by intraclass correlation coefficient (ICC). All

LA reservoir, conduit and booster pump strain and strain rate parameters exhibited excellent intra- and interobserver correlation, with ICC values > 0.92.

Table 8
ICCs for intra- and interobserver variability for LA reservoir, conduit and booster pump strain and strain rate

Variable	Interobserver variability		Intraobserver variability	
	ICC	95% CI	ICC	95% CI
S-reservoir	0.973	0.945–0.987	0.959	0.916–0.980
S-conduit	0.982	0.963–0.991	0.982	0.963–0.992
S-booster pump	0.976	0.950–0.989	0.975	0.948–0.998
Sr-reservoir	0.925	0.848–0.963	0.952	0.902–0.977
Sr-conduit	0.971	0.940–0.986	0.975	0.949–0.988
Sr-booster pump	0.967	0.933–0.984	0.982	0.963–0.992

Discussion

The main findings of the study were that EHT patients without LVH and with LVH showed the decreased LA reservoir, conduit and booster pump functions and increased LA stiffness when compared to normal subjects. What's more, we found that LA conduit function was strongly correlated with LA stiffness.

Previous studies had demonstrated that hypertension leads to LA enlargement and physic dysfunction. Demir M, et al [17] had compared LA function between dipper and nondipper hypertension patients, and demonstrated that patients with nondipper hypertension had decreased LA global strain and increased LA stiffness. LA stiffness and strain can be used for the assessment of LA function in patients with nondipper hypertension. Miyoshi H, et al [18] had demonstrated that in EHT patients, an elevation in systolic blood pressure (SBP) leads to increased LA stiffness during ventricular systole and LV diastolic stiffness, in association with continued and further advanced LV diastolic dysfunction. Liu Y, et al [19] had evaluated the LA physic function of hypertensive patients with or without coexisting diabetes by using STE, and found abnormal LA reservoir and conduit functions. They concluded that STE-derived strain and strain rate imaging were sensitive methods for evaluating LA function. Xu TY, et al [20]had investigated LA function in relation to hypertension using STE in patients with preserved LVEF, and found that hypertension was associated with impaired LA function, as assessed by STE, even before LA enlargement or after LV remodel. Jarasunas J, et al [21] had found that patients with paroxysmal AF and primary arterial hypertension have decreased reservoir, conduit and pump LA functions even in the absence of echocardiographic signs of LV diastolic dysfunction.

Our results were accordance with previous studies. Volume-derived values in EHT patients revealed impaired LA functions compared with normal subjects. Strain and strain rate showed LA reservoir,

conduit and booster pump function were damaged, and LA reservoir and conduit function were more serious in EHT patients with LVH than without LVH. LA stiffness in EHT patients with LVH was significantly larger than without LVH and normal subjects. EHT not only leads to LV myocardial hypertrophy and myocardial fibrosis, but also leads to LA myocardial fibrosis. In normal aging process, there was a decrease in conduit volumes together with an increase in active atrial emptying. These changes were probably because of a compensatory mechanism to overcome the normal age-related decrease in LV relaxation [8]. The increased LA stiffness could also rise LV end diastolic pressure and filling pressure, at last, the LA conduit function was impaired more serious. In EHT patients, the decreased reservoir, passive and booster pump function maybe a composite measure of LV diastolic function. Subgroup analysis also showed that LA volumed-derived values and LA strain and strain rate for detecting LA dysfunction were complement to each other.

Correlation test showed that LA stiffness had a strong correlation with LA conduit function both in EHT patients without LVH or LVH. ROC analysis showed the AUC values were higher for detection LA conduit function than LA reservoir and booster pump function in EHT patients. LA expansion index and LA stiffness also have the higher AUC values for detection LA dysfunctions in EHT patients. The results demonstrated that LA stiffness can assess the LA conduit dysfunction in EHT patients, also LA stiffness can reflect LV remodelling with preserved LVEF in EHT patients without LVH or LVH.

Conclusions

In this study, increased LA stiffness, combined LA volume-derived values, strain and strain rate may conclude that LA reservoir, conduit and booster pump function were impaired in EHT patients without LVH and with LVH. 2D strain is a sensitive and reproductive tool for detecting the impairment of LA dysfunction. LA stiffness maybe a predictor for LV remodelling in EHT patients without LVH and with LVH.

Declarations

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Authors' Contributions:

Huang J and Ni CF designed the study and carried out the study, data collection and analysis, Huang J wrote the manuscript and Ni CF revised the manuscript. Yan ZN and Fan L designed part of the experiments, and collected the EHT patients and normal controls. Yang C performed the statistical analysis.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the ethics committee of Changzhou No.2 People's Hospital and the First Affiliated Hospital of Soochow University.

Consent for publication

All participants provided their written, informed consent.

Competing interests

The authors declare that they have no competing interests.

Conflicts of Interest

There are no conflicts of interest to disclose.

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Figures

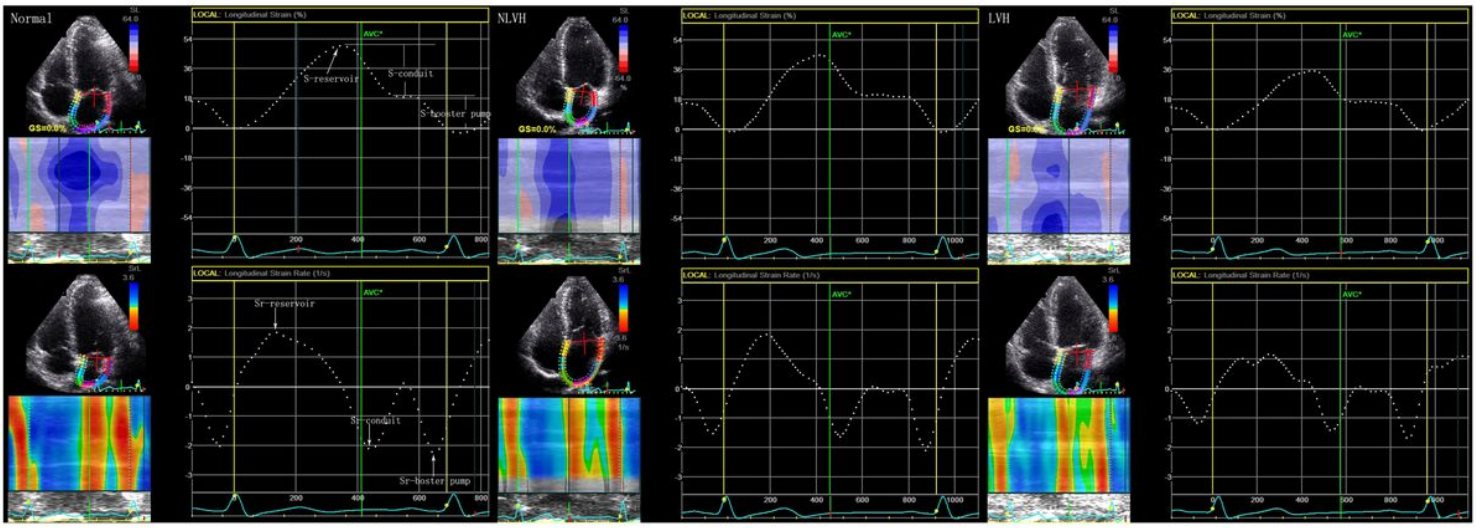

Figure 1

LA functions in apical 4-chamber views in normal subjects and EHT patients (without LVH and with LVH) by using EchoPAC. S-reservoir, S-conduit and S-booster pump, as well as SR-reservoir, SR-conduit and SR-booster pump, corresponded to the LA reservoir, conduit and booster pump functions, respectively. The strain and strain rate index decreased in EHT patients.

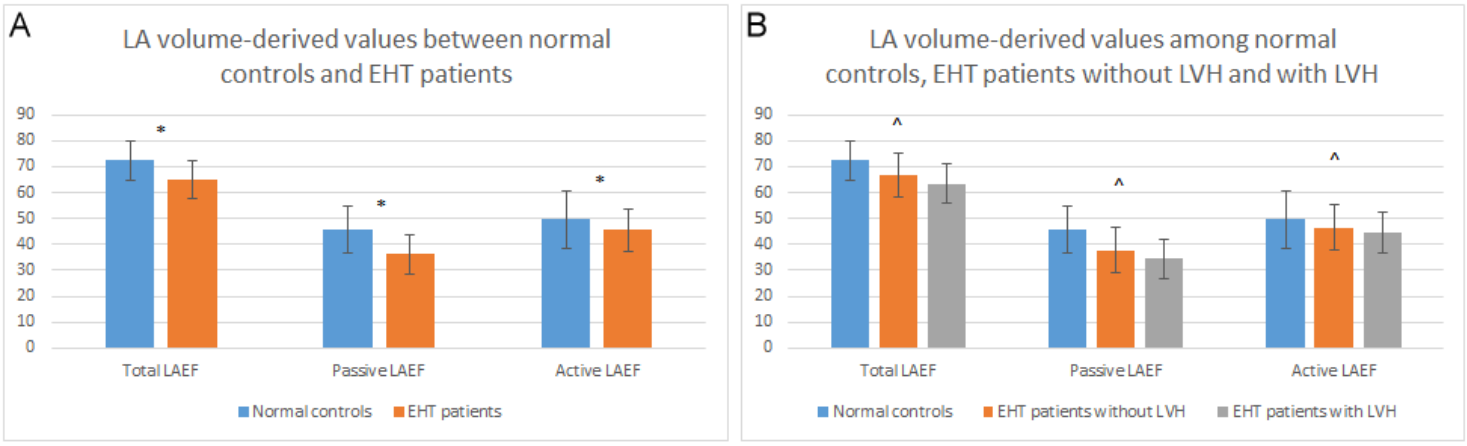

Figure 2

A: LA volume-derived values (Total LAEF, passive LAEF and active LAEF) between normal controls and EHT patients (* means $p < 0.05$). B: LA volume-derived values (Total LAEF, passive LAEF and active LAEF) among normal controls, EHT patients without LVH and with LVH (^ means $P < 0.05$).

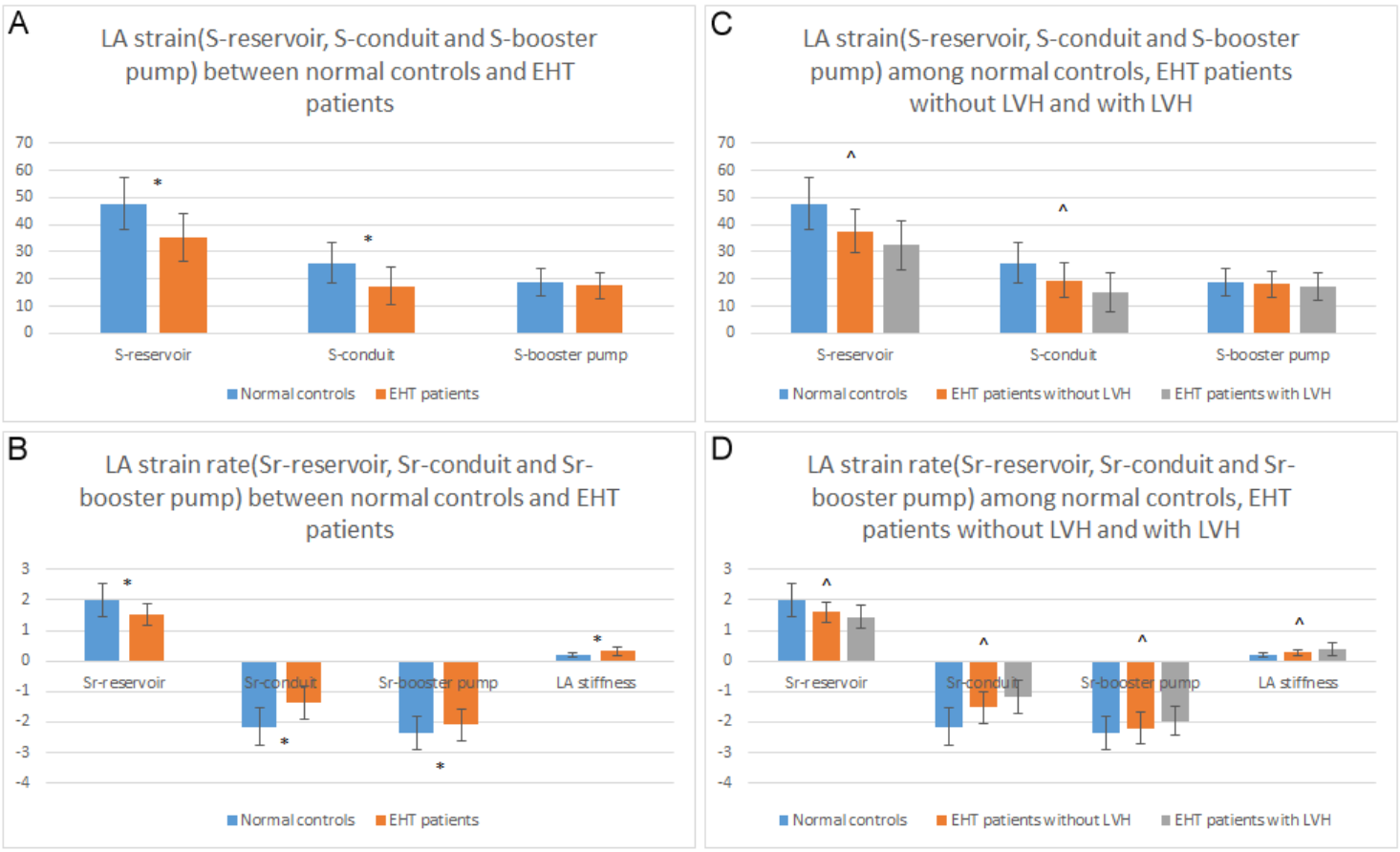

Figure 3

LA strain (A) and strain rate (B) between normal controls and EHT patients (* means $p < 0.05$). LA strain (C) and strain rate (D) among normal controls, EHT patients without LVH and with LVH (^ means $p < 0.05$).

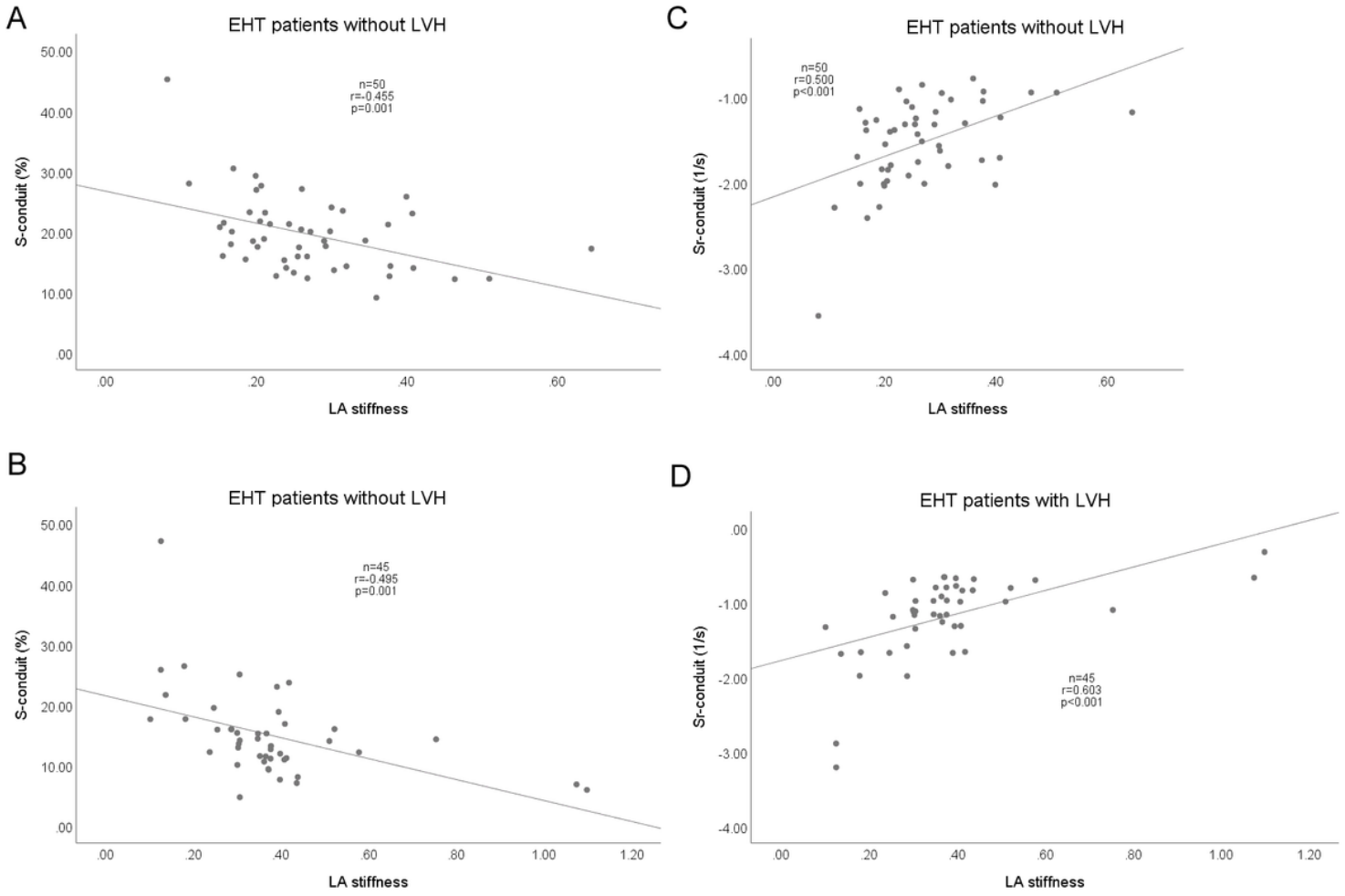

Figure 4

Correlation tests showed S-conduit in EHT patients without LVH (A) and with LVH (B) were negatively correlated with LA stiffness. Correlation tests showed Sr-conduit in EHT patients without LVH (C) and with LVH (D) were positively correlated with LA stiffness.

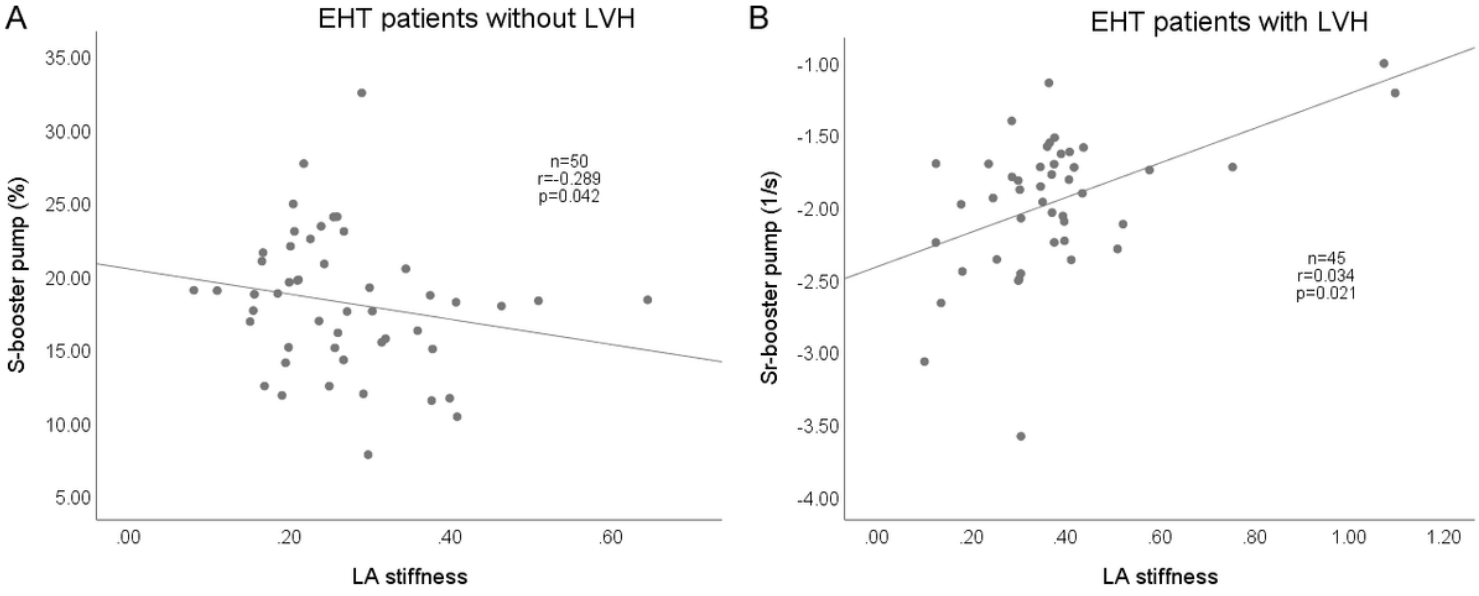

Figure 5

A: Correlation test showed S-booster pump in EHT patients without LVH was negatively correlated with LA stiffness, B: Correlation test showed Sr-booster pump in EHT patients with LVH was positively correlated with LA stiffness.

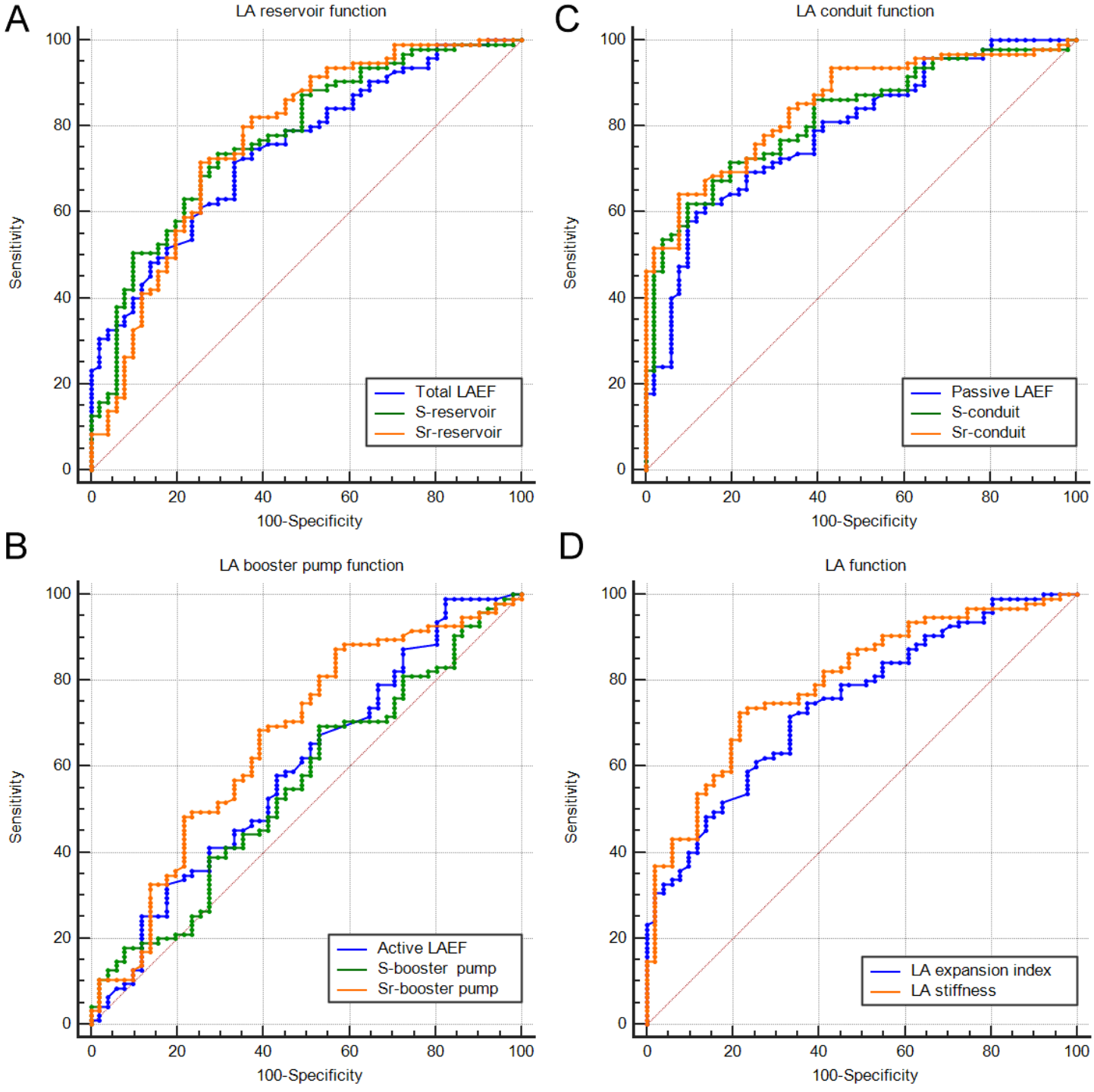

Figure 6

ROC analysis showed the AUC for detection LA reservoir, conduit, booster pump functions (A, B, C) and LA dysfunction (D).