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ORIGINAL

EVALUATION OF LEFT VENTRICULAR FUNCTION IN HYPERTENSIVE ATHLETIC PATIENTS WITH DIFFERENT CIRCADIAN RHYTHMS USING STRATIFIED STRAIN TECHNIQUE

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ABSTRACT

Purpose: With the stratified strain approach, the changes in the longitudinal mechanical condition of the left ventricular myocardium in hypertensive athletic patients with a normal left ventricular ejection fraction (LVEF) have been evaluated. Materials and Methods: Based on circadian rhythm, 48 dippers and 53 non-dippers are selected among 103 hypertension athletic patients with normal LVEF (LVEF > 50%). The stratified strain approach is used to measure the longitudinal strain (GLS) of the subendocardial, middle, and epicardial myocardium during left ventricular systole. The relationship between the stratified strain and the circadian rhythm in hypertensive individuals has been analysed. Results: show that the levels of IVST, LVPWT, and LVMI in the non-dipper group are considerably higher than those in the dipper group, while there is not statistically significant between the two groups in terms of LVDd, LVDs, LA, or EF. Myocardial strain analysis reveals that the left ventricular long axis strain (GLS) in the non-dipper group is considerably greater than that in the dipper group, And the difference is statistically significant ($P< 0.05$). But the GLSendo between the non-dipper group and the dipper group did not vary significantly ($P<0.05$). In GLSMid, GLSepi, there is no significant difference, and the difference is not statistically significant($P>0.05$). Conclusion： Ultrasonic stratified strain technique can quantitatively measure and analyze the longitudinal stratified strain of the myocardium in each segment of the left ventricle in hypertensive athletic patients and evaluate their early left ventricular mechanics changes, providing a better diagnostic method for early clinical determination of myocardial involvement in athletic patients.

KEYWORDS: Echocardiography, Hypertension, Stratified strain technique, Circadian rhythm

1. INTRODUCTION

Essential hypertension (EH), one of the most frequent chronic disorders in the world, is the primary cause of myocardial infarction, stroke, renal disease, congestive heart failure, and other ailments. Hypertension, with a high risk of disability and mortality, is the "silent killer" of cardiovascular and cerebrovascular disorders， increasing the strain and stress on society, medical resources, and families.

Normal blood pressure has regular features of falling blood pressure at night and rising blood pressure during the day. Typically, the maximum value is around 9:00-11:00 and 15:00-18:00 in the day, while the lowest value is at 2:00-3:00. When waking up, the human body's blood pressure progressively rises, resulting in "double peaks and one valley" or "double peaks and double valleys."

The dipper rhythm refers to the circadian rhythm of blood pressure. The blood pressure circadian rhythm is initially classified as dipper type (nocturnal blood pressure decline rate ≥10%) and non-dipper type (<10%), and then further classified as dipper type (10%~20%), non-dipper type (0%~10%), anti-dipper type (<0), and super dipper type (> 20%).

According to the study, the improper function of target organs is directly related to the imbalance of blood pressure regulation in athletic patients, and the effects of different types of circadian rhythm on heart disease are radically different. Furthermore, there is no evident clinical expression of subclinical heart disease in hypertensive individuals, standard detection procedures are difficult to detect possible myocardial injury.

Hence, this research delves into the relationship between several forms of blood pressure circadian rhythm and cardiac function impairment, as well as the early detection of subclinical cardiac damage in athletic patients, which is critical for guiding clinical timely intervention(Unger et al., 2020). Speckle tracking imaging (STI) has received increasing attention in myocardial strain characterization and quantitative evaluation of cardiac function.

The most recent ultrasonic stratified strain approach may extract strain parameters of cardiac tissue at all levels by speckle tracking the motion trajectories of subepicardial myocardium, middle myocardium, and subendocardial myocardium. Myocardial contractile function can theoretically be assessed more precisely and quantitatively. The ultrasonic stratified strain technique is utilized in this work to examine the relationship between left ventricular longitudinal delamination strain and circadian rhythm in athletic patients in order to uncover probable subclinical myocardial contractile function loss in this condition(Domenech, Berruezo, Molina, Mont, & Coca, 2013).

2. Materials and Methods

A total of 103 athletic patients from January 2020 to December 2021 with hypertension and normal left ventricular ejection fraction (LVEF) without intervention in Shunde Hospital of Southern Medical University are selected. There are 55 males and 48 females, aged from 30 to 70 years, with an average age of 51.6 ±7.2years(Chowdhury et al., 2018).

2.1 Inclusion Criteria

1) All athletic patients signed informed consent and know it and are able to cooperate independently. 2) Meet the diagnostic criteria of hypertension: systolic blood pressure ≥ 140mmHg and diastolic blood pressure ≥ 90mmHg. 3) The athletic patients who participated in this study are initially diagnosed with hypertension, but did not undergo clinical intervention.

2.2 Exclusion Criteria

1) Acute hypertension. 2) Secondary hypertension. 3) Acute infectious disease. 4) Accompanied by multi-functional organ damage. 5) Suffering from malignant tumor. 6) Severe cardiopathy. 7)Acute myocardial infarction. 8) Severe anemia. 9) Hyperthyroidism. 10) Severe liver and kidney disease. 11) Taking antihypertensive drugs. 12) Unwilling to cooperate with athletic patients.

2.3 Grouping Standard

24-hour ambulatory blood pressure is measured by DMS non-invasive portable blood pressure monitor. In the day (6:00 to 22:00) and at night (22:01 to 05:59), athletic patients' blood pressure needs to be monitored dynamically in real time. During the testing process, the blood pressure of the patient needs to be measured every 20 minutes during the day and every half an hour at night(Boddi, 2017).

The subjects whose effective blood pressure readings are more than 70% of the times should be tested, and the blood pressure indexes of the athletic patients are obtained by the instrument. After calculation, the percentage of nocturnal blood pressure decrease is obtained, which is ≥ 10% in the dipper group and < 10% in the non-dipper group(Parati et al., 2014).

2.4 Instruments and Methods

Using Philips color Doppler ultrasound diagnostic instrument, the model is EPIQ7C, equipped with M5S probe, frequency 1~5MHz. The athletic patients at rest take the left decumbent position and connect the electrocardiogram. The two-dimensional dynamic images of left ventricular long axis section, apical four-chamber section, two-chamber section and three-chamber section are collected at 40-80 frames per second. The left atrial diameter (LAD), end-diastolic interventricular septum thickness (IVSD), left ventricular posterior wall thickness (LVPWD) and left ventricular end-diastolic diameter (LVEDD) are measured respectively(Kario et al., 2019; Perrone-Filardi et al., 2017).

Routine parameters such as LVEDD and left ventricular mass index (LVMI). LVEF is measured by biplane Simpson method. The forward mitral flow spectrum is taken, (Chen et al., 2018)and the tissue Doppler spectrum of mitral septum is obtained by TVI mode. At the same time, the early and late peak flow velocity (E, A) of mitral orifice diastole and the early diastolic velocity (e') of mitral septal tissue are measured(Ozawa et al., 2015).

2.5 Image Post-processing

Close the examination, select the patient and enter the CMQ mode, select the two-dimensional dynamic images of the apical three-chamber heart, four-chamber heart and two-chamber heart in turn, and frame at the end of systole for STI analysis(Hermida, 2016; Lopez-Sublet et al., 2019).

The software automatically tracks the myocardial intima and longitudinal strain curve as shown in Fig.1 and records the measured values of longitudinal strain (LS) of each layer of the basal, intermediate and apical segments of the left ventricle during systole. The global longitudinal strain (GLSendo) of the subendocardial myocardium, the global longitudinal strain of the middle myocardium (GLSmid) and the global longitudinal strain of the epicardium (GLSepi) are measured(Stergiou, Malakos, Zourbaki, Achimastos, & Mountokalakis, 1997).

2.6 Statistical Methods

Based on the SPSS20.0 statistical tool, the normal distribution test is carried out, and the data in accordance with the normal distribution is expressed by the average ±standard deviation, the data between groups is expressed by t-test,(Kalaycıoğlu et al., 2015) the data that does not accord with the normal distribution is represented by the interval between median and quartile, and the data between groups is tested by nonparametric test. The counting data are expressed in frequency (%), and the data between groups are tested by chi-square test(Boggia et al., 2007).

3. Results

3.1 General Clinical Data

A total of 103 athletic patients are enrolled in this study. There are 55 males and 48 females, ranging in age from 18 to 70 years old, with an average age of 51.6 ±7.2 years. According to the circadian rhythm, there are 48 cases in the dipper group and 55 cases in the non-dipper group.

There are no significant difference in the basic data between the two groups (P > 0.05), so there is comparability between the two groups. The FPG index of non-dipper group is higher, and the difference between the two groups is statistically significant (P < 0.05).

Table 3-1: Comparison of General Clinical Indicators in Each Group

TARGET		CONFIGURATION		AMOUT	T/X2 VALUES	P VALUES
		DIPPER TYPE	NON-DIPPER TYPE			
AGE		51.60±7.15	52.01±7.50		-0.286	0.776
SEXUAL DISTINCTION	Man	25	30	55	0.062	0.803
	Woman	23	25	48		
SMOKING HISTORY	Deny	23	29	52	0.237	0.626
	Correct	25	28	51		
HISTORY OF DRINKING	Deny	21	27	48	0.294	0.588
	Correct	27	28	55		
HEART RATE		71.39±5.10	71.74±4.92		-0.354	0.724
CREATININE		80(70.25~90)	86.8(69.2~95.2)		-1.157	0.247
BMI		23.14±1.99	23.34±2.07		-0.495	0.621
TG		1.54(1.02~2.10)	1.51(1.14~2.15)		-0.221	0.825
TC		5.00(3.90~5.75)	4.76(3.82~5.53)		-0.784	0.433
HDL-C		1.19(1.02~1.33)	1.09(0.98~1.41)		-0.519	0.604
LDL-C		2.71(2.14~3.06)	2.54(2.04~3.00)		-0.883	0.377
FPG		5.85(5.17~7.00)	6.58(5.50~8.00)		-2.539	0.011*

pour：：P<0.05*

3.2 Blood Pressure Variability and Circadian Rhythm

The 24-hour ambulatory blood pressure indexes of the two groups are analyzed. The results show that the 24hSBP, 24hDBP, nSBP and nDBP of athletic patients with hypertension in dipper group are lower, and the difference between the two groups is statistically significant. There is no significant difference in dSBP and dDBP between the two groups.

Table 3-2: Comparison of 24-hour ABPM between two groups of athletic patients

TARGET	CONFIGURATION		T VALUES	P VALUES
	Dipper type (n=48)	Non dipper type (n=55)		
24hSBP	135.06±9.07	140.80±9.83	-3.062	0.003*
24hDBP	75.00±6.43	78.85±5.20	-3.358	0.001*
nSBP	124.46±6.70	131.04±6.39	-5.097	<0.01**
nDBP	73.23±3.41	76.52±3.72	-4.657	<0.01**
dSBP	145.62±8.91	146.31±7.51	-0.423	0.673
dDBP	79.25±6.70	79.34±6.25	-0.075	0.941

pour：：P<0.05， **：P<0.01*

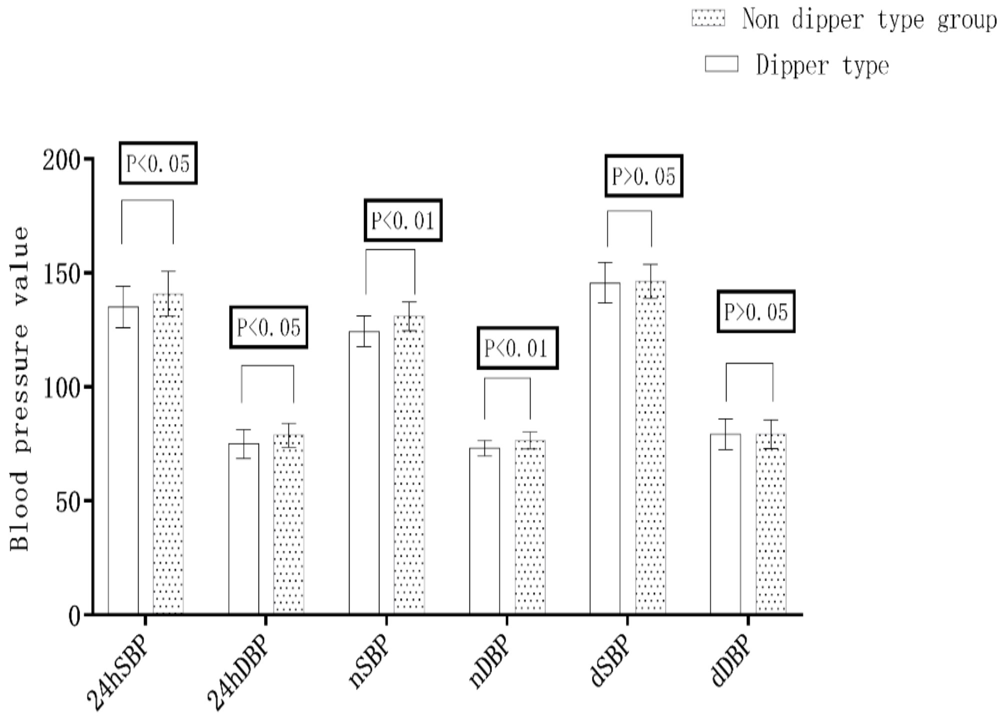


Figure 3-2: Comparison of 24-hour ABPM between the dipper group and the non dipper group

3.3 Structure and Function of Cardiac Ultrasound

According to the table 3-3, the results show that the indexes of IVST, LVPWD and LVMI in the dipper group are lower, and the difference between the two groups is statistically significant. There is no significant difference in LVIDd, LVIDs, LA and LVEF between the two groups.

The GLS of left ventricle in athletic patients with non-dipper hypertension is lower, and there is significant difference between the two groups(P＜0.05). In contrast, the differences in E /A, e', and E /e' between the two groups are not statistically significant.

Table 3-3: Comparison of cardiac structure and function

TARGET	CONFIGURATION		*T value*	*P value*
	DIPPER TYPE (n=48)	NON-DIPPER type (n=55)		
LVIDD	44.79±0.72	45.31±0.72	-0.504	0.615
LVIDS	27.52±0.41	27.49±0.37	0.054	0.957
LA	36.67±0.95	37.13±0.86	-0.360	0.720
LVEF	63.13±0.96	63.75±0.95	-0.458	0.648
IVST	10.46±1.34	11.85±1.31	-5.268	<0.01**
LVPWD	10.23±1.32	11.49±1.29	-4.873	<0.01**
LVMI	151±23.15	161±23.05	-2.075	0.041*
E/A	1.03±0.02	1.02±0.02	0.464	0.644
E'	6.1±0.21	6.18±0.2	-0.295	0.769
E/E'	11.3±0.37	12.05±0.45	-1.278	0.204
LONGITUDINAL STRAIN VALUE	17.3±2.79	16.09±2.84	2.182	0.031*

pour：：P<0.05；**：P<0.01*

3.4 Comparison of Incidence of Left Ventricular Wall Thickening Between Dipper Group and Non-dipper group

It can be seen from Table 3-4 that the left ventricular wall end-diastolic thickness ≥11mm is taken as the diagnostic criterion of LVH, and the incidence of LVH in dipper group and non-dipper group is taken as the research object, and univariate logistic regression is carried out. It can be seen from the table 3-4 that the proportion of LVH in non-dipper group is significantly higher than that in dipper group(P<0.05).

Table 3-4. Analysis of the relationship between non dipper group, dipper group, and LVH

GROUP	WITH LVH	WITHOUT LVH	X2 VALUE	P VALUE	OR	95%CI
Dipper type(n=48)	7(14.6%)	41(85.4%)	5.937	0.015*	3.347	1.267-8.845
Non dipper type(n=55)	20(36.4%)	35(63.6%)				

pour：：P<0.05*

3.5 Analysis of Delamination Strain Chart of Dipper and Non-dipper

It can be seen from table 3-5 that the order of the myocardial stratified strain parameters of dipper and non-dipper athletic patients is as endocardial layer > middle layer > outer layer of myocardium. The GLSendo of athletic patients with hypertension in non-dipper group is higher than that in dipper group, and the difference is statistically significant(P<0.05). However, there is no significant difference in GLSmid and GLSepi between non-dipper group and dipper group, as shown in figure 3-3.

Table 3-5. Comparison of myocardial layered strain values

TARGET	CONFIGURATION		T VALUE	P-VALUE
	Dipper type (n=48)	Non dipper type (n=55)		
GLSEND	21.2+3.51	19.1+3.34	3.019	0.0024*
GLSMID	17.6+4.12	16.5+4.33	1.315	0.191
GLSEPI	15.3+3.71	14.3+3.32	1.444	0.151

pour：：P<0.05。*

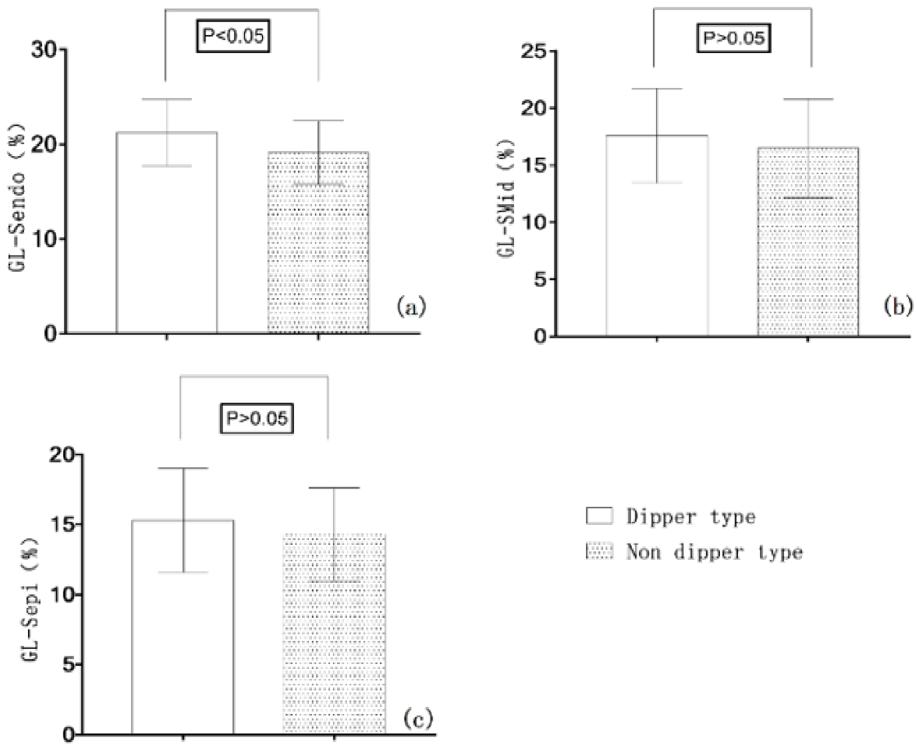


Figure 3-3. Comparison of myocardial layered strain values

4. Discussion

4.1 The Occurrence and Influence of Circadian Rhythm of Abnormal Blood Pressure

Normal blood pressure's physiological model can be characterized as "two peaks and one valley." Simply said, the average blood pressure during the day is higher than that during sleep at night, resulting in a blood pressure pattern with a long-stemmed structure. This is clinically known as dipping blood pressure. (Możdżan et al., 2013)The primary reason is that the variations in neurohumoral fluid in the body during the day are compatible with the stable expression of the internal environment, indicating a circadian rhythm(Luers & Maisch, 2011). At the same time, the circadian regularity of blood pressure is critical in safeguarding the body's vital organs such as the heart, brain, and kidneys. The decline in nocturnal blood pressure in athletic patients is less than that in normal persons, resulting in a heavy load on the heart, brain, kidney. Other critical organs are in a state of high load for a long time, and the body organ damage is more serious(Nakatani, 2011). Subclinical cardiac damage in athletic patients with early hypertension has no clear clinical symptoms, and most systolic function measures of traditional echocardiography are normal, making it difficult to adequately assess the subclinical myocardial(Kappetein et al., 2011; Yoon & Bella, 2009) function damage induced by circadian rhythm disturbances. This study found significant differences in left ventricular wall thickness and LVMI between the dipper and non-dipper groups, which is consistent with the findings of Wu Xueyi et al., who found that non-dipper EH is associated with an increased incidence of LVH that is independent of hypertension.

The causes of this phenomenon describe as: In individuals with non-dipper EH, there is no substantial change in nocturnal blood pressure relatived to daytime blood pressure because the heart is in high load for a long time due to high systolic blood pressure and no significant decline at night. The results of this study shows that the non-dipper EH group has higher values of n-SBP, n-DBP, 24h-SBP, and 24h-DBP, which demonstrates this point of view(Fagard et al., 2009; Higashi et al., 2002).

4.2 Evaluation of Myocardial Function

The typical left ventricular myocardium is composed of three layers: oblique epicardial myocardial fibers, circular middle muscle fibers, and longitudinal endocardial myocardial fibers. The earlier ultrasonic global strain technique analyzed myocardial function by considering the motion of the entire ventricle wall, but neglected the unique layered spiral structure and function of myocardium, (Tamura et al., 2007) because the effects of illnesses on different layers of myocardium are different.

The diseased status of myocardial cannot be effectively assessed by analyzing each layer of myocardium as a whole. The ultrasonic stratified strain approach can track the stable sound spots in each of the three layers of myocardial and calculate their strain levels. Theoretically, this technique can analyze the morphological and functional alterations of each layer of myocardial correctly, promptly, and statistically. Because STI is more reliable in measuring strain in the long axis direction than in the radial direction, only myocardial LS characteristics are examined in this study. Several research in recent years have confirmed the predictive utility of LS parameters acquired by two-dimensional speckle tracking imaging in many diseases.

In this study, the non-dipper group has higher IVSD, LVPWT, and LVMI than the dipper group because nocturnal blood pressure decreased in athletic patients with non-dipper hypertension, resulting in long-term vascular hypertension and ventricular wall thickening, which is consistent with previous studies. There is no statistically significant difference between the two groups in LVIDd, LVIDs, LA, or LVEF. Recent research has demonstrated that when there is only a minor change in left ventricular systolic function, LVEF cannot accurately reflect the change. As a result, traditional echocardiography has certain limitations in detecting modest changes in cardiac function in the early stages of hypertension. More sensitive approaches for evaluating early myocardial function are needed to support early clinical diagnosis and treatment.

4.3 Application of Strain Parameters in Hypertension

Current clinical research is focused on heart failure with retained ejection fraction in heart disease. The European Heart Association published an expert agreement on heart failure with normal ejection fraction in 2007. It states that athletic patients need to meet three conditions to confirm these diseases: their left ventricular ejection fraction must be within the normal range or mildly abnormal, and they must have relevant clinical indications of heart failure. The heart's diastolic function is impaired or the relaxation is inadequate.

The early manifestation of impaired body function in hypertensive athletic patients is primarily a decrease in cardiac diastolic function, and the gradual development of hypertension is accompanied by left ventricular remodeling, mainly in the form of left ventricular hypertrophy, an increase in ventricular mass index, and an improvement in ventricular mass. Left ventricular remodeling in hypertensive individuals includes not only hypertrophy of individual cardiomyocytes, but also an increase in collagen fiber tissue and intercellular matrix, which leading an increase in left ventricular myocardial stiffness.

Echocardiography's diagnostic role in heart failure can fully answer the following questions: whether the patient's left ventricular ejection fraction is abnormal, whether the structure is abnormal, and whether the abnormal cardiac structure can be explained. At the same time, relevant heart association specialists stated that individuals with suspected or confirmed heart failure should have echocardiography and evaluation of their cardiac function once a year. Suggestions are also given for subsequent patient therapy. Currently, mitral flow spectrum, pulmonary vein flow spectrum, color Doppler ultrasonography, tissue Doppler imaging, and speckle tracking technologies are the major indicators of echocardiography.

In recent years, there has been a growing interest in using two-dimensional speckle to obtain layered strain parameters in clinical diseases. The mainly reason is that this approach can detect myocardial injury earlier than LVEF or the examination of conventional measures of left ventricular function, and it has a superior accuracy in identifying ventricular systolic and diastolic function. This study also discovers that in both dipper and non-dipper athletic patients, the myocardial stratification strains all following the order: subendocardial myocardium > middle myocardium > subepicardial myocardium.

The results could be attributed to a difference in curvature rate between the endocardium, media, and epicardium, resulting in varying local tension. Maintaining the SSL gradient between all levels of myocardium is critical for maintaining appropriate cardiac contraction and rest. The findings of this study also reveals that the expression of SSI in the non-dipper group is significantly lower than that in the dipper group in the subendocardial myocardium（$P<0.05$）, while there is no difference in the expression of the above parameters in the middle and epicardium ($P >0.05$).

The above findings suggest that if the expression of ventricular systolic function in hypertensive athletic patients is within the normal range, the endocardial myocardial contractility has diminished, and the damage in the non-dipper group is more visible than in the dipper group. The reason is that coronary blood flow travels from the epicardium to the endocardium, and the endocardium is firstly to show signs of myocardial function deterioration. Second, in the early stages of hypertension, the contractile capacity of the subendocardial myocardium is reduced due to a rise in peripheral capillary pressure, which affects myocardial fibrinogen formation and thus leads to subendocardial myocardial fibrosis.

Because the subendocardial myocardium is relatively less tolerant to ischemia and hypoxia, myocardial ischemia first affects the energy supply to the subendocardial myocardium. Endocardial strain was impaired in pre-HT athletic patients, while medial and epicardial myocardium strain did not change significantly. Endocardial strain is also considered to be one of the sensitive indices for monitoring subclinical cardiac function injury in athletic patients with pre-HT. The study also researched the association between left ventricular endocardial strain and blood pressure variability. According to the findings, blood pressure variability is a major predictor of cardiovascular adverse outcomes.

There is a significant linear correlation between endocardial strain and blood pressure fluctuations, demonstrating that there is a relationship between the change of degree of blood pressure and the decrease in left ventricular endocardial response in athletic patients with pre-HT. Regardless of systolic or diastolic blood pressure, the greater the degree of change, the more noticeable decrease in left ventricular endocardial strain. Although the influence of body mass index is controlled in this study, the above association still exists. This is consistent with prior research, which indicates that stratified strain can be used to treat hypertension and accompanying early heart function impairment.

4.4 Limitations

This study can objectively evaluate the left ventricular systolic function in hypertensive athletic patients, but it has limitations: (1) Because the sample size is small, the results can only be used as a preliminary study result. (2) There is no follow-up analysis of different courses of disease in hypertensive athletic patients. (3) The picture quality of stratified strain technique is easily affected by operators and patients.

In conclusion, ultrasonic stratified imaging can quickly, accurately, and quantitatively measure the longitudinal stratified strain parameters of each segment of the left ventricle in hypertensive athletic patients, as well as objectively and accurately evaluate the early regional systolic function of the left ventricle. It gives a more accurate way for detecting myocardial involvement in hypertensive athletic patients.

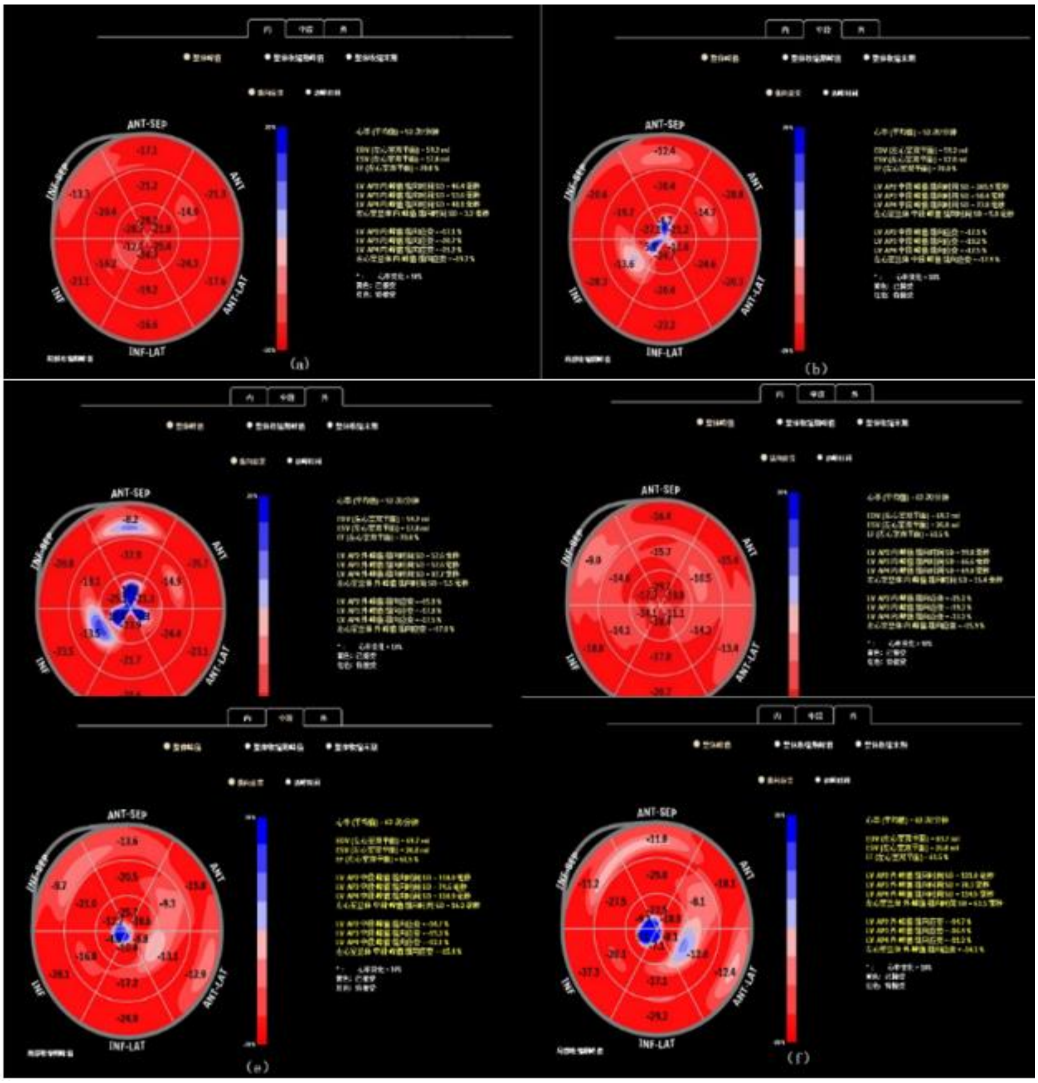
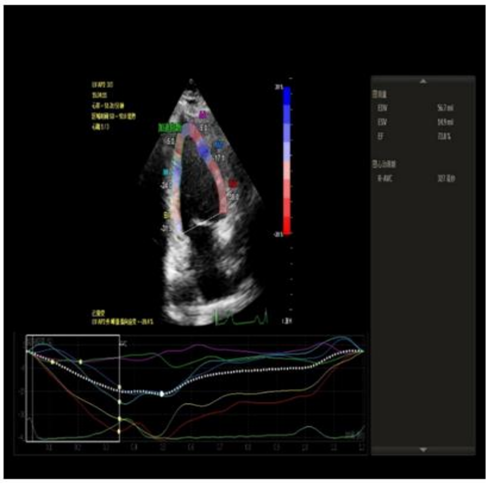
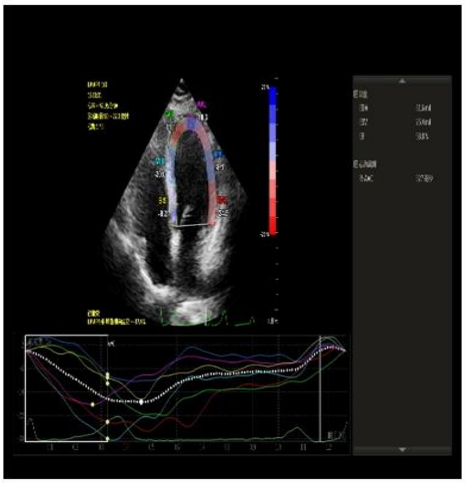
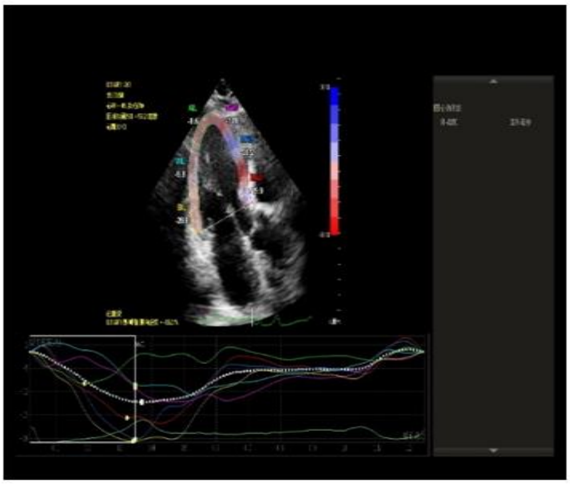


Figure 3-4







The strain parameters of each layer of myocardium in the dipper type and non dipper type groups are shown in Figures a-c, which show the strain parameters of the inner layer, middle layer, and outer layer of myocardium in the dipper type group; Figure d-f shows the strain parameters of the inner, middle, and outer layers of the non-dipper type group, respectively.

Declaration of Competing Interest

The authors declare that the research is conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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