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Early Detection of Left Atrial Dysfunction by Speckle Tracking Echocardiography in Hypertensive Patients with Normal Left Atrial Size

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ABSTRACT

Background: Arterial hypertension adversely affects LA size and function, effect on function may precede effect on size. This effect is reflected on patient's morbidity and mortality risks. Many techniques were used to assess LA function but with many pitfalls.

The objectives: early detection of left atrial dysfunction with speckle tracking echocardiography in hypertensive patients with normal left atrial size.

Patients And Methods: The study was conducted on 50 hypertensive patients and 50 age matched normotensive controls , all with normal LA size and free from any other cardiovascular disease that may affect the LA size or function. They were all subjected to history taking, clinical examination and echocardiographic study, both the conventional measures and speckle tracking then both groups were compared regarding LA strain representing LA function.

Results: Our study found that hypertensive patients had significantly reduced LA function as measured by speckle tracking when compared to normotensive controls (P-value < 0.001). Also, many factors were associated with worse LA function in hypertensive patients as old age, high BMI, DM, LV diastolic dysfunction, high LV mass index, larger LA size, lower LA expansion index and higher systolic BP.

Conclusion: Speckle tracking echocardiography is a useful novel technique in detecting LA dysfunction in hypertension even before LA enlargement occurs.

Keywords: hypertension, left atrium, speckle tracking.

INTRODUCTION

Arterial hypertension is associated with morphologic and functional left atrial (LA) abnormalities. An increase in LA size in patients with hypertension is a common finding in clinical practice, and the mechanisms underlying this enlargement have been extensively analyzed. *(1)*

Most of studies included patients regardless of LA size. This raises the question of whether LA dysfunction in patients with hypertension may be detected in the absence of LA enlargement. This question may be of clinical interest, because LA size is often used as a surrogate marker of LA function in clinical practice. *(2)*

Also, LA enlargement and dysfunction are considered risk factors for development of atrial fibrillation and cerebrovascular strokes in hypertensive patients. *(3)*

Speckle-tracking echocardiography (STE) allows direct and angle-independent analysis of myocardial deformation, thus providing sensitive and reproducible indices of myocardial fiber dysfunction that overcome most of the limitations of Doppler-derived strain measures. *(4)* The assessment of LA strain dynamics by STE in hypertensive patients may be of particular interest in those with no evidence of LA enlargement, because it may provide additional information for the early detection of LA abnormalities. *(5)*

PATIENTS AND METHODS

Study subjects: This study included 50 patients with arterial hypertension and 50 age matched non hypertensive control subjects.

Inclusion criteria for patients group:

1- Patients with ***systemic arterial hypertension*** ;defined as : Systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg **or** Antihypertensive treatment with a documented history of hypertension.

2- All patients should have an echocardiographic evidence of ***normal LA size***; defined as: LA volume index < 28 ml / m^2.

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Exclusion criteria:

Cardiac conditions that affect LA size and function

1- Documented coronary artery disease (defined as ; history of MI or revascularization , SWMA on echocardiography or any positive stress test)

2- Any type of cardiomyopathy (e.g. Dilated, ischemic, hypertrophic ….)

3- Mitral valve disease.

4-Atrial fibrillation.

5- Atrial flutter.

METHODS

The selected patients and controls were subjected to the following:

a. Thorough history taking with particular stress on:

- Age, gender, risk factors including: diabetes mellitus, hypertension, smoking, dyslipidemia and positive family history of cardiac disease.
- Full drug history (types of medications used, doses, duration).
- History of any cardiac problem (e.g. ischemic heart diseases , heart failure , arrhythmias)
- Any paracardiac problems specially (renal disease, bronchopulmonary disease, and chronic liver disease).

b. ***General and local cardiac examination:***

Including arterial blood pressure, pulse, body weight , body surface area and body mass index

c. ***Echocardiogram:***

Studies were performed using a high-quality echocardiograph (Vivid S5 or Vivid 9 ; GE Medical Systems). A standard echocardiographic study using 2D , M-mode and Doppler techniques was performed for all subjects in addition to speckle tracking for LA.

Standard assessment of left atrium :

LA volumes were calculated from apical four-chamber and two-chamber views using the biplane modified Simpson's rule. Maximal and minimal LA volumes were measured just before mitral valve opening, and at mitral valve closure, respectively. Then the LA volume index was calculated in ml/m2.

The following indices of LA function were calculated:

- Total LA stroke volume (LASV) could be obtained as the difference between maximal and minimal LA volumes.
- LA expansion index could be obtained as the ratio of total LASV to minimum LA volume × 100

Speckle tracking echocardiography:

Recordings were processed using an acoustic-tracking software (Echo Pac, GE, USA), allowing off-line semi-automated analysis of speckle-based strain. In particular, LA endocardial surface was manually traced in both four- and two-chamber views by a point and-click approach. An epicardial surface tracing was then automatically generated by the system, thus creating a region of interest (ROI).

Lastly the software generated the longitudinal strain curves for each segment and a mean curve of all segments that reflect the pathophysiology of atrial function**.**

Global peak atrial longitudinal strain was then determined which is the most robust measure of LA function (mainly the reservoir function which is the most affected LA function in hypertension***)***

LV systolic function :

Was measured in 2D apical 4-chamber and 2-chamber views using biplane method of discs (modified Simpson's rule)

LV diastolic function :

Was determined using peak E velocity, peak A velocity, E/A ratio, and the deceleration time. The early diastolic E′ velocity and late diastolic A′ velocity were estimated by Doppler tissue imaging, by placing the sample volume at the septal annulus of the mitral valve and E/E' ratio was calculated.

LV wall thickness :

LV mass (LVM, in grams) was calculated using the Penn formula :

$LVM = 1.04\ [(LVIDd + PWTd + IVSTd)3 – LVIDd] – 13.6\ g$

where LVIDd is LV end-diastolic internal diameter ; PWTd, diastolic posterior wall thickness; and IVSTd, diastolic interventricular septal thickness.

LVM was subsequently indexed to body surface area (BSA) to obtain LV mass index.

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. Qualitative data were presented as number and percentages while quantitative data were presented as mean, standard deviations and ranges.

The comparison between two groups with qualitative data were done by using ***Chi-square test*** and/or ***Fisher exact test*** was used instead of Chi-square test when the expected count in any cell was found less than 5.

The comparison between two independent group regarding quantitative data with parametric distribution were done by using ***Independent t-test.***

RESULTS

The 2 groups were compared regarding demographic data and risk factors

Comparison between hypertensive and non-hypertensive patients regarding anthropometric measures and risk factors

Both groups were matching regarding age, gender, HR, BMI and BSA (non-significant difference). DM was more common among the hypertensive group while smoking was more common among the control group.

Comparison between hypertensive and non-hypertensive subjects regarding LV measurements

All the studied subjects had normal LVEF, hypertensive group had significantly higher LV mass index and subsequently the LV diastolic dysfunction was significantly more prevalent in the hypertensive group.

Comparison between hypertensive and non hypertensive subjects regarding LA parameters

Although the LA volume index was within the normal range in all studied subjects, total LA stroke volume (which represents the contractile function of the LA) was significantly lower in hypertensive group meaning that the contractile function of LA is affected in hypertensive patients even before the LA size is enlarged, the LA expansion index (which represents the reservoir function of the LA) was significantly lower in hypertensive group meaning that the reservoir function of LA is also affected before LA enlargement occurs.

Global PALS (peak atrial longitudinal strain) was significantly lower in hypertensive group.

i.e. changes in global PALS (as an index of LA global dysfunction, specifically describing the reservoir function of LA) as well as other indices of LA dysfunction occurred even before abnormalities in LA volume occurs**.**

The LA size (LA volume index) as well as the different indices of LA dysfunction (Total LA stroke volume, LA expansion index and global PALS) were significantly lower in the hypertensive group despite the normal LV volume index in all the studied subjects.

Here we tried to find the effect of different parameters and risk factors of the studied subjects on global PALS

Correlation of global PALS to different risk factors of the studied subjects (i.e How much did these risk factors affect global PALS)

Diabetics had lower global PALS , also patients with LV diastolic dysfunction had lower global PALS

Correlation of global PALS (%) with all the studied parameters in the study subjects (i.e How did the different anthropometric measures and echocardiographic criteria affect the global PALS)

Older subjects, those with higher systolic BP and those with higher BMI had lower global PALS (all these are risk factors for LA dysfunction).

Subjects with higher LV mass index (a common complication of hypertension) had lower global PALS.

Larger LA volume index was associated with lower global PALS (although all values of LA volume index were within the normal range).

Regarding conventional indices of LA function, subjects with lower LA expansion index had lower global PALS while total LA stroke volume didn't affect global strain significantly (because global PALS mainly represents the reservoir function of LA more than its contractile function).

We thought about finding a cut off value for global PALS below which we can detect impairment of LA function (assessed by global PALS) even if the LA is of normal size in hypertensive patients. So we used the above

receiver operating characteristic (ROC) curve that showed this cut off value to be ≤ 35 % with sensitivity of 98% and specificity of 98% which means that below this value, the studied subject had LA dysfunction before LA enlargement with a sensitivity of 98% and specificity of 98%.

DISCUSSION

Arterial hypertension is one of the common diseases associated with the increased incidence of heart failure and is one of the independent risk factors for atrial fibrillation through perpetual structural and functional changes in the left atrium which is in turn responsible for increased cardiovascular mortality. Hypertension alters atrial dynamics significantly and so hypertensive patients are at risk of structural and functional changes in the LA. *(6)*

In recent years, strain rate imaging (SRI) has been shown to be an accurate method for quantifying regional myocardial function independent of cardiac rotation and tethering effect. Meanwhile, a few studies have focused on quantifying LA function in hypertensive patients. *(7)*

In this study we tried to detect early LA dysfunction in hypertensive patients and we meant by early that it's before changes in LA size represented in LA volume. We used 2D speckle tracking echocardiography for estimation of LA function. Also, we tried to find a correlation between different risk factors and parameters found in hypertensive patients and LA function (strain).

Choice of controls:

We used a control group of 50 healthy subjects whom we chose to be matching with the hypertensive group regarding their criteria ; age, gender, heart rate, BMI and BSA, this aimed at minimizing the impact of these factors on LA function while comparing it between both groups.

Many studies didn't match all these criteria between the diseased and control groups, in a study done by Mondillo S et al., both groups were age matched but not matching in BMI *(8)*.

Also Miyoshi H et al matched both groups regarding age but not regarding BMI *(9)*

In another study assessing LA function by strain rate imaging both groups were age matched but not matching in BMI .*(10)*

In 2014, Sahebjam M et al matched their candidates regarding age, HR and BSA but not regarding gender and BMI. *(11)*

Regarding LV measurements:

Both groups were matching for LVEF only, but the hypertensive group had greater LV mass index and worse LV diastolic function and this was expected as a result of hypertension.

This was in concordance with a recent Egyptian study in Cairo University carried by Hassanin N in 2015. *(12)*

Also, this was corresponding to the study carried by Miyoshi et al in which hypertensive group had greater LV mass and higher grade of LV diastolic dysfunction. *(9)*

In another study in 2014, both groups had no significant difference in LVEF but more LV mass and worse diastolic function in hypertensive group. *(13)*

Regarding LA parameters:

The keypoint in our study was to ensure that all the studied subjects had normal LA size , and the best to express this is LA volume index. This was important for early detection of LA dysfunction before LA enlargement.

This keypoint was also evident in a study by Mondillo et al in 2011 where all the subjects had normal LA size. *(8)*

Though, hypertensive group had larger LA volume compared to the control group. Furthermore, LA function measured in conventional methods named total LA stroke volume and LA expansion index was more affected in the hypertensive group.

This was similar to a study done by Eshoo S et al in 2009 in which hypertensive group had larger LA volume index than the control group. *(14)*

This was different than a study by Cameli et al in which both groups had LA volume indices with no significant difference. *(15)*

In a study by Tsai W et al in 2012 , the hypertensive group had also larger LA volume but there was no significant difference between the 2 groups regarding corresponding parameters of LA function. *(16)*

Regarding global peak atrial longitudinal strain:

In our current study, global PALS was impaired in hypertensive group compared to the control group. Global PALS represents LA function, mainly the reservoir function which is affected early in patients with arterial hypertension.

This was in concordance with the results of Mondillo S et al in 2011 where they found that hypertensive patients had early LA strain abnormalities compared to normal subjects. *(8)*

Also, a study conducted by Cameli et al showed that one of early effects of hypertension was affection of LA deformation indices expressed in longitudinal strain which indicated preclinical LA dysfunction**.** *(15)*

Furthermore, another study by Hassanin N in 2013 concluded that LA longitudinal strain representing its reservoir function was reduced in hypertensive group with highly significant P-value, i.e. < 0.001 *(12)*

In 2007, a study was conducted by Kokubu N et al to test the effect of RAS inhibition on LA function, they concluded that LA deformation indices were reduced in hypertensive patients and RAS inhibitors could preserve or improve LA reservoir function**.** *(10)*

Sahebjam M et al in 2014 concluded that hypertension significantly affected LA reservoir function (detected by LA speckle tracking) and the effect of hypertension on LA reservoir function was independent of age, sex, heart rate, LV mass index and LVEF. *(11)*

The correlation of different risk factors and studied parameters with global LA strain:

Risk factors that were found to affect LA strain adversely are DM, older age and higher BMI , this could be explained by that these factors have a negative impact on LA function.

Diabetes mellitus:

Mondillo S et al in 2011 stated that DM adversely affected LA strain and these changes were independent of LA dilatation and are more prominent in patients with hypertension and DM together. *(8)*

In 2015, Tadic et al stated the effect of type II DM on LA remodeling expressed in LA strain using speckle tracking echocardiography. *(17)*

In contrary, a study conducted by Sahebjam et al found that DM didn't affect LA strain in hypertensive patients. *(11)*

Age:

A study conducted by Okamatsu K et al concluded that aging adversely affects LA size and function (detected through LA strain). *(18)*

On the other hand, Sahebjam et al in 2014 found no correlation between age and LA strain in hypertensive patients. *(11)*

Body mass index:

A recent study in 2015 stated that overweight and obese hypertensive patients had worse LA function (measured by 2D strain) compared with hypertensive patients with normal BMI. *(17)*

Corresponding results were found by Miyoshi H et al , BMI independently affected LA strain by 2D speckle tracking echocardiography**.** *(9)*

Other parameters that were related adversely to global LA strain in the current study were systolic blood pressure, LV diastolic function, LV mass index, LA volume index and LA expansion index.

Systolic blood pressure:

In a study conducted in 2014, systolic blood pressure adversely affected LA strain in hypertensive patients. *(9)*

Also, Tadic M et al found that blood pressure variability (poor control of blood pressure) in hypertension was correlated to reduced LA strain. *(17)*

LV diastolic function:

In a study conducted by Miyoshi et al in 2014 , they found a significant correlation between LV diastolic dysfunction (E/e') and LA systolic strain. *(9)*

Tsai W et al conducted a study that showed a negative impact of LV diastolic dysfunction on LA conduit function. *(16)*

LV mass index:

In early 2015, a study by Xu Ty showed that LV mass index was significantly associated with all the LA deformation indices, i.e. higher LV mass index correlates with reduced LA function assessed by speckle tracking. *(19)*

Also, in the formerly mentioned study carried by Miyoshi H et al, LV mass index adversely affected LA strain. [9]

In contrary, Kokubu N et al found no correlation between LV mass index and LA systolic strain. [10]

LA volume index:

In a study conducted by Cameli M et al , higher LA volume index was found to be an independent predictor of reduced LA systolic strain.[15]

Similarly, Miyoshi et al found a similar correlation between LA size and LA function expressed in LA strain by 2D speckle tracking. [9]

This correlation is somewhat logic because changes in both LA size and function are the 2 arms by which systemic hypertension affects LA hemodynamics.

LA expansion index:

In a study done by Saraiva RM et al, they found that LA expansion index correlated well with global LA strain representing LA conduit function. [5]

This could be explained by that both LA expansion index and global LA strain represent LA conduit function which is affected early in hypertensive patients.

LA stroke volume:

In our study, LA stroke volume didn't correlate significantly with global peak atrial longitudinal strain which could be explained by that LA stroke volume represents LA booster pump function which is not expressed fully in the global PALS.

LV ejection fraction:

Regarding LVEF, it didn't affect LA strain significantly. A possible explanation for this is that all the studied subjects in the current study had normal LVEF and so it may be of significant impact in the reduced LVEF values.

This was corresponding to Kokubu N et al in their study that showed no correlation between LVEF and LA strain. [10]

Also, a study conducted by Mondillo S et al found LVEF not significantly affecting LA deformation indices by speckle tracking.[8]

In contrary, Dogan et al found a significant impact of LVEF on LA strain.[20]

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Tables and Figures

		No HTN	HTN	Independent t-test	
		No. = 50	No. = 50	t	p-value
ge	ean±SD	54.06 ± 8.35	56.04 ± 10.72	-1.030	0.305
ender	emale ale	25 (50.0%) 25 (50.0%)	30 (60.0%) 20 (40.0%)	0.646	0.421
		No HTN	HTN	Independent t-test	
		No. = 50	No. = 50	t	p-value
R (bpm)	ean±SD	77.24 ± 10.68	79.94 ± 10.87	-1.253	0.213
MI (Kg/m2)	ean±SD	25.20 ± 2.73	25.96 ± 3.61	-1.188	0.238
SA (m2)	ean±SD	1.76 ± 0.09	1.73 ± 0.09	1.528	0.130
		No HTN	HTN	Chi-square test	
		No. = 50	No. = 50	X^2	p-value
M	egative ositive	40 (80.0%) 10 (20.0%)	26 (52.0%) 24 (48.0%)	8.734	**0.003**
moking	egative ositive	29 (58.0%) 21 (42.0%)	42 (84.0%) 8 (16.0%)	8.208	**0.004**

Table (1): Comparison between both groups regarding anthropometric measures and risk factors

		No HTN	HTN	Independent t-test	
		No. = 50	No. = 50	t	p-value
VEF (%)	ean±SD	67.02 ± 5.90	69.50 ± 6.72	-1.961	0.053
V mass index (gm/m2)	ean±SD	77.18 ± 11.70	84.50 ± 22.71	-2.026	**0.045**

LV diastolic dysfunction	No HTN	HTN	Chi-square test	
	No. = 50	No. = 50	X^2	p-value
I	12 (24.0%)	29 (58.0%)	31.926	**0.001**
II	0 (0.0%)	10 (20.0%)		
Non	38 (76.0%)	11 (22.0%)		

Table (2): Comparison between both groups regarding LV measurements

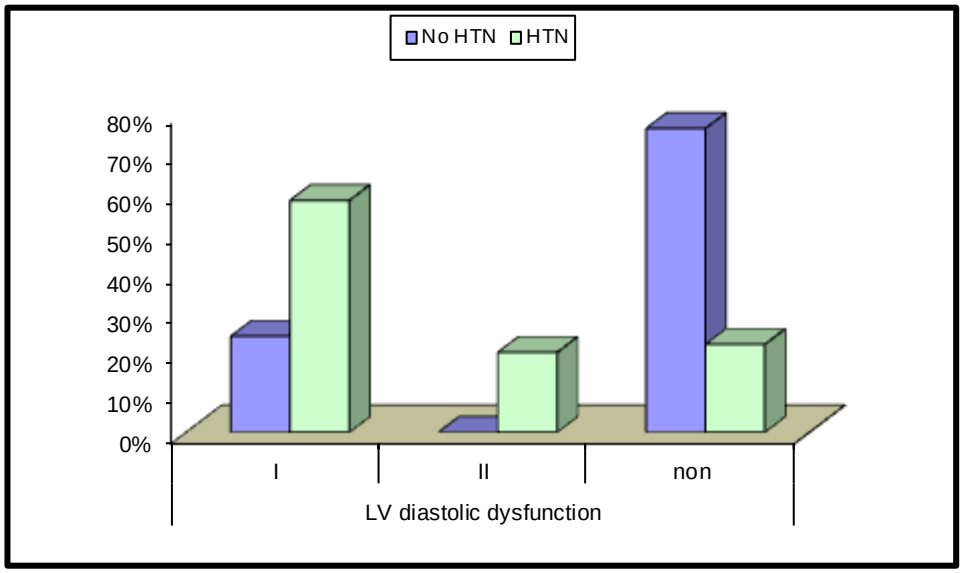

Figure (1): Comparison between both groups regarding LV diastolic function

		No HTN	HTN	Independent t-test	
		No. = 50	No. = 50	t	p-value
A volume index (ml/m2)	ean±SD	17.78 ± 2.71	20.74 ± 4.69	-3.869	**0.001**
otal LA stroke volume (ml)	ean±SD	29.30 ± 3.69	27.02 ± 5.18	2.534	**0.013**
A expansion index (%)	ean±SD	257.58 ± 19.05	223.68 ± 41.96	5.202	**0.001**
obal PALS (%)	ean±SD	41.36 ± 2.86	24.00 ± 6.92	16.399	**0.001**

Table (3): Comparison between both groups regarding LA parameters

		Global PALS (%)	Independent t-test	
		Mean ± SD	t	p-value
ender	emale ale	23.51 ± 5.25 22.47 ± 9.02	0.728	0.468
M	egative ositive	28.35 ± 4.24 19.29 ± 6.15	6.098	**0.001**
moking	egative ositive	20.95 ± 5.51 19.75 ± 3.73	1.205	0.231
V diastolic dysfunction	one	28.55 ± 3.5 25.52 ± 5.74 14.6 ± 3.66	23.737	**0.001**

Table (4): Correlation of global PALS with different risk factors

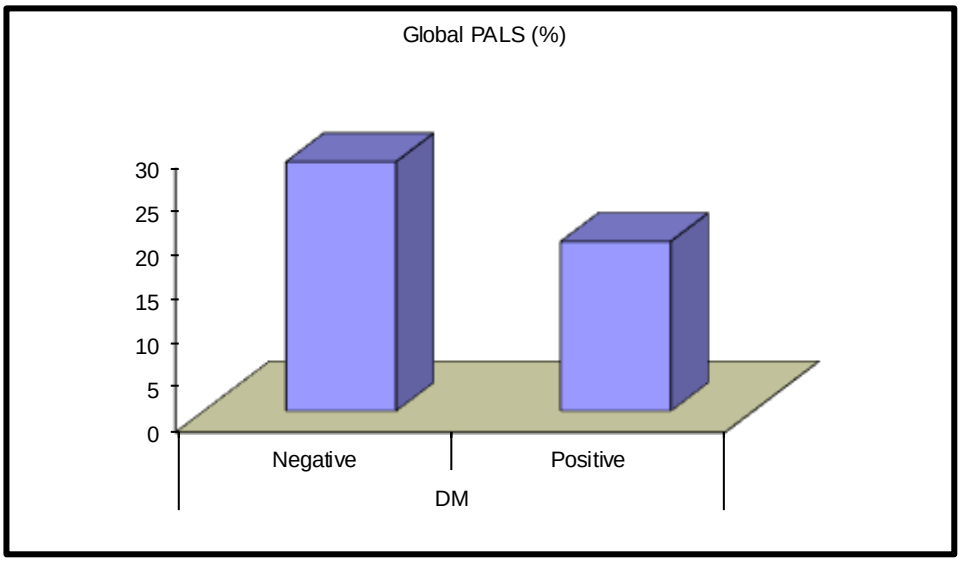

Figure (2): Correlation of global PALS with DM

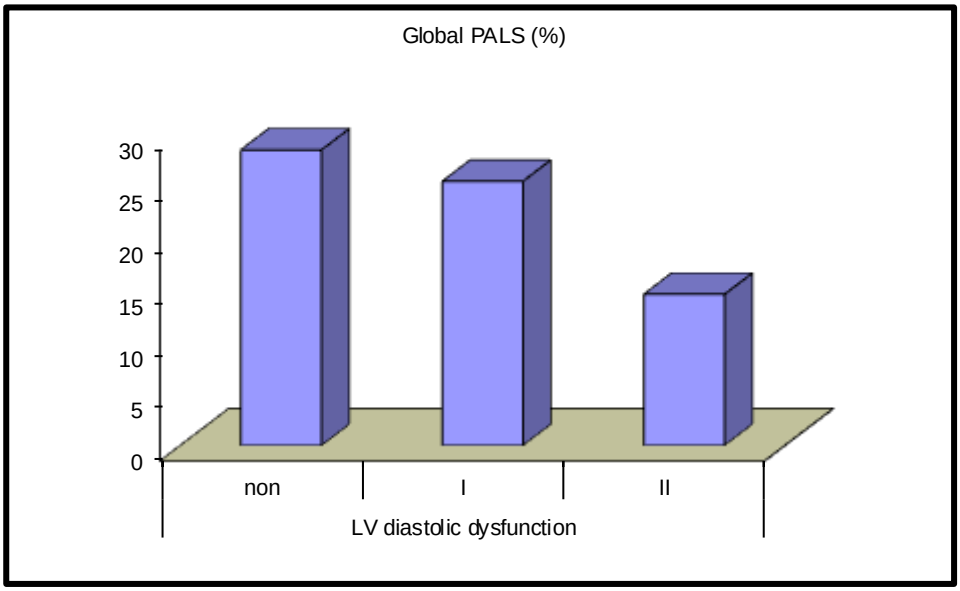

Figure (3): Correlation of global PALS with LV diastolic dysfunction

	Global PALS (%)	
	r	**p-value**
ge	-0.866**	**0.001**
ystolic	-0.633**	**0.001**
iastolic	-0.113	0.563
R (bpm)	-0.252	0.078
MI (Kg/m2)	-0.764**	**0.001**
SA (m2)	-0.167	0.246
A volume index (ml/m2)	-0.668**	**0.001**
otal LA stroke volume (ml)	-0.072	0.820
A expansion index (%)	0.828**	**0.001**
VEF (%)	0.024	0.718
V mass index (gm/m2)	-0.655**	**0.001**

*: Significant **: Highly significant

Table (5): Correlation of global PALS (%) with the studied parameters

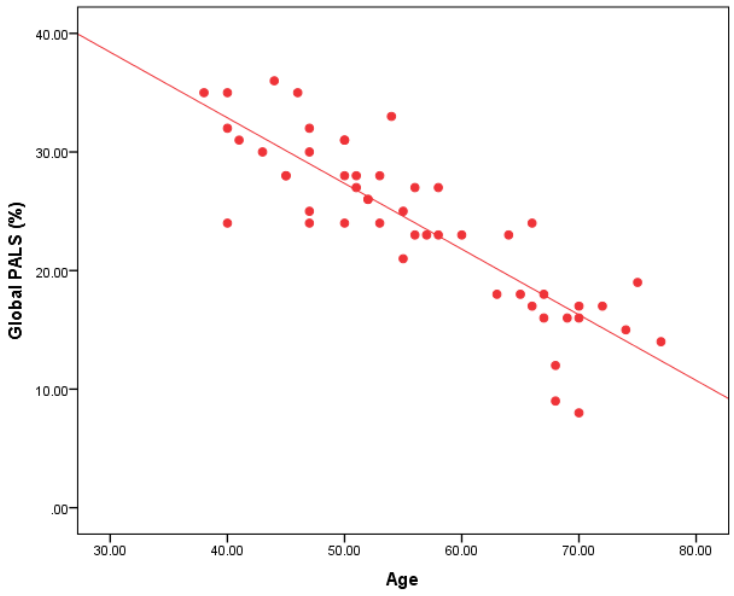

Figure (4): Correlation of global PALS with age

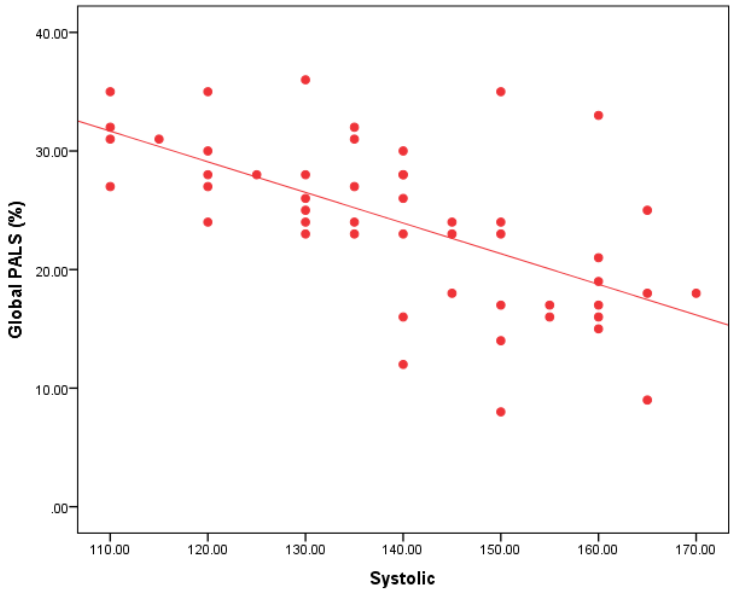

Figure (5): Correlation of global PALS with SBP

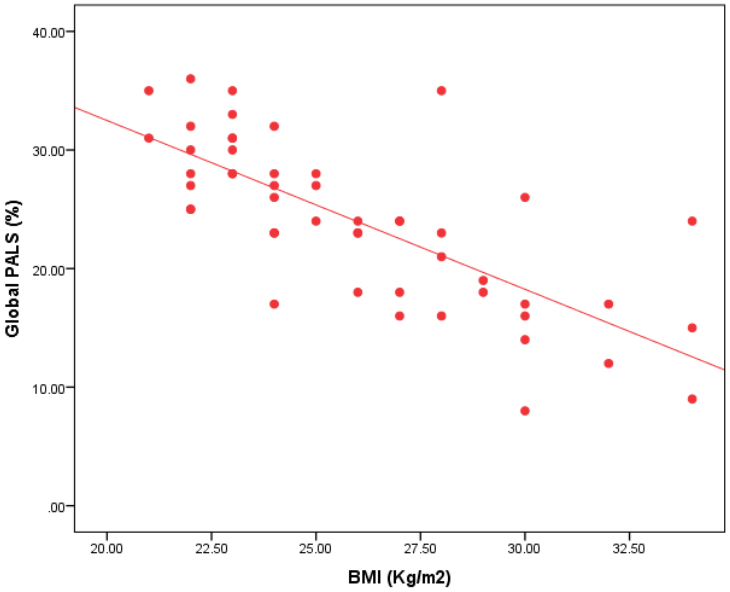

Figure (6): Correlation of global PALS with BMI

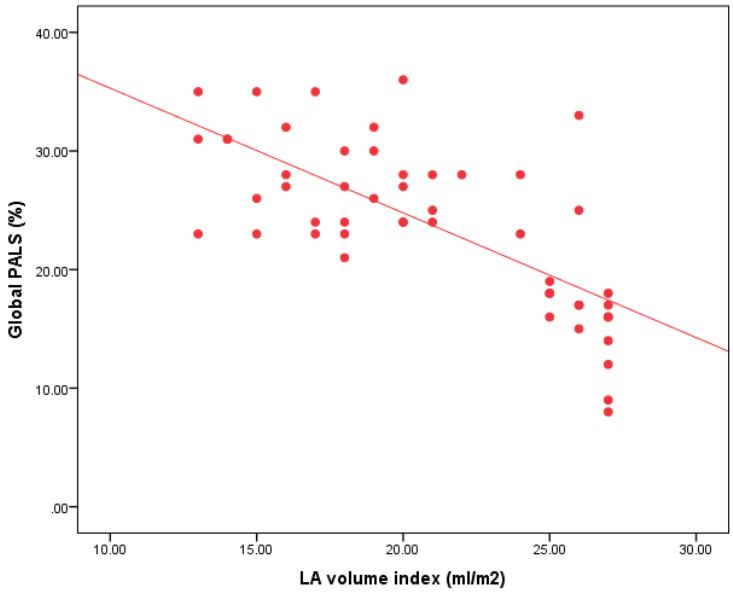

Figure (7): Correlation of global PALS with LA volume index

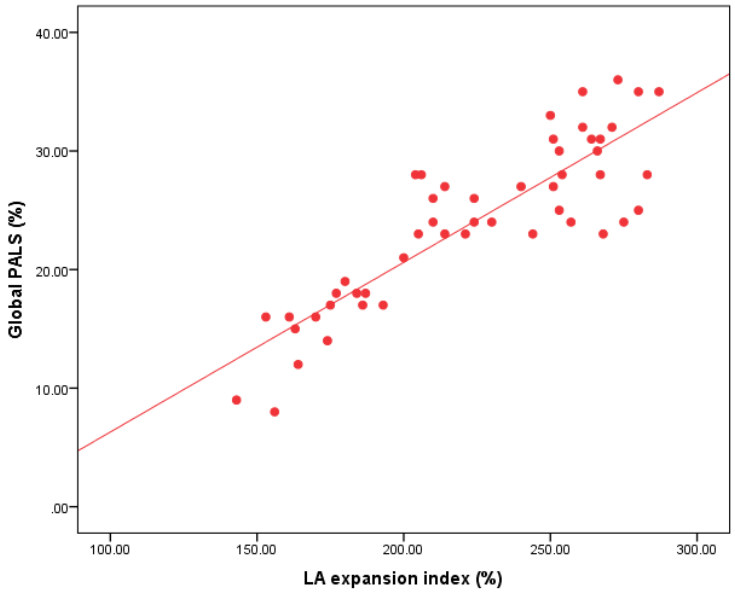

Figure (8): Correlation of global PALS with LA expansion index

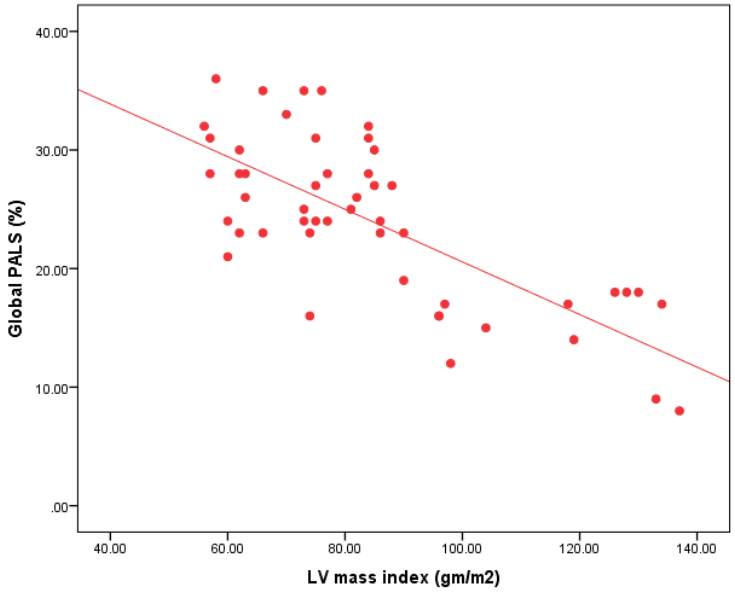

Figure (9): Correlation of global PALS with LV mass index

Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
≤35	0.999	98.00	98.00	98.0	98.0

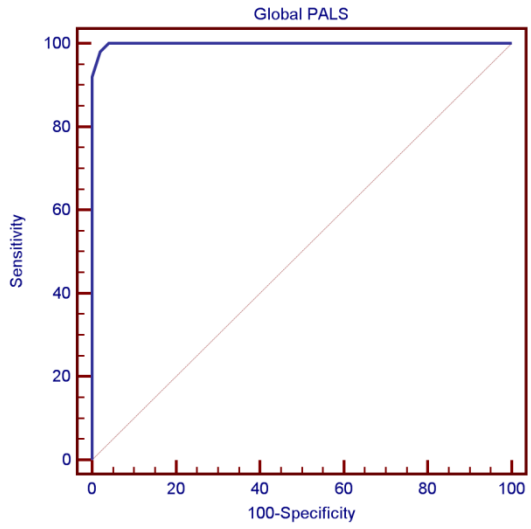

Figure (10): ROC curve for global PALS