Echocardiographic assessment of Left Ventricular Dyssynchrony in Hypertensive Patients with Normal Systolic Function

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ABSTRACT

Background: Normal Left Ventricular systolic function is present in nearly 50% of patients with congestive heart failure, the majority of such patients have systemic hypertension. Recent studies have demonstrated Left Ventricular dyssynchrony among patients with heart failure and normal systolic function. The co-existence between Left Ventricular dyssynchrony and hypertension with normal systolic function (with no clinical evidence of heart failure) is less well understood.

Objective:

To assess the Left Ventricular dyssynchrony among hypertensive patients with normal systolic function by using Tissue doppler imaging.To find out the associations between the LV dyssynchrony and other global echocardiographic findings like (LA volume index, LVmassindex , LV sephericity and LV filling pressure E/E`)

Type of the study: Prospective case- control study

Methods: The study conducted in Baghdad Teaching Hospital from 1st of June 2015 to 30th of May 2016 .Study included two groups of people, 40 patients, age_ matched healthy (control) group (group1) and 60 patients with established hypertension (group 2). A Complete 2-D and TDI echocardiography studies with simultaneous ECG were performed for all patients. Examination involved LV septal and posterior wall thicknesses, internal dimensions, left atrial size, ejection fraction and tissue doppler derived waves velocities E', E/E.' Dyssynchrony was determined by measuring T-P max (the maximal time difference from the onset of QRS to peak systolic velocity on TDI between any opposing LV wall in 3 apical views) .

Results: The study included 40 age -matched control people, 27males (67.5%) and 13 females (32.5%) with a male to female ratio was 1.8 :1, ranging from (42.4-58y) with mean age was (50.2 ±7.8y) (group 1) and 60 hypertensive patients, 38 males (63.3%) and 22 females (36.7%) with a male to female ratio was 1.7 :1, ranging from (48.5- 66.5y) with mean age of (57.5± 9.0 y) (group 2) . Left Ventricular dyssynchrony was identified in 20 of 60 patients (33.3%) .Dyssynchrony had no significant association with age and BSA. But it was significantly associated with LA volume index (r = 0.61, p=0.001), LV mass index(r=0.52 ,p=0.001) , LV sphericity index (r= 0.5, p = 0.003)) and LV filling pressure(r=0.6 , p value=0.001) . Dyssynchrony had significant negative correlation with (E`) velocity (r= - 0.7 ,P =0.001) .

Conclusion: Left Ventricular dyssynchrony is frequent among hypertensive patients with normal LV systolic function .The Left Ventricular dyssynchrony is significantly related to LA volume, LV mass, LV sphericity and LV filling pressure.

Key words: LV, Tissue Doppler, LA, Hypertension.

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Systemic Hypertension is an important public health challenge in both developing and developed countries, it present in approximately 26% of the adult population all over the world[1]. Such individuals are predisposed to the development of major cardiovascular events. LV dyssynchrony is a difference in the timing or lack of synchrony in contractions of the LV . Large differences in timing of contractions can reduce cardiac efficiency and is correlated with HF[2].LV systolic and diastolic dyssynchrony are not uncommon in patients with hypertension. Dyssynchrony is associated with increasing incidence of HF, cardiovascular morbidity and mortality [3]

systemic hypertension: Hypertension also known as **high blood pressure**, is a long term medicalcondition in which the blood pressure in the arteries is persistently elevated[4]. HT isa major risk factor for stroke and cardiovascular diseases and is associated withsignificant morbidity and mortality(5).There are two types of HT:

***Primary (essential) hypertension*: -** there is no identifiable cause of HT. Thistype tends to develop gradually over many years[6].

***Secondary hypertension*: -** Various conditions and medications can lead to secondary HT, including:Kidney problems,Adrenal gland tumors

Thyroid problems,Congenital cause such as coarctation of aorta ,Certain medications such as contraceptive pills, decongestants, over-the counter pain relievers, cocaine and amphetamines[7].

Definition of Dyssynchrony:

Dyssynchrony means differences in the timing of contraction or relaxation between the different myocardial segments, There are different classification of dyssynchrony :

1-mechanical or electrical dyssynchrony.

2- Atrioventricular, interventricular, intraventricular.

3- Systolic or diastolic [8].

Specific Echocardiography Methods to Evaluate CardiacDyssynchrony:[9] .

1. Septal-to-posterior wall motion delay (SPWMD).
2. Inter-ventricular mechanical delay (IVMD).
3. Tissue doppler imaging indices:

a. Mechanical dyssynchrony index.

b. Basal septal-to-lateral wall Ts. (T-P max).

4. Systolic dyssynchrony index (SDI-16) (Real time 3D – echo)
5. Speckle tracking radial strain..

Markers of dyssynchrony[10]*:*

1- M-mode septum to posterior delay > 130ms.

2- Inter-ventricular delay > 40ms.

3- Dyssynchrony index > 33 ms by TDI..

4- Septal to posterior wall delay > 60ms by TDI.

5- T-P max >50 ms By TDI..

6- Systolic strain (% delayed contraction > 30).

Aim of the study

1- To assess the LV dyssynchrony in HT patients with normal systolic function by using Tissue dopplerimaging .

2- To find out the associations between the LV dyssynchrony and other global echocardiographic findings like (LA volume index, LV mass index , LV sephericity and LV filling pressure E/E`) .

Patients:

Patients' design :case- control descriptive study.

Setting : Prospective study conducted in Baghdad Teaching Hospital
(cath.unit).

Duration : From 1st of June 2015 to 30th of May 2016 .

Inclusion Criteria*:*

1- (group 1) normal healthy people (normotensive) (control group).

2- (group 2) patients with established hypertension of variable duration
and normal QRS duration(<120 msec) (ECG) .

Exclusion criteriawere as follows:

1- Congestive heart failure , EF<54%

2-Ischemic Heart Disease with segmental wall motion abnormalities .

3- Evidence of valvular heart disease (regurgitation more than mild or
any degree of stenosis).

4- Pulmonary hypertension.

5- Pericardial disease .

6- Atrial fibrillation .

7- Any cause of secondary HPT such as kidney ,adrenal and thyroid
problems ,Coarctation of aorta .

8-patients with hypertrophic cariomayopathy.

Methods

Questionnaire: Data collection was done using questionnaire which included the personal data (Age ,Gender, Height ,Weight) and clinical Examination Included (chest examination, abdominal examination, BP , PR and JVP) .

ECG was performed for all patients using Schiller device (Schiller AG, Cardiovit CH-6341,Baar, Swiss made) and transthoracic echocardiography (2-dimensional and Doppler) study using available equipment (Vivid GE 9) equipped with phased array transducer of 2.5 MHZ with simultaneous ECG tracing.

TDI recordings were obtained in basal and mid-LV segments from 3 apical views.LV measurements were made according to recommendations of the ASE. LeftAtrialvolume ,LVmassand LV sphericity index were calculated , LV diastolic function and LV Fillingpressure were also assessed. LV dyssynchrony was assessed by measurements of time intervals from onset of the QRS complex to the peak systolic velocity on the pulsed tissue Doppler waveform (T-P) in the 3 apical views. The maximum T-P was measured as the maximaldifference of T-Pbetween any 2 opposing LV walls . T-Pmax value of 50 msec. was selected as the cut point for LV dyssynchrony.

TDI method to measure the T-P value

Statistical analysis was done using computerized statistical software; statistical package for social sciences (SPSS) (version 16).

1- Mean and standard deviation were done for all quantitative continuous variables.

2- Two -Pearson correlations with 2-tailed analysis were used to test associations between continuous data sets (e.g., between LV mass and dyssynchrony, and between LA size and dyssynchrony and others associations). Significant result is considered when P-value <0.05, and highly significant when <0.001, and non-significant when >0.05.

Results: The study included 40 age -matched control people, 27males (67.5%) and 13females (32.5%) with a male to female ratio was 1.8 :1, (group 1) and

60hypertensive patients, 38 males (63.3%) and 22 females (36.7%) with a male tofemale ratio was 1.7 :1, (group 2) .Table 1 shows the distribution of studied groups according to their demographic characters as the age of normal (control) group was ranging from (42.4-58y) with mean age of (50.2 ±7.8y) and hypertensive patients wasranging from (48.5-66.5y) with mean age of (57.5± 9.0y) . Mean of BSA incontrol group was (1.89 ± 0.14) which is nearly similar to hypertensive group(1.92 ±0.23) , mean systolic blood pressure in control group was (110 ±10.1mmHg) which is less than that of hypertensive group (147.4 ± 22.5 mmHg) and theQRS duration in control group was nearly similar to that seen in hypertensivepatients (84.1 ± 10.5 msec) , (86.5 ±11.7 msec) respectively.

(Table 1): The distribution of studied groups according to their demographic characters

Demographic character	NormaL mean±SD	Hypertensive patient mean±SD
Age(Y)	50.2 ± 7.8	57.5 ± 9.0
Height (m)	1.64 ± o.41	1.69 ± 0.11
BSA (m^2)	1.89 ± 0.14	1.92 ±0.23
Systolic blood pressure (mmHg)	110 ±10.1	147.4 ±22.5
QRS duration(msec) ECG	84.1 ± 10.5	86.5 ± 11.7

Hypertensive Patients were on a variety of antihypertensive medications including 32 of 60 patients taking 2 drugs (53.3%) and 28 (46.7%) taking 3 ormore antihypertensive medications.Table 2show the echocardiographic findings in normal and hypertensive patients so we found the mean of LA volume (ml) , LA volume index(ml/m2) innormal group was (29.1 ±4.18) , (20.4 ±3.57) respectively this proved to bestatistically significant less than hypertensive group (55.9 ± 9.38 ml), (32.7±5.18ml/m2) (p=0.0001).The same table shows the mean of LV mass in normal group was (150 ± 13.4) , LV mass index was (90.4 ±6.5) both of them significantly lower thanhypertensive group (210.3 ± 38.43g) ,(115.1 ±7.11 g/m2) respectively (P=0.0001). Mean of LV sphericity index in normal group was (0.46 ± 0.43) whichis more than hypertensive group (0.36 ± 0.03) (p =0.0031) . The mean of LVseptal thickness in normal group was (0.7 ± 0.09 mm) which significantly less thanhypertensive group (13.0 ± 0.13mm) (P =0.0001) . The mean EF of normal groupwas nearly similar to hypertensive group (64 ± 5.3%) (65.1 ± 4.1%) respectively (P =0.18)(not significant) .The mean of lateral mitral relaxation velocity (E`) innormal group was significantly higher than hypertensive group (9.8± 1.1), (7.2±0.5) respectively (P =0.045) , mean of LV filling pressure (mitral inflow tomitral relaxation velocity ratio) (E/E`) in normal group was (9.5 ±2.9) which issignificantly lower than hypertensive group (13 ± 1.1) (P =0.0001) . Finally themean of T_Pmax (marker of dyssynchrony) in normal group was (30.6 ±4.75msec) which is whithin normal range and significantly lower than hypertensive group (56.5± 25msec) (P =0.001). The LV dyssynchrony in hypertensive patients (T-P max > 50msec) (ranging from 51 to 83 msec) was identified in 20 of 60 patients (33.3%)of hypertensive patients.

(Table 2) : Echocardiographic findings in hypertensive and control groups.

Echo findings	Normal (control) Mean ± SD	Hypertensive patient Mean ±SD	P-Value
LA volume (ml)	29.1 ±4.18	55.9 ± 9.38	0.0001
LA volume index (ml/m^2)	20.4 ±3.57	32.7 ± 5.18	0.0001
LV mass (g)	150 ± 13.4	210.3 ± 38.43	0.0001
LV mass index (g/m^2)	90.4 ±6.5	115.1 ± 7.11	0.0001
Sphericity index	0.46 ± 0.43	0.36 ± 0.03	0.0031
LV septal thickness (mm)	0.7 ± 0.09	13.0 ± 0.13	0.0001
EF%	64 ± 5.3	65.1 ± 4.1	0.18
E` (cm/s)	9.8± 1.1	7.2± 0.5	0.045
E/E`	9.5 ±2.9	13 ±1.1	0.0002
TP-max to systole (msec)	30.6 ±4.75	56.5 ± 25.0	0.0001

The T-P max had no significant association with age (p = 0.2) and BSA(P=0.4) (Table 6).

Table 4 shows the correlation of LV dyssynchrony which assessed by T-Pmaxwas significantly associated with LA volume (r = 0.63, p=0.001) or LA volumeindex (r = 0.61, p = 0.001) i.e greater LVdyssynchrony was observed withincreasing LA volume or index . A similar relationship was observed between TPmax and LV mass (r=0.64 ,p=0.001) or LV mass index (r= 0.52, p = 0.001) .LV dyssynchrony was significantly associated and positively correlated withLVsphericity index (r = 0.5,

p =0.003) .The T-P max had significant negativecorrelation with (E`) velocity ( r = - 0.7 ,p = 0.001) and finally the T-P max hadsignificant association with LV filling pressure (E/E`) (r=0.6 , p=0.001) .

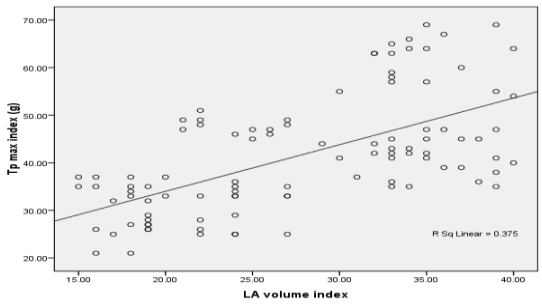
(Table 3) :pearson correlations of LV Systolic dyssynchrony with Age and BSA

Varaible	Pearson correlation (r)	p- value
Age	+0.3	0.2
BSA	-0.07	0.4

(Table 4) :pearson correlations of LV Systolic dyssynchrony with Echo.findings data.

LV dyssynchrony (T-P max)	Pearson correlation (r)	P_value
LA volume	0.63	0.001
LA volume index	0.61	0.0001
LV mass	0.64	0.001
LV mass index	0.52	0.001
Sphericity index	0.5	0.003
E` velocity	-0.7	0.001
E/E`	0.6	0.001
EF%	- 0.08	0.4

Figure 1 show the diagram of positive correlation between LV dyssynchronyand LA volume index which mean greater LV dyssynchrony was observed withincreasing LA volume index (r = 0.61, p = 0.001) .



(Figure 1) : correlation between LV dyssynchrony (T-P max) and LA volume index

Figure 2 show the diagram of significant positive correlation between LVdyssynchrony and LV mass index (r= 0.52, p = 0.001). **Figure 3** show the diagram of positive correlation between LV dyssynchronyand LV sphericity index (r = 0.5, p = 0.003).

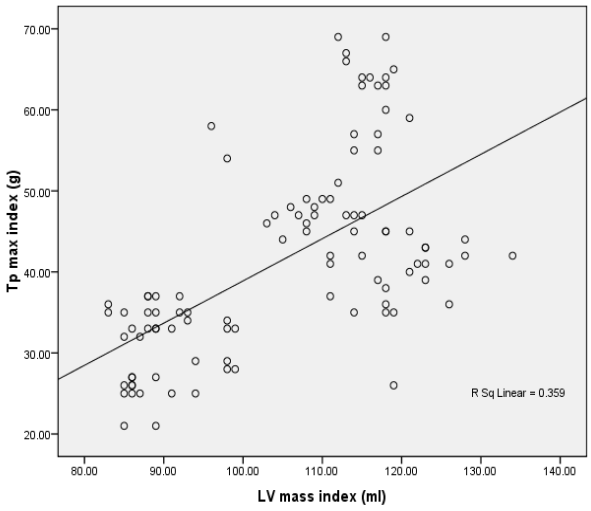
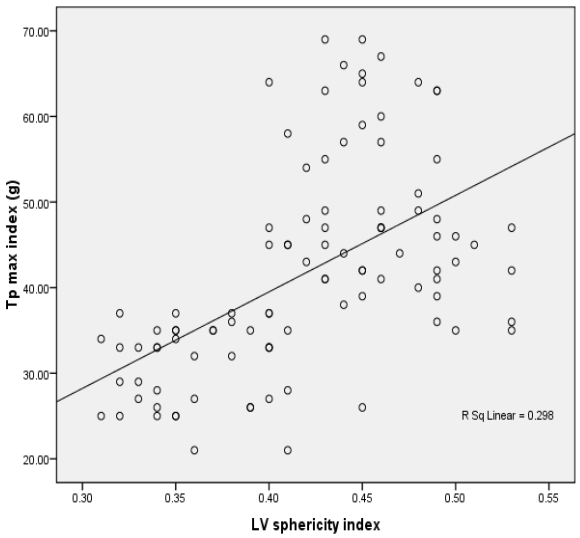


Figure 2) : correlation between LV dyssynchrony (T-P max) and LV massindex



(Figure 3) : correlation between LV dyssynchrony (T-P max) and LV sphericityindex

Discussion: Age of the patients was ranging from (48.5-66.5y) that show no relationwith LV systolic dyssynchrony (p-value =0.2) which is similar to that foundby Benjamin Yang et al [(11)].

Left ventricular systolic dyssynchrony (T-Pmax>50 msec) was identified in20 patients (33.3%) in the hypertensive group which is similar to that reportedby

Wang et al (33%) [12] and less than that reported by Yu et al (39%) [13]andBenjamin Yang et al (41%) [11] .
Hypertensive patients show higher LA volume index (32.7±5.18 ml/m2) (p-value=0.0001) and LV mass index (115±7.11 g/m2) (p-value=0.0001) than normalcontrol group. LV dyssynchrony was strongly associated with LA volume index(P-value=0.0001) and LV mass index (P-value=0.001) ,these findings are similarto that reported by McKee PA et al [14]. The LV dyssynchrony among suchpatients is related to the magnitude of LV hypertrophy and LA size. Thissignificant relationship provide further insight into the effects of hypertension onLV function and the potential mechanism for the development of clinical HF inpatients with normal systolic function. HT cause LV hypertrophy , increased LVfilling pressure and ultimately increased LA volume. The latter has beendemonstrated to have important prognostic implications for cardiovascular events[15,16].
LV systolic dyssynchrony was significantly associated with LV Sphericityindex, the T-P max showed negative correlation to LV sphericity(p= 0.003)which is similar to that reported by Benjamin Yang et al [11]. LV remodeling(abnormal LV sphericity) parallels thedevelopment of hypertrophyand changes in LA size. These changes are accompanied by changes in ventricularsynchrony that may precede the development of clinical heart failure [17]. we found that LV dyssynchrony was considered as important cause in developing the mechanisms of LV remodeling which is the same result found byYuda S et al [17].The T-P max had significant negativecorrelation with (E`) velocity (Pvalue= 0.001) i.e greater LV dyssynchrony was strongly associated withlowerearly diastolic relaxation assessed by E′ which is similar to that found by OpdahlA. et al (P-value =0.0001) [18] .T-P max had significant association with LV filling pressure (E/E`) (Pvalue=0.001) Which is nearly similar to that reported by Chang et al (P-value=0.0005) [19].

Conclusion:

1- LV dyssynchrony is frequent among hypertensive patients with normal LVsystolic function .

2- The LV dyssynchrony is significantly related to LA volume, LV mass, LVremodeling and LV filling pressure.

Recommendation:

1- Follow-up study will be necessary to determine whether LV dyssynchronyin hypertensive patients is associated with the subsequent development ofHF and to determine patients who may benefit from more intensivehypertension control at an earlier stage in their disease process.

2- Another imaging methods such as Strain , strain rate and speckle tracking inaddition to TDI consider addifrent methods used for evaluation of LVdyssynchrony.

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