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, LV mass index, 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 waves). 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 sephericity 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 sephericity and LV filling pressure.

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

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Systenmic 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. 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. LV systolic and diastolic dyssynchrony are not uncommon in patients with hypertension. Dyssynchrony is associated with increasing incidence of HF, cardiovascular morbidity and mortality.

**Systemic Hypertension:** Hypertension is a long term medical condition in which the blood pressure in the arteries is persistently elevated. HT is a major risk factor for stroke and cardiovascular diseases and is associated with significant morbidity and mortality. There are two types of HT:

- **Primary (essential) hypertension:** - there is no identifiable cause of HT. This type tends to develop gradually over many years.

- **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.
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.

Specific Echocardiography Methods to Evaluate Cardiac Dyssynchrony:
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:
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 Doppler imaging.
2- To find out the associations between the LV dyssynchrony and other global echocardiographic findings like (LA volume index, LV mass index, LV sphericity 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 Criteria were 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 cardiomyopathy.

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. Left Atrial volume, LV mass and LV sphericity index were calculated, LV diastolic function, and LV Filling pressure 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 maximal difference of T-P between any 2 opposing LV walls. T-P max value of 50 msec. was selected as the cut point for LV dyssynchrony.

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
60 hypertensive patients, 38 males (63.3%) and 22 females (36.7%) with a male to female 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 was ranging from (48.5-66.5y) with mean age of (57.5 ±9.0y). Mean of BSA in control group was (1.89 ±0.14), 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 the QRS duration in control group was nearly similar to that seen in hypertensive patients (84.1 ± 10.5 msec), (86.5 ±11.7 msec) respectively.

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 or more antihypertensive medications. Table 2 show the echocardiographic findings in normal and hypertensive patients so we found the mean of LA volume (ml), LA volume index(ml/m2) in normal group was (29.1 ±4.18), (20.4 ±3.57) respectively this proved to be statistically 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 than hypertensive group (210.3 ±38.43g), (115.1 ±7.11 g/m2) respectively (P=0.0001). The T-P max had no significant association with age (p =0.2) and BSA (P=0.4) (Table 6).

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) | Hypertensive patient | P-Value |
|---------------|------------------|----------------------|---------|
| LA volume (ml) | 29.1±4.18        | 55.9±9.28            | 0.0001  |
| LA volume index (ml/m2) | 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/m2) | 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           | 9.3±2.0          | 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-Pmax was significantly associated with LA volume (r = 0.63, p<0.001) or LA volume index (r = 0.61, p = 0.001) i.e greater LV dyssynchrony was observed with increasing 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 with LV sphericity index (r = 0.5,
Echocardiographic assessment

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The T-P max had significant negative correlation with (E'/E) velocity (r = -0.7, p = 0.001) and finally the T-P max had significant association with LV filling pressure (E/E') (r=0.6, p=0.001).

(Table 3): Pearson correlations of LV Systolic dysynchrony with Age and BSA

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

(Table 4): Pearson correlations of LV Systolic dysynchrony with Echo findings data.

| LV dysynchrony (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     |

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

Left ventricular systolic dyssynchrony (T-Pmax>50 msec) was identified in 20 patients (33.3%) in the hypertensive group which is similar to that reported by...
Wang et al (33%) (12) and less than that reported by Yu et al (39%) (13) and Benjamin 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 normal control group. LV dyssynchrony was strongly associated with LA volume index (P-value=0.0001) and LV mass index (P-value=0.0001). These findings are similar to that reported by McKee PA et al (14). The LV dyssynchrony among such patients is related to the magnitude of LV hypertrophy and LA size. This significant relationship provide further insight into the effects of hypertension on LV function and the potential mechanism for the development of clinical HF in patients with normal systolic function. HT cause LV hypertrophy, increased LV filling pressure and ultimately increased LA volume. The latter has been demonstrated to have important prognostic implications for cardiovascular events (15,16). LV systolic dyssynchrony was significantly associated with LV Sphericity index. 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 the development of hypertrophy and changes in LA size. These changes are accompanied by changes in ventricular synchrony 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 by Yuda S et al (17). The T-P max had significant negative correlation with (E') velocity (Pvalue = 0.001) i.e greater LV dyssynchrony was strongly associated with lowerdiastolic relaxation assessed by E' which is similar to that found by Opdahl A 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 LV systolic function.

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

Recommendation:

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

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

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