The evaluation of left ventricle stiffness index in patients suffering from hypertension

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Abstract

Many diseases can produce cardiac overload, of these disease hypertension, valve disease congenital anomaly in addition to many other disease. One of the most common diseases causing left ventricle overload is hypertension. A long term hypertension can cause myocardium hypertrophy leading to changes in the cardiac contractility and reduced efficiency. The investigations were carried out using conventional echocardiography techniques in addition to the tissue Doppler imaging (TDI) from which many noninvasive measurements can be readily obtained. The study has involved the effect of hypertension on the myocardium stiffness index through the measurement of early diastolic filling (E) and the early velocity of lateral mitral annulus (E_a) from which left ventricle filling pressure can be obtained. Our aim was to investigate the changes in the myocardium index of diastolic stiffness using TDI for patients suffering from systemic hypertension. We studied 263 hypertensive patients (105 males and 158 females of average age of 54.07± 12.7) and 166 healthy subjects (age range 40.06± 12.8,53 males and 113 females) as a control group. Measurements were carried out using tissue Doppler imaging (TDI) of the mitral annulus in addition to other echocardiographic measurements for the assessment of left ventricle end diastolic dimension (LVEDD), Doppler peak early (E) and late (A) diastolic filling velocities. Results reveal that mitral annular early diastolic velocity (E_a) measured by TDI, that (E_a) was significantly lower for the hypertensive group in comparison with the control group (E_a 9.81 ± 2.87 cm/s for hypertensive vs. 12.90 ± 2.395 cm/s for control p value <0.001. Hypertensive group also showed a significantly higher mitral annular late diastolic velocity (Aa) in comparison with control group as Aa 11.21 ± 2.504 cm/s for hypertensive vs. 9.787 ±2.201cm/s for control, p value <0.001.. In conclusion, LV myocardial diastolic stiffness index is increased in hypertensive patients.

Key words

Left ventricular myocardial Stiffness, hypertension, tissue Doppler echocardiography.

Article info.

Received: Jan. 2014
Accepted: Feb. 2014
Published: Apr. 2014

تقييم معامل صلابة البطين الأيسر في المرضى الذين يعانون من ارتفاع ضغط الدم

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الخلاصة

يمكن للعديد من الأمراض أن تولد زيادة في الجهد على القلب، من هذه الأمراض ارتفاع ضغط الدم، و تشوه الصمام الخلقي بالإضافة إلى أمراض كثيرة أخرى. إن احد أكثر الأمراض شيوعا والذيّ يتسبب في زيادة الآجهاد على البطين الأيسر هو مرض ارتفاع ضغط الدم. إن استمرار ارتفاع ضغط الدم لمدة طويلة يمكن أن يسبب تضخم عضلة القلب مما يؤدي إلى تغير في القابلية الأنقباضية للقلب وبالتالي انخفاض كفائته. أجريت الدراسة باستخدام جهاز تخطيط صدى القلب التقليدية بالإضافة إلى استخدام جهاز دوبلر للانسجة حيث يمكن

إجراء القياسات بسهولة. تشتمل الدراسة على دراسة تأثير ارتفاع ضغط الدم على معامل صلابة عضلة القلب من خلال قياس السرعة المبكرة لأمتلاء البطين الأيسر عند انبساط عضلة القلب كذلك قياس بداية سرعة الصمام الاكليلي الحلقي الجانبي ومنها يمكن احتساب معامل الصلابة من خلال ضغط امتلاء البطين الايسر. الهدف من الدراسة: للتحقيق من التغيرات في مؤشر عضلة القلب الناتج من التصلب الانبساطي باستخدام تصوير دوبلر للانسجة للمرضى الذين يعانون من ارتفاع ضغط الدم النظامي. شملت الدراسة 263 من مرضى ارتفاع ضغط الدم (105 ذكور و 158 إناث، متوسط العمر12.7±54.07 و (166 شخصا سليما تتراوح أعمارهم 12.8,40.06± 53 رجال و113 نساء) تم إجراء القياسات باستخدام تصوير دوبلر للأنسجة للصمام الإكليلي الحلقي بالإضافة إلى استخدام جهاز تخطيط صدى القلب لقياس أبعاد البطين الأيسر عند نهاية انبساط عضلة القلب، كذلك لقياس بداية ونهاية سرعة امتلاء البطين الأيسر عند انبساط عضلة القلب. واستخدم تصوير دوبلر للأنسجة في قياس سرعة الصمام الإكليلي الحلقي ومن هذه القياسات تم إيجاد معامل صلابة الانبساط عن طريق احتساب [E/Ea/LVEDD]. أظهرت النتائج إن السرعة الانبساطية المبكرة للصمام الإكليلي الحلقي (E_a) هي اقل بكثير عند المرضى المصابين ارتفاع ضغط الدم(9.81 ± 2.87 cm/s) مقارنة بالأشخاص السليمين (12.90 ± 2.395 cm/s) تكون ذات فروق معنوية إحصائيا0.001> p value. كما أظهرت الدراسة إن السرعة الانبساطية المتأخرة للصمام الإكليلي الحلقي (Aa) هي أعلى بكثير عند المرضى المصابين ارتفاع ضغط الدم (11.21 ± 2.504 cm/s) مقارنة بالأشخاص السليمين (9.787 ±2.201cm/s) تكون ذات فروق معنوية إحصائيا 0.001> p value . الاستنتاج: وجد إن معامل تصلب عضلة القلب الانبساطي تزداد في المرضى المصابين بارتفاع ضغط الدم كذلك تغير في سرعة انتقال الدم عبر الصمام الإكليلي.

Introduction

Hypertensive heart disease is defined as the response of the heart to afterload imposed on the left ventricle by the progressively increasing arterial pressure and total peripheral resistance produced by hypertensive vascular disease [1].

Left ventricle hypertrophy can be resulted from increased hemodynamic demand, the heart augment the cardiac output by means of growth of cardiomyocytes. It is known that LVH is in part the result of this morphological adaptation to the chronic pressure-overload and is characterized by thickening of the myocardial walls. The adaptation further increases LV diastolic dysfunction because growth of cardiomyocytes causes increased stiffness of muscular fibers [2].

LV diastolic dysfunction is caused directly by raised blood pressure, or by structural changes related to LV hypertrophy remains controversial but hypertensive patients may present with normal transmitral inflow filling patterns or with the more typical presentation is one of diastolic dysfunction. To more accurately assess left ventricular diastolic and systolic function, it is necessary to find a less load-dependent method of analysis [3].

Tissue Doppler echocardiography (TDE) is a recent non-invasive technique to evaluate regional systolic and diastolic function. The Doppler tissue signal may be displayed as a color or pulse Doppler image [4–5]. In the latter technique the wall motion is converted into a temporal pattern of velocity waves from which peak velocity, duration and time–velocity integrals can be quantified [6].

Tissue Doppler echocardiography (TDE) is directly measures myocardial velocities. Diastolic tissue Doppler velocities reflect myocardial relaxation, and in combination with conventional Doppler measurements, the index of diastolic stiffness can be calculated. The measurements have included the calculation of the ratio of (transmitral early diastolic velocity / mitral annular early diastolic velocity [E/E_a]) which has been reported to give noninvasive estimation of left ventricular (LV) filling pressure [7]. The ratio E/E_a to LV end diastolic diameter (LVEDD), represents the index of diastolic stiffness ((E/E_a)/LVEDD) that represents a pressure – volume relationship of the left ventricle. This echo Doppler index of diastolic LV myocardial stiffness was previously studied on the left ventricular hypertrophy [8].

Abbreviations and Acronyms

E_a : Peak mitral annular early diastolic Velocity.
A_a : Peak mitral annular late diastolic velocity.
E/E_a : The ratio of early diastolic mitral inflow velocity to early diastolic tissue Doppler mitral annular velocity.
TDI : Tissue Doppler imaging.
E : Peak mitral early filling velocity.
A : Peak mitral atrial phase filling velocity.
LV : Left ventricular.
LVEDD: Left ventricular end diastolic diameter.
LVIDS: Left ventricular end systolic diameter.
LVH: Left ventricular hypertrophy.
SLV: Stiffness of left ventricular.
dv: Change in volume.

Patients and methods

In the present study patients with hypertension were chosen. Patients were examined for other diseases which can interfere with LV stiffness. A total of 429 subjects were included in the study, 263 patients with an established diagnosis of hypertension (HT group), 105 males and 158 females of average age of 54.07± 12.7 and 166 healthy subjects (age range 40.06± 12.8, 53 males and 113 females) as (C group). The study was performed during the period from January 2013 until October 2013, at the echo unit of the Baghdad/ medical city teaching hospital.

The plan of the study consisted of the following steps:-

Case history, Electrocardiography (ECG), Chest X- ray and Echocardiographic examination.

The echocardiography was performed for each subject using SONOACE X8 equipped with a transducer operating at 2-5 Hz, Left ventricular internal dimension at diastole (LVIDD) and systole (LVIDS),were measured, using M-mode echocardiography to asses left ventricular systolic and diastolic function. Pulse Doppler tracing of the transmittal flow velocity curve were obtained from the apical four-chamber view during quite respiration with the patients lying on the left lateral position. Measurement of the early velocity E and A peak velocity at atrial contraction, these two parameter (E, A) are very good indicators for diastolic performance [9].

Tissue Doppler Imaging (TDI) of the mitral annulus velocity measurements was obtained from the apical four-chamber view, using a 1-2 mm sample volume placed at the lateral sides of the mitral valve annulus. The TDI mitral annular velocities were measured including the early (E_a), late (A_a) [10]. All TDI velocities were taken as an average of the lateral readings of five cardiac cycles. The mean values of Ea velocities were used to calculate the E/E_a ratio. Myocardial diastolic stiffness index was calculated by using the equation of Stiffness index= $[(E/E_a)/LVEDD]$ [11].

All values were expressed as mean value with standard deviation ±1. The comparison between the mean values for both groups was tested by paired student's t-test. p- value <0.05 was considered as the level of significant.

Results

The study included 263 hypertensive patients (158 females and 105 males, age 54.07± 12.7 years) and 166 healthy subjects (113 females and 53 males, age 40.06± 12.8 years).

Table 1: Conventional M mode and two dimensional echocardiographic findings, ages from 20-80 years.

	Control	hypertensive	Change% = (HT-C/C)×100	p-value
LA cm	3.177± 0.43	3.46± 0.49	8.907	<0.05
LVIDD cm	4.73± 0.56	4.742 ± 0.693	0.211	>0.05
IVSd cm	0.941 ± 0.648	1.33 ± 0.263	41.33	<0.05
PWTd cm	0.861 ± 0.175	1.194 ± 0.249	38.67	<0.05
E(mm/s)	73.06 ± 9.804	69.63 ± 16.47	-4.69	<0.05
A(mm/s)	56.80 ± 11.04	76.62 ± 15.33	34.89	<0.05
E\A	1.322 ± 0.250	0.936 ± 0.261	-29.19	<0.05

LA= Left atrium, LVEDD= Left ventricular end-diastolic diameter, IVS= Interventricular septum, PW= Posterior wall. P <0.05= Significant, P >0.05= Non significant.

Table 1 shows conventional echo-Doppler findings obtained from the study population. The hypertensive group showed increased LV wall thickness compared with control group (IVS 1.33 ± 0.263 for hypertensive vs. 0.941 ± 0.648 mm for control, P < 0.001), and (PWT 1.194 ± 0.249 for hypertensive vs., 0.861 ± 0.175 mm for control, P <0.001), while LVIDD showed no significant difference between both groups (P > 0.05), and LA diameter showed significant difference between both groups (P<0.05).

Mitral inflow Doppler Indices of LV diastolic function is presented in (Table 1). The hypertensive group showed a significantly higher A wave velocity compared with control group (A 76.62 ± 15.33 for hypertensive vs., 56.80 ± 11.04 cm/s for control, P <0.001), the results show significantly lower E/A ratio in hypertensive group compared with control group (E/A 0.936 ± 0.261 for hypertensive vs., 1.322 ± 0.250 for control, P <0.05), and a decrease in E wave (E 69.63 ± 16.47 for hypertensive vs., 73.06 ± 9.804 ms for control, P <0.05).

Table 2:- Doppler Tissue Imaging Annular Velocities.

	control	hypertensive	change% = (HT-C/C)×100	p-value
E_a mm/s	12.90 ± 2.395	9.81 ± 2.87	-23.95%	<0.05
A_a mm/s	9.787 ±2.201	11.21 ± 2.504	14.53%	<0.05
E/E_a	5.797±1.065	7.567± 2.4801	30.53%	<0.05
Stiffness index	1.238 ± 0.267	1.637 ±0.628	32.22%	<0.05

P <0.05= Significant, P >0.05= Non significant.

Mitral annular TDI early diastolic velocity E_a was significantly lower in the hypertensive group compared with the control group (E_a 9.81 ± 2.87 for hypertensive vs., 12.90 ± 2.395 mm/s for control, P <0.05.

Hypertensive group also showed a significantly higher value in late diastolic velocity in comparison with control group (A_a 11.21 ± 2.504 for hypertensive vs., 9.787 ± 2.201 mm/s for control, P <0.05. The LV stiffness index and E/E_a were

significantly higher in hypertensive compared with control (LV stiffness index 1.637 ±0.628 for hypertensive vs., 1.238 ± 0.267 for control, P <0.001), and (E/E_a for hypertensive patients is 7.567± 2.4801) and control is 5.797±1.065, p <0.05) (Table 2).

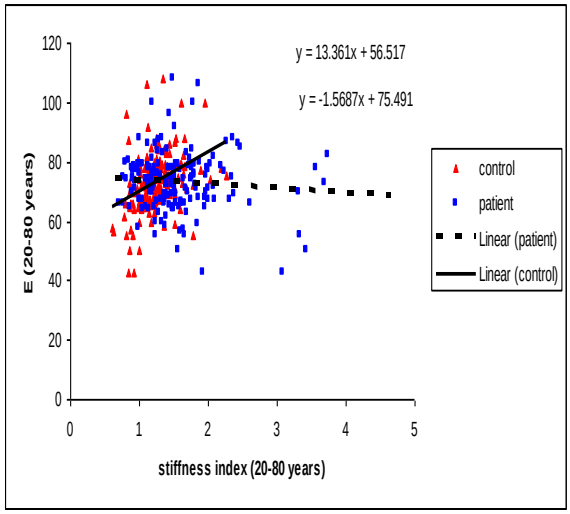

Fig.1: The relation between stiffness index and peak early (E) diastolic filling velocities.

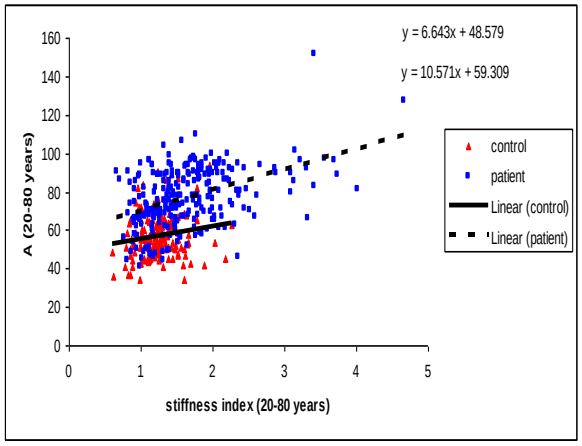

Fig. 2: The relation between stiffness index and peak late (A) diastolic filling velocities.

Discussion

Most patients who have clinical diastolic dysfunction have hypertensive heart disease. Long-standing arterial hypertension augments LV systolic stress, inducing myocardial fiber hypertrophy and increasing LV wall thickness [12].

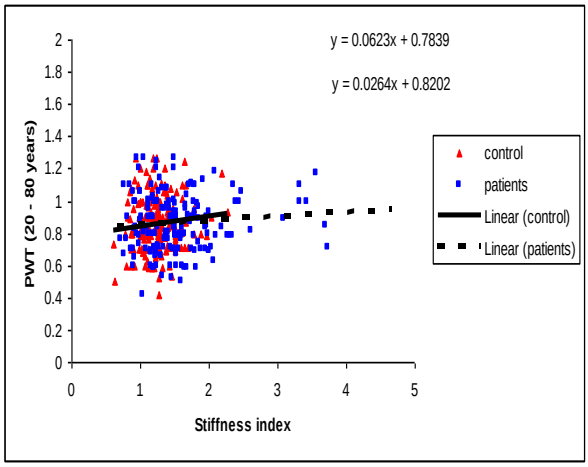

Fig. 3: The relation between stiffness index and posterior wall(PWT).

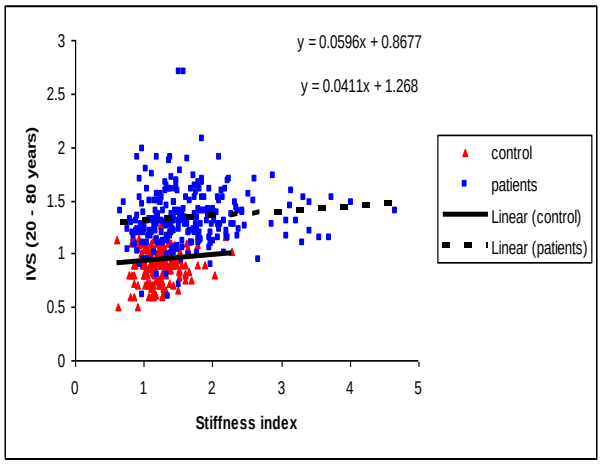

Fig. 4: The relation between stiffness index and interventricular septum(IVST).

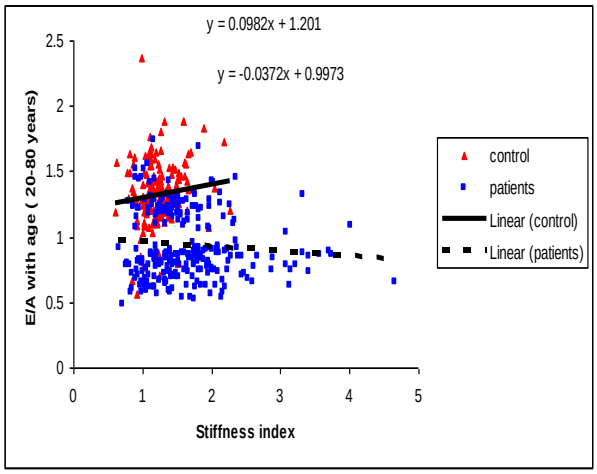

Fig.5: The relation between stiffness index and E/A ratio.

This physiologic adaptation eventually leads to increased LV chamber stiffness. Ventricular relaxation is also prolonged because of the increased proportion of collagen fibers and because of the slow sequence of electrical repolarization that leads to nonuniform relaxation [13]. A non invasive assessment of LV myocardial stiffness for hypertensive patients using an echo-Doppler and TDI index based on the pressure volume relation ((E/E_a)/LVEDD).

To determine the stiffness of LV (SLV) none invasively we have to measure the change of volume (dV) in diastole together with the corresponding change in magnitude of pressure (dP) Therefore.

With the use of tissue Doppler (dp) can be calculated from the ratio of E/E_a The early transmitral velocity (E) can be measured by conventional Doppler while E_a is measured by TD which measures the velocity of mitral annular which is related with the stiffness of the LV. Because the transmitral velocity E is related with the transmitral pressure difference and the extent of myocardial stiffness also related with the transmitral pressure. This determines a relationship between volume and pressure in the ventricle. In our results a sharp increase in E for control with the increase in (SLV) whiles a very significant reduction in the slope for patients Fig. 1. At the same time the graph between the late (active) transmitral velocity (A) with the ventricular stiffness is rising steeper for patients than controls this result may be explained on the bases of that, as the volume of the LV increases during diastole, the intracavitary pressure also increases. The magnitude of pressure change (dP) over a given change in volume (dV) defines the operating stiffness of the LV (SLV). Therefore, with increasing LV filling volume (preload) there is a proportionately larger increase in LV pressure and SLV this is what we have observed for control as LV relax faster than patients (Fig.2). Paradoxically, a slow LV relaxation rate decreases the apparent SLV during early filling, because myocardium continues to relax during this period [14], which tends to decrease LV cavity pressure. LV relaxation usually does not affect SLV during late diastole, when it is determined mostly by passive properties.

In this study the E/E_a ratio was significantly higher in patients with hypertension compared with the control group. This may be due to the early diastolic velocity (E_a) decreases progressively is reduced in patients that leading to an impaired relaxation such as LVH or restrictive cardiomyopathy, [15]. Results of this study have shown that the ratio E/A is decreased in hypertensive patients compared with normal, this may indicate myocardial relaxation is delayed, patients have a prolonged mitral filling pattern, decreased E-wave velocity and increased A wave, since more of the ventricular filling happens to occur at the beginning of diastole than at the end of it, with atrial contraction. In addition, increased filling pressure can mask these changes in mitral velocities. An E/A ratio < 1 have high specificity for abnormal LV relaxation, but can be seen with either normal or increased filling pressures, depending on how delayed LV relaxation is [16]. The relationship between blood flow derived velocities and regional myocardial wall motion derived velocities, measured by tissue Doppler echocardiography, and expressed as the ratio of peak early diastolic velocities E/E_a, [17]. Transmitral flow can be influenced by the increased fibrosis in the LV is known to be a part of the pathological process in hypertensive patients can slow the LV relaxation [18].

We have also shown by using combined conventional echocardiography and TDI index the diastolic stiffness was significantly higher in hypertensive patients compared to healthy subjects (Table 2). This may be due

to the fact that patients with hypertension experienced certain morphologic and structural changes of the left ventricle including left ventricular hypertrophy reducing LV compliance and increasing myocardial stiffness. This is in agreement with Lorell, et al., who suggested that chronic hypertension is the most common cause of diastolic dysfunction and failure as it leads to LV hypertrophy and increased connective tissue content, both of which decrease cardiac compliance [19].

A similar findings have been reported by Borlaug, et al., who suggested that myocardial contractility increases to match arterial load in asymptomatic hypertensive heart disease, and that progression to heart failure may be mediated by processes that simultaneously impair myocardial contractility and increase passive myocardial stiffness[20]. We have also shown increased LV diastolic stiffness index showed a significant relation with the degree of (PW and IVS thickness). These findings support the previous assumption that certain morphologic changes do occur in hypertensive patients leading to left ventricular hypertrophy and increased LV mass that increase myocardial stiffness and LV filling pressure.

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