Original Article

Assessment of Left Ventricular Diastolic Function in Hypertensive Patients Under Different Hemodynamic Conditions: Comparative Study Between Transmitral and Tissue Doppler Echocardiography

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OBJECTIVE

To evaluate the behavior of LV diastolic displacement velocities of basal posterior septum near mitral ring segment obtained by tissue Doppler in relation to mitral flow velocities of hypertensive subjects, submitted to preload increase by left inferior limbs elevation for 5 minutes, and during 1 minute of handgrip (conditions 1 and 2, respectively).

METHODS

Twenty five outpatients (15 men, 52 ± 11 years), with arterial hypertension > 3 years, by the transmitral flow Doppler variables: E, A and E/A, and of tissue Doppler: E', A' and E'/A', in basal situation and in conditions 1 and 2. For comparison of results in basal situation with conditions 1 and 2 a paired t test was applied.

RESULTS

E(cm/s) varied from $68,88 \pm 11,94$ to $75,82 \pm 15,71*$ and E'(cm/s) varied from $8,22 \pm 2,30$ to $8,31 \pm 2,24$ in condition 1 ($p<0.05$). In addition, a comparison of variation percent (%) of Doppler transmitral indices with corresponding tissue Doppler indices variation % showed a significant difference between E and E', with preload increase ($p=0.01$).

CONCLUSION

Patients with left ventricular adaptation to systemic arterial hypertension showed less modification of the index E´ than E, after preload increase maneuver, an evidence that may suggest its more ample utilization in the context of echocardiographic left ventricular diastolic function evaluation.

KEY WORDS

Left ventricular diastolic function; arterial hypertension; tissue Doppler.

Left ventricular (LV) diastolic dysfunction has been recognized as one of the leading causes of congestive heart failure (CHF)[1]. Several studies have indicated that 30% to 50% of CHF patients have normal or slightly impaired left ventricular systolic function. Some researchers propose that these patients should be designated as a "diastolic" heart failure group[2].

Since then, transmitral flow velocity profile at the LV entry pathway has been routinely assessed by spectral Doppler in the search for patterns that may characterize such a diagnosis and reveal something about disease prognosis[3]. Although this method had initially determined what would become known as diastolic measurement pattern, soon it was realized that evaluation results varied and reproducibility was limited[4].

A few studies showed the lack of a pattern of normality even with a clear clinical condition of diastolic dysfunction and heart failure. This lack of a pattern began to be designated as "pseudonormal pattern"[5]. Such a pattern results from increased left atrial pressure that becomes higher than the effects of LV relaxation. This dependence on velocity and the isovolumetric relaxation time in relation to LV relaxation, as well as to left atrial pressure, was noticed long ago, and these variables set a framework that conveys the limitations of the methods based on transmitral flow assessment[5].

This pattern may take place due to the fact that flow variables at the LV entry pathway are data determined by pressure differences between the left atrium and the LV during diastole. Evaluation of volume changes has the theoretical advantage of being less preload-dependent than TMD variables[6].

Tissue Doppler (TD) assesses high-amplitude and low-velocity signals from the myocardium[7]. This resource has been useful as a quantitative index of LV segmental function for analysis of both diastole[8] and systole[9]. Diastolic dysfunction studies have shown that this is relatively independent of preload[6] and it has been documented that probability of the same "pseudonormalizaton" seen with TMD appearing is low

TD assessment of the diastolic function may even be used to yield a highly accurate diastolic segmental analysis, as shown in a recent study[10], in which interrogation of multiple sites with this technique was possible using color tissue Doppler data and processing signals from all LV segments.

This clinical study was designed to assess the behavior of LV diastolic indices obtained by TDI as compared to those obtained by TMD under hemodynamic overload conditions – induced by changes in preload (leg-lifting) – and postload – by isometric exercise, (handgrip manouvre) – during analysis of the diastolic function of this chamber. The study population consisted of patients with systemic arterial hypertension (SAH) for at least three years, whose left ventricles had adapted to this condition.

METHODS

Patient selection - Twenty-five outpatients with SAH for at least three years were consecutively evaluated. Exclusion criteria were: clinical, electrocardiographic or echocardiographic signs of myocardial ischemia, valvar diseases, cardiac arrhythmias, coronary heart diseases and peripherical diseases. Moreover, chronic renal failure and diabetic patients were also excluded.

Investigators did not interfere with cardiac medications for SAH treatment. All individuals who underwent the test signed the written consent form expressing their agreement with the protocol approved by the institution Ethics Committee under the name "Assessment of the left ventricle diastolic function by pulsed-wave tissue Doppler in hypertensive patients", at the meeting held on January 19, 2001 (number 99376).

Echocardiography - The echocardiograms were performed with the HDI 5000, Philips-ATL, Seattle, WA equipment with patients at rest, lying down in the left lateral decubitus position. The images were acquired in standard tomography slices of the LV (longitudinal and transversal parasternal and, apical 4-, 5-, and 2- chamber views) with a 3.5 MHz transducer in harmonic mode. The images were archived on VHS tapes, and all analysis of spectral mitral and tissue Doppler, as well as the measurements of cavities and analysis of LV kinesis were performed on-line and off-line.

Parietal thicknesses of the interventricular septum (Psiv) and of the posterior wall (Pw), as well as LV diastolic (Dd) and systolic (Sd) diameters were obtained using the M mode; LV hypertrophy (LVH) was defined as a mass index $\geq$110g/sq m for women and 125g/sq m for men; AE dimension was also measured during late systole. Ventricular mass was automatically calculated by the equipment (mass formula: LV = 1.04 x [(Dd + Pw + Psiv)^3 – Dd^3]), and LV systolic and diastolic volumes, as well as ejection fraction, were obtained by the Teichholz method.

Transmitral flow velocities - LV apical four-chamber transthoracic images were recorded with standard 2.5 MHz transducer equipment. The volume sample was placed on the free-edge of mitral valve leaflets, at the apical four-chamber view. Flow velocity was recorded with the pulsed-wave Doppler method using the mean of three representative heart beats. Peak early diastolic velocity (E), peak atrial systolic velocity (A) and E/A ratio were determined.

Tissue Doppler imaging - Myocardial velocities were measured by activation of the color Tissue Doppler function, to record low-velocity and high-intensity signals, using a high number of frames (120 MHz) with a temporary resolution of 8 ms. After this period, the volume sample was placed at the basal portion of the posterior septum, and the peak early standard velocity pattern (E' cm/s), the peak velocity corresponding to the

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atrial systole or late diastolic filling (A' cm/s) and the E'/A' ratio were recorded[11].

Changes induced to hemodynamic conditions - Flow velocity profiles were obtained under baseline conditions, after manoeuvres to increase LV preload (condition 1) –by uniform and supported lifting of both legs to a 45-degree angle in relation to the bed during a continuous five-minute period – and after manoeuvres to increase LV postload (condition 2) – during a continuous one-minute period of sustained handgrip with a manual dynamometer at 30% of its maximum capacity.

Reproducibility - Interobserver variability – calculated as the difference between two measurements taken on the same patient by two different observers who had undergone the same training, divided by the mean value of the difference – varied from 1.5 to 2.6% for transmitral flow indices, and 0.8 to 1.7% for pulsed-wave tissue Doppler.

Statistical analysis - All values were presented as mean ± standard deviation (SD). The variables obtained at rest (baseline), through mitral Doppler and tissue Doppler were compared to the conditions associated with lower limb lifting (condition 1) and to the handgrip manouevre (condition 2). The mean TMD and TD differences between the baseline state and conditions 1 and 2 were compared by paired Student's t-test.

The percentage of variation of TMD indices under conditions 1 and 2, in relation to the baseline and compared to corresponding percentage values (%) of the variation of TD indices under conditions 1 and 2, also in relation to the baseline, were calculated in a second assessment. It was then verified that the mean values of the difference in percentages of variation (∆ %) were smaller than the standard deviation. The conclusion that data did not have a normal distribution led to the use of the Wilcoxon t-test to compare these variables. A value of $P < 0.05$ was considered statistically significant.

RESULTS

Sample characteristics - The sample consisted of twenty-five patients, aged 32 to 75 years (52 ± 10.9), with borderline anthropometric indices (body mass index = 27.9) who did not present extreme variations in mean arterial blood pressure or heart rate during the exam (MAP=108±20.7mmHg and HR=69.7±13.1bpm). Mean indices of systolic functions were normal, with an ejection fraction of 66.9±9.6% and a systolic shortening fraction of 37.5±7.1%, and adequate left ventricular mass (182.6±65.3g.) (table 1).

Baseline values - Under baseline conditions, values for velocities calculated by TMD were: E = 68.88 ± 1.94cm/s. A = 61.88 ± 12.99cm/s. E/A = 1.16 ± 0.31. Under baseline conditions, values for velocities calculated by TD were: E' = 8.31 ± 2.31cm/s. A' = 9.12 ± 1.93cm/s. E'/A' = 0.92 ± 028 (Table 2).

Table 1 - Sample clinical, echocardiographic and anthropometric data		
	Mean	**SD(±)**
Age (years)	52.0	10.9
EF (%)	66.9	9.6
SF (%)	37.5	7.1
LV MASS (g.)	182.6	65.3
MAP (mmHg)	108.7	20.7
HR (bpm)	69.7	13.1
BMI	27.9	4.8

EF- LV ejection fraction; SF- LV systolic shortening fraction; MAP- LV mean arterial blood pressure during the exam; HR- mean heart rate during the exam; BMI- body mass index.

Comparison between variations recorded by mitral Doppler and by tissue Doppler - The comparison between the percentages of variation in mitral flow velocities after changes in hemodynamic conditions and the percentages of variation obtained by tissue Doppler analysis revealed a significant difference between the ∆% recorded for the E wave ∆% *vs.* that of the E' wave (6.1% vs. 0%, P=0.01), which corroborates the nonvariability of E' following increase in preload (Table 2).

By comparing the magnitude of changes observed in the variables evaluated by both methods under baseline hemodynamic conditions, lower limb lifting and handgrip, and by applying the Wilcoxon t-test to evaluate differences between the measurement medians, it becomes clear that there is a significant difference between variations in the E waves measured by mitral Doppler and the E' waves measured by tissue Doppler.

DISCUSSION

Diastole and preload/postload interference - Transmitral flow pulsed-wave Doppler echocardiography is the most conventional method to evaluate diastole. The test, however, shows an important variation in E and A wave indices, and in the ratio between both waves (E/A) in view of changes induced by LV preload.

Tissue Doppler is the method that assesses segmental myocardial velocity at both diastole and systole. In a study comparing the interventricular septum on TD with that of transmitral flow in twenty patients with standard relaxation deficit (E/A wave ratio <1), who received an infusion of 700 ml of physiological saline, a significant change was observed in the E/A velocity ratio measured by transmitral flow (E/A=0.7 ± 0.1 *vs.* 0.9 ± 0.1 p < 0.01), which was not observed in the TD measurements (E'/A'=0.5 ± 0.1 vs. 0.5 ± 0.1. p=NS)[6].

These results point to the fact that assessment of segmental ventricular wall motion by TD is relatively independent from ventricular preload, as has already been suggested[12].

Table 2 - Transmitral flow Doppler and Tissue Doppler under baseline conditions and changes to pre- and postload

	Transmitral flow Doppler			Tissue Doppler		
	E	A	E/A	E`	A`	E`/A`
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Baseline	68.88 ± 11.94	61.88 ± 12.99	1.16 ± 0.31	8.22 ± 2.30	9.12 ± 1.93	0.92 ± 0.28
Condition 1	75.82 ± 15.71*	63.34 ± 16.61	1.30 ± 0.52	8.31 ± 2.24	10.05 ± 2.36*	0.86 ± 0.25*
Condition 2	70.30 ± 17.49	66.44 ± 17.55	1.14 ± 0.47	7.54 ± 1.86*	9.60 ± 2.20	0.81 ± 0.27*

*statistically significant difference compared to baseline with $p<0.05$. E- early transmitral diastolic flow velocity; A- late transmitral diastolic flow velocity; E'- early diastolic myocardial wall motion velocity; A'- late diastolic myocardial wall motion velocity.
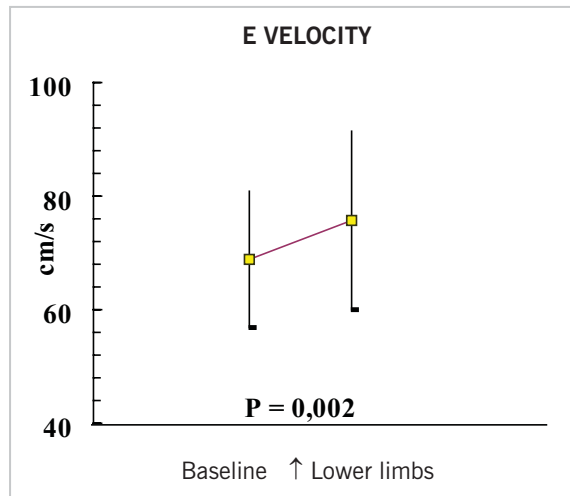

Fig. 1 - Change in E transmitral flow velocity at baseline state and after LV preload elevation by tilting lower limbs to 45°.
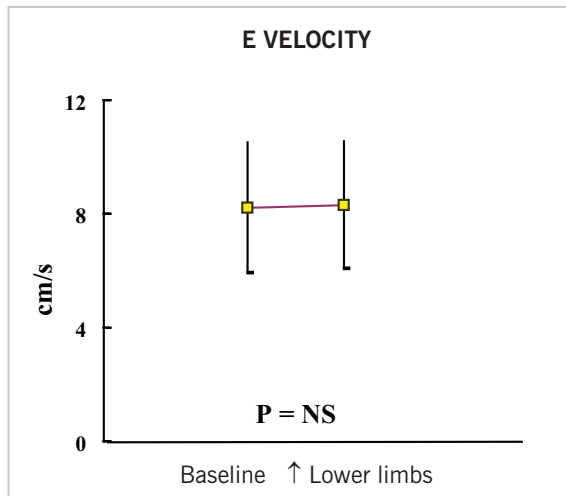

Fig. 2 - Change in E' myocardial motion velocity at baseline state and after LV preload elevation by tilting lower limbs to 45°.

Table 2 - Differences between percentages of variation (∆%) of TMD and TDI indices under conditions of pre- and postload elevation (C.1 and C.2, respectively) in relation to the baseline state

	TMD	TD	P
∆% E-E' C.1/baseline	6.1	0.0	0.010
∆% E-E' C.2/baseline	1.1	-7.1	0.045
∆% A-A' C.1/baseline	-1.2	10.0	NS
∆% A-A' C.2/baseline	10.7	8.2	NS
∆% E/A-E'/A' C.1/baseline	8.0	-6.3	0.001
∆% E/A-E'/A' C.2/baseline	-8.0	-14.3	NS

∆% E-E' C.1/baseline: difference in percentages of variation between E and E' waves after preload elevation; ∆% E-E' C.2/baseline: difference in percentages of variation between E and E' waves after postload elevation; ∆% A-A' C.1/baseline: difference in percentages of variation between A and A' waves after preload elevation; ∆% A-A' C.2/baseline: difference in percentages of variation between A and A' waves after postload elevation; ∆% E/A-E'/A' C.1/baseline: differences in percentages of variation between E/A and E'/A' ratios after preload elevation; ∆% E/A-E'/A' C.2/baseline: differences in percentages of variation between E/A and E'/A' ratios after postload elevation.

Concerning postload, both transmitral flow study and TD show variations. Oki et al[13], conducted a detailed study of pulsed-wave tissue Doppler. The authors[13] evaluated systolic and diastolic functions in twenty healthy individuals by echocardiogram before and after acute postload elevation, secondary to the infusion of angiotensin II (until they obtained a 30 mmHg elevation in mean arterial blood pressure). By doing so, the authors observed that all diastolic parameters (TMD and TD) underwent significant variations.

These findings suggested that neither method is entirely independent of postload-variations. This fact, however, enables their utilization to detect and follow-up the effect of LV postload variations, which could be useful, for instance, to keep track of clinical progression or, perhaps, to quantify response to drug therapies.

Motion of mitral annulus and adjacent segments of the ventricular myocardium - In view of the relatively fixed position of the ventricular apex during the cardiac cycle[14] – with LV relatively preserved as to its geometry – changes on the longitudinal axis would reflect volumetric changes, as indicated by Sohn et al[16]. In this study,

the analysis of the wall motion in the basal portion of the interventricular was deliberately chosen, since this myocardial portion adjacent to the mitral annulus moves in a more parallel fashion than the others (such as the anterior, lateral and inferior face), as already highlighted by Sohn et al[16].

As seen on Figure 3, the tissue Doppler exam captured, on the segment analyzed, two different movements towards the atrial chamber: one known as (E'), which starts simultaneously with the beginning of blood flow towards the LV entry pathway, where its peak velocity always occurs earlier than the peak flow velocity measured by mitral Doppler and is ended well before the blood inflow through the mitral orifice ends. The E' peak velocity is higher than the peak of another wave (A'), which is similar to the normal pattern of transmitral flow. As emphasized by Sohn et al[6], on their classical study**: "Mitral inflow after the end of left ventricular lengthening in the long-axis dimension. whether it is driven by pressure gradient or inertia. would lead to an increase in left ventricular volume in the short-axis dimension. which would mean higher compliance of the ventricular chamber in the short-axis dimension. Therefore, it may be assumed that a relaxation abnormality reflected in the long-axis dimension could potentially be evident earlier than clinical manifestation of global left ventricular relaxation abnormality".

This particular aspect in the methodology suggests that mitral Doppler analysis of the variables yields data concerning velocities, whereas with tissue Doppler measurements, data would reflect changes in volume.

Tissue Doppler: independence of preload changes - Data analysis in this study showed independence of E' values to the leg-lifting manouevre (condition 1, corresponding to change in preload). Other researchers – such as Garcia et al[12] – had already observed that E' velocity had only a slight relationship to E peak velocity, which indicated the relative independence of E' peak velocity obtained by tissue Doppler.

With this study, it is shown for the first time that, even with simpler and noninvasive bedside manoeuvres, no significant changes were observed in the peak early E' velocity of the mitral annulus on tissue Doppler (in contrast to E velocity on mitral Doppler), after a change in preload induced by elevation of the lower limbs.

Lower limb elevation and handgrip manoeuvres as a means to study adaptation of the heart to new hemodynamic conditions - Both manoeuvres used in this study, aiming at provoking new hemodynamic levels as a means to evaluate adaptive responses of circulation and the myocardium, have been employed for a long time. The preload increase mechanism with corresponding elevation of systemic arterial blood pressure was recently correlated to the release of powerful endothelial-action vasoconstrictors[15].

The mechanism of hemodynamic change induced by increase in preload (lower limb lifting), using the same protocol applied to the subjects in this study, has also already been established[16]. Comments made concerning magnitude of the impact of the manoeuvres on these hemodynamic variables warrant analysis. As seen in Figures 1 and 2 (with > preload), the magnitude of the changes was enough to interfere with behavior of the E variable, obtained by mitral Doppler in this study, but did not have any impact on the E' variable measured by tissue Doppler.

Tak et al observed a significant effect of the handgrip manoeuvre on preload and, consequently, on diastolic indices[17]. Other publications ratified the use of the manoeuvre to produce isometric exercise and an effective postload elevation, by applying 30% to 50% of maximal force over a period of 1 to 5 minutes[18,19]. We observed that a few patients had difficulties to maintain the same handgrip strength during the set time (five minutes), and a few individuals were only able to sustain a smaller load over a shorter time, even though this has been a commonly reported problem in studies previously published regarding utilization of similar-type isometric exercises.

Diagnosis of diastolic dysfunction of the basal segment of the interventricular septum as measured by tissue Doppler - The findings in this study point to a preload-independence, considering the E' wave
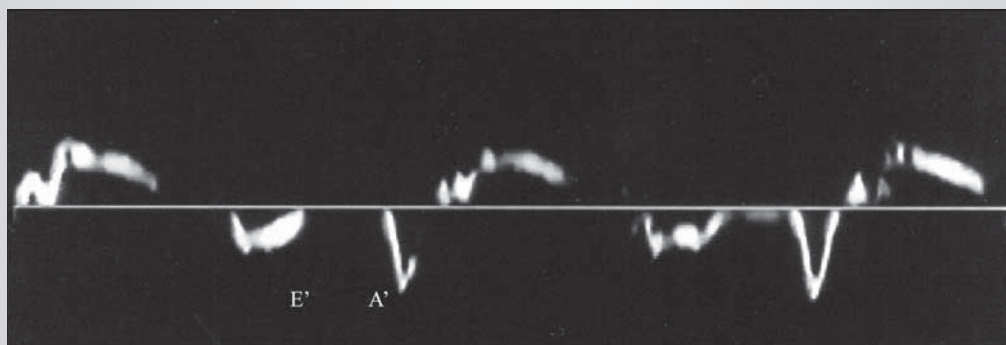

Fig. 3 - *Recording of myocardial diastolic motion E' and A' waves as measured by pulsed-wave tissue Doppler echocardiography.*

velocity. Statistical data and results obtained from the analysis of all variables are consistent with findings in literature[6,12,13,16].

Application of the findings in this study to clinical practice - In patients with the 'pseudonormalization" pattern, whose parameters may be obtained both by mitral Doppler and tissue Doppler, the variation of peak E and E' velocities, as well as the E/A ratio in relation to the E'/A' ratio, may be employed to differentiate this 'pseudonormal' pattern from a normal filling pattern.

Considering that the most common practice in echocardiographic procedures has been to try to differentiate this 'pseudonormal' pattern from normal diastolic function pattern by analyzing the pulmonary vein flow pattern – which is not always useful for this purpose in this subgroup of patients – the adoption of the simple manoeuvres proposed in this study may be useful for these patients. Moreover, variation in TD indices after the postload changes reported in this study suggest that these indices may be used to monitor the diastolic function of hypertensive patients being treated with medication to reduce postload.

Study limitations - This study, similarly to others previously published, has several practical limitations. Among them: 1) considering that patients with left ventricular asynergy were left out, it is possible that patients with kinesis abnormalities (for instance, those affecting the basal segment of the interventricular septum) may present abnormalities in the profiles of the variables analyzed, which does not express the overall behavior of the ventricle, which may be normal for the behavior of its diastolic function parameter[16]; 2) we have opted to measure myocardial velocity at the region more adjacent to the annulus on the interventricular septum, which corresponds more exactly to the basal segment of the posterior interventricular septum. However, due to the fact that it is subject in a lower degree to the translational movement of the myocardium, this approach has the disadvantage of being affected whenever the right ventricular function is altered. For instance, secondarily to pulmonary hypertension, especially if this chamber also presents signs of associated dysfunction[16]; 3) since one of the exclusion criteria was that patients should not be in sinus rhythm, it is possible that these findings may not be applicable to those with atrial fibrillation, for instance; 4) although less affected than mitral Doppler analysis, the constraining aspect of an inadequate acoustic window has to be taken into consideration. The Doppler diastolic evaluation is usually also affected by tachycardia, valvar diseases and cardiac rotational movement[20].

Conclusions - In patients with the left ventricle adapted to arterial hypertension, the diastolic motion of the myocardial segment adjacent to the mitral annulus measured by tissue Doppler was less dependent on preload than when assessed by the transmitral flow Doppler. This fact suggests the validity of the method as a coadjuvant index for assessment of LV diastolic function in this group of patients. We may also conclude that TD indices were significantly affected by postload variation, and that they could be used to monitor and follow-up the diastole after antihypertensive treatment with postload-reducing drugs.

Potencial Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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