Pulse pressure/stroke volume: a surrogate index of arterial stiffness and the relation to segmental relaxation and longitudinal systolic deformation in hypertensive disease

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Aims Pulse pressure/stroke volume (PP/SV) is regarded as a surrogate index of arterial stiffness (AS). Strain echocardiography is a novel method to evaluate systolic and diastolic left ventricular (LV) function. The aim of this study was to investigate the effect of AS on segmental relaxation and systolic deformation in hypertensive disease.

Methods and results We evaluated 70 hypertensive patients and 30 non-hypertensive volunteers. The patients were divided as follows: without global diastolic dysfunction (HTN-N) and with global diastolic dysfunction (HTN-DD). The segmental and global longitudinal strain (S) and strain rate (SR) and early and late diastolic SR were recorded from 18 segments. The number of segments with abnormal relaxation (SR/E/SR/A < 1.1) was calculated as segmental DD. Pulse pressure/SV index was used as a surrogate marker of AS. Arterial stiffness was higher in HTN-N and was more pronounced in the HTN-DD group compared with the control (1.45 ± 0.38 vs. 1.79 ± 0.36 vs. 1.21 ± 0.31 mmHg m²/ml, all P < 0.05). HTN-N had increased segmental DD compared to control despite the normal conventional indices of diastolic dysfunction. Global longitudinal deformation of the HTN-N group was similar to the control; HTN-DD also showed evidence of LV hypertrophy (LVH) and had more extensive segmental DD and deteriorated global systolic deformation compared with the control, despite the normal ejection fraction (segmental DD: 11 ± 3 vs. 4 ± 2, P < 0.05 and strain: 17.7 ± 2.8 vs. 21.2 ± 2.3%, P < 0.05). The deterioration of AS in the hypertensive group was accompanied with a particular distribution of segmental DD that was more pronounced at the basal regions compared with apical LV territories. Arterial stiffness and LV mass index are found to be independent predictors of segmental DD, mean Ea, and global systolic deformation.

Conclusion Arterial stiffness and LVH are independently related to abnormal segmental relaxation and global longitudinal systolic deformation in hypertensive disease.

Introduction

The pathophysiological background of systemic hypertension involves not only the classical hallmark of altered vascular resistance but also changes in vascular stiffness, which refers to conduit arteries, mainly of the aorta, and its principal branches. Increased arterial stiffness (AS) is regarded as an independent predictor of all causes of cardiovascular mortality in patients with essential hypertension. Among several methods that have been described for the evaluation of AS, the pulse pressure (PP)-to-stroke volume (SV) method (PP/SV) is regarded as a surrogate index to measure AS or total arterial compliance in humans. The PP method has been used in large-scale studies such as the LIFE study, and it has been utilized for the estimation of AS on treated or untreated hypertensive patients.

Previous studies have investigated the effects of increased AS on the left ventricle (LV). These studies have shown that structural and functional myocardial abnormalities such as diastolic dysfunction or longitudinal systolic dysfunction can be related to increased AS, as a result of ageing or disease. However, the estimation of diastolic dysfunction

KEYWORDS
Arterial stiffness; Hypertrophy; Diastolic dysfunction; Strain

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was usually based on conventional indices that represent the global status. Recent studies have demonstrated that altered segmental relaxation, based on strain echocardiography, may be a better method to evaluate changes in diastolic function in hypertension, as it is evident before global indices of diastolic dysfunction become informative.\(^\text{10,11}\)

Although longitudinal dysfunction based on annular velocities has also been found to be related to increased AS,\(^\text{9}\) the effect of AS on LV deformation has not been extensively investigated.

Hence, the aim of this study is to investigate the effect of AS on segmental relaxation, evaluated by strain techniques, global longitudinal systolic deformation, and LV remodelling in middle-aged hypertensive patients under treatment.

**Methods**

**Study subjects**

The study population consisted of 70 patients with essential hypertension recruited from the hypertension outpatient clinic and the Echocardiography Department and 30 non-hypertensive volunteers for control.

Participants were excluded if they were not in sinus rhythm or if they had a history of coronary artery disease, regional wall motion abnormalities, mitral or aortic stenosis, congenital disease, cardio-myopathy, mitral or aortic regurgitation, pericardial disease, or cor pulmonale. All patients had a history of hypertension for more than 1 year and were currently under medical treatment. The control group consisted of volunteers who were normotensive, according to their BP measurements and medical records. The advanced age of some participants appeared to be the main risk factor for diastolic abnormalities in that group.

All subjects were evaluated for global diastolic dysfunction according to published guidelines of the European Working Group, based on known conventional echocardiographic criteria [E/A, deceleration time (DT), isovolumic relaxation time (IVRT), pulmonary veins S, D, A, and A flow velocities], along with tissue Doppler parameters (E/E\(_\text{a}\)).\(^\text{12-15}\)

The diagnosis of global diastolic dysfunction was based on the following criteria: E/A\(_\text{50y} = 1.0 \) and DT\(_\text{50y} > 220 \) ms, E/ A\(_\text{50y} < 0.5 \) and DT\(_\text{50y} > 280 \) ms, and/or IVRT\(_\text{50y} > 92 \) ms, IVRT\(_\text{50y} > 100 \) ms, and/or pulmonary S/D\(_\text{50y} > 1.5 \) or S/D\(_\text{50y} > 2.5 \) and/or E/E\(_\text{a}\) mean > 15. The Valsalva manoeuvre, pulmonary venous recordings, and annular tissue Doppler tracings were also used for the diagnosis of pseudonormal type of diastolic dysfunction.

The patients were divided into two groups: hypertensive without global diastolic dysfunction (HTN-N) and hypertensive with global diastolic dysfunction (HTN-DD). The estimation of AS was conducted in all the participants and was based on the PP method.

The study was approved by the Local Research Ethics Committee.

**Echocardiography**

All the participants were studied by using standard two-dimensional and Doppler echocardiography with Toshiba Aplio model SSA-770A. Parasternal and apical projections were obtained according to the recommendations of the American Society of Echocardiography (ASE).\(^\text{16}\) LV ejection fraction (EF) was derived using Simpson’s modified biplane method. Left ventricular mass was estimated with the area-length formula as described in detail in the ASE document on LV quantification.\(^\text{17}\) Left ventricular mass index (LVM\(_i\)) was then calculated using the formula: LV mass/BSA, where BSA is the body surface area. Relative wall thickness (RWT) was estimated according to the formula: RWT = 2\(r\) / posterior wall thickness(LVEDD), where LVEDD is the left ventricular end-diastolic diameter. Hypertrophy was defined as LVM\(_i\) > 115 g/m\(^2\) in men and > 95 g/m\(^2\) in women.\(^\text{17}\)

Pulsed-wave Doppler of transmural LV inflow was performed in the apical four-chamber view, with the sample volume placed at the level of the mitral valve tips. Peak velocities of E and A waves and their ratio E/A, DT, and LV isovolumic relaxation time (IVRT) were measured. Pulsed tissue Doppler recordings from the septal and lateral sites were also recorded from the apical four-chamber view. Mean Ea was estimated averaging the septal and lateral values. Left ventricular filling pressures were estimated by calculating the E/E\(_\text{a}\) mean ratio.

**Tissue Doppler imaging samples acquisition for strain–strain rate analysis**

Tissue Doppler images of cine loops of three cardiac cycles from the lateral, septal, anterior, inferior anteroseptal, and posterior walls from the apical four-, three-, and two-chamber views were acquired separately at end-expiratory apnoea and stored digitally. To optimize the tissue velocity signals, the two-dimensional image was optimized to obtain a clear differentiation between the myocardium and the blood pool. We used the narrowest image sector angle possible (30\(^\circ\)) to achieve the maximum colour Doppler frame rate, typically > 150 frames/s. The recorded wall was positioned in the centre of the sector, so that the direction of the motion interrogated was as near as possible parallel to the direction of the insonating beam, giving an insonation angle < 15\(^\circ\) in all the recordings in order to avoid underestimation of values due to angle dependency. The insonation frequency was set at 2.8 MHz. Filter harmonic imaging was set as a standard for all the recordings. The PRF was adjusted accordingly, avoiding aliasing, and was typically ~4.2 kHz.

**Strain–strain rate off-line analysis**

The analysis of strain and strain rate (SR) parameters was performed off-line using the incorporated USTQ-770A programme of the Toshiba Aplio System. One sample volume region of interest (ROI) was placed at the basal part of each LV segment, so that there was no migration beyond the limits of the selected myocardium. An automatic ROI tracking mode was activated in order to ensure that measurements reflected the motion of a myocardial tissue segment throughout the cardiac cycle. We used a 6 mm × 9 mm oval ROI for longitudinal measurements. The systolic SR parameters of basal, mid, and apical segments were analysed separately from each LV wall in the longitudinal direction, and the average of the values of three consecutive cycles was calculated for each parameter. The myocardial systolic strain parameters were calculated by integrating the SR profiles over time and compensating for drifting over the cardiac cycle. End-systolic strain was determined.

In order to define the end of systole, timing information was used from blood pool pulsed or continuous wave Doppler tracings recorded from cycles with comparable R-R interval. The aortic valve closure click was considered as the end of the systole.

Eighteen LV segments (basal, mid, and apical of each wall) were averaged from each patient in order to estimate the mean (Global) longitudinal strain (S) and SR values.

The same sample volume (ROI) was used to measure diastolic SR parameters. The eighteen LV segments were also assessed for segmental diastolic dysfunction. Early and late diastolic SR parameters S\(_\text{E}\) and S\(_\text{A}\) of basal, mid, and apical segments were recorded separately from each LV wall in the longitudinal direction, and their ratio E/A, DT, and L V isovolumic relaxation time (IVRT) were measured. Pulsed tissue Doppler recordings from the septal and lateral sites were also recorded from the apical four-chamber view. Mean Ea was estimated averaging the septal and lateral values. Left ventricular filling pressures were estimated by calculating the E/E\(_\text{a}\) mean ratio.

**Arterial stiffness**

Haemodynamic measurements were performed in a quiet laboratory. After supine rest, the patients’ peripheral blood pressure was recorded over the brachial artery of the right arm using a validated semi-automated oscillometric device (Omron CP-705; Omron
Healthcare, Milton Keynes, UK). Three measurements were taken 2 min apart. The mean value of the last two measurements was taken as a representative of brachial blood pressure. Pulse pressure was estimated by the formula: PP = systolic blood pressure (SBP) – diastolic blood pressure (DBP). Mean arterial pressure (MAP) was estimated by the formula: MAP = DBP + 1/3 (SBP – DBP).

Stroke volume was calculated by the invasively validated method given by the formula: SV = aortic annular cross-sectional area × (Doppler velocity–time integral of aortic flow), as previously described, and indexed for BSA (SVi) to account for differences in body size.

Arterial stiffness was then calculated using the formula: AS = PP/SVi.4

Statistical analysis

Data were analysed using SPSS 12 software (SPSS, Chicago, IL, USA). Continuous variables, expressed as mean ± SD, were compared using the Student’s t-test for independent groups if the assumption of normality of distribution was justified, and if not, the Mann–Whitney U-test was employed. The two-tailed \( t \)-test was used to test the null hypothesis for categorical variables. Linear regression was used to investigate the relation between two parametric variables. Pearson’s correlation was used to evaluate bivariate linear relations.

Multiple linear regression was performed, applying an enter method, in order to estimate independent predictors for diastolic dysfunction (segmental DD and mean Ea) and longitudinal systolic dysfunction (systolic strain).

Segmental DD, mean Ea, and mean strain were set as dependent variables sequentially. Arterial stiffness (PP/SVi), hypertrophy (LVMI), age, gender, and BMI were set as independent parameters.

Results

Characteristics of the study population

General and standard echocardiographic parameters as well as clinical details of the study groups are summarized in Tables 1 and 2. Males outnumbered women, especially in the control group. Hypertensive patients had similar BSA, but were more obese and had higher blood pressure measurements compared with the control. Relative wall thickness and LVMI were progressively higher in the HTN-N and HTN-DD groups compared with the control group. Hypertrophy was present in 72.5% (29/40) of the HTN-DD group and borderline LV hypertrophy (LVH) in 10% (3/30) of the HTN-N group. None of the control group had evidence of LVH. Patients with diastolic dysfunction had hypertension

| Table 1 General and echocardiographic characteristics of the study groups |
|--------------------|-----------------|-----------------|
|                     | Control, n: 30  | HTN-N, n: 30    | HTN-DD, n: 40  |
| Age (years)         | 47.5 ± 6.6     | 49.5 ± 8.2      | 51.3 ± 7.8     |
| Male                | 76.7% (23)     | 60% (18)        | 57.5% (23)     |
| WT (mm)             | 8.9 ± 1.1      | 9.8 ± 1.0*      | 11.9 ± 1.8*†   |
| RWT                 | 0.37 ± 0.03    | 0.41 ± 0.06*    | 0.50 ± 0.10†   |
| LVMi (g/m²)         | 91.3 ± 16.0    | 101.5 ± 17.1*   | 127.2 ± 23.7†  |
| BSA (m²)            | 1.95 ± 0.24    | 2.93 ± 4.9*     | 28.8 ± 4.6*†   |
| BMI (kg/m²)         | 26.4 ± 3.3     | 1.69 ± 11.6     | 16.7 ± 10.5†   |
| Height (m)          | 1.74 ± 0.11    | 7.3 ± 6.1*      | 10.2 ± 6.8†    |
| HTN (years)         | –              | 136.0 ± 15.4*   | 148.1 ± 19.4†  |
| SBP (mmHg)          | 122.8 ± 9.0    | 83.0 ± 8.1*     | 82.6 ± 9.3*    |
| DBP (mmHg)          | 80.0 ± 4.2     | 101.4 ± 10.9*   | 104.1 ± 11.8*  |
| MAP (mmHg)          | 95.0 ± 5.6     | 52.6 ± 12.6*    | 64.9 ± 14.5†   |
| PP (mmHg)           | 43.7 ± 8.3     | 47.6 ± 7.4     | 46.2 ± 7.7     |
| LVEDD (mm)          | 48.2 ± 6.1     | 19.0 ± 3.6     | 28.4 ± 4.1     |
| LVEESD (mm)         | 30.3 ± 4.3     | 24.0 ± 2.8      | 24.3 ± 2.5     |
| LVEDD (mm/m²)       | 24.7 ± 2.4     | 74.4 ± 7.3      | 68.0 ± 9.1     |
| LVMI (g/m²)         | 180.4 ± 27.3   | 189.6 ± 41.5    | 238.9 ± 42.9†  |
| EF (%)              | 84.3 ± 15.8    | 86.5 ± 18.4     | 130.6 ± 19.6†  |
| DT (ms)             | 70.4 ± 10.2    | 73.1 ± 10.7     | 59.5 ± 15.5†   |
| IVRT (ms)           | 50.1 ± 10.9    | 55.8 ± 12.8     | 72.1 ± 18.5†   |
| E/A                 | 1.36 ± 0.23    | 1.31 ± 0.28     | 0.82 ± 0.21†   |
| HR (bpm)            | 73.5 ± 9.3     | 69.3 ± 11.1     | 68.5 ± 14.2    |
| LA (mm)             | 36.2 ± 4.4     | 37.8 ± 3.9      | 42.8 ± 4.3†    |
| ACE inhibitor (%)   | –              | 66*             | 70*            |
| β-blocker (%)       | –              | 40.5*           | 39*            |
| Ca++ inhibitor (%)  | –              | 33*             | 46*            |
| Diuretic (%)        | –              | 15*             | 28*            |
| Hypercholesterolaemia (%) | 20 | 45* | 53* |
| Diabetes (%)        | 4              | 5               | 4.5            |
| Smoking (%)         | 7              | 7               | 9              |

HTN-DD, hypertensives with diastolic dysfunction; HTN-N, hypertensive without diastolic dysfunction.

*P < 0.05: HTN-N or HTN-DD vs. control.
†P < 0.05: HTN-DD vs. HTN-N.
for longer periods (HTN years) and were taking more angiotensin-converting enzyme (ACE) inhibitors, Ca inhibitors, and diuretics, compared with those without diastolic dysfunction (HTN-N). There was no significant difference in EF among the study groups.

Diastolic dysfunction

All the patients with global DD (HTN-DD) appeared to have two or more conventional echocardiographic indices (DT, E/A, IVRT, and pulmonary S/D), suggestive of diastolic dysfunction. The HTN-DD group had lower septal and mean early diastolic mitral annulus velocities, higher filling pressures (E/Ea), and more segments with abnormal relaxation pattern (segmental DD) compared with HTN-N and the control group (Table 2, Figure 1). Hypertensive patients without global DD, based on conventional indices, had an increased per cent incidence of abnormal relaxation at the basal, mid, and apical segments compared with controls. However, patients with global DD appeared to have the highest per cent incidence of segments with abnormal relaxation at basal, mid, and apical territories, compared with both HTN-N and the control groups.

Longitudinal systolic dysfunction

Strain echocardiography revealed that hypertensive patients with diastolic dysfunction had lower mean (global) longitudinal strain and SR, compared with HTN-N and control, despite the normal EF estimated by conventional echocardiography. Hypertensive patients without global diastolic dysfunction (HTN-N), although that they had a tendency to have lower global longitudinal strain and SR, appeared to have statistically similar global longitudinal function compared with controls.

Arterial stiffness

Arterial stiffness (PP/SVi) was higher in the hypertensive groups and appeared to be more pronounced in patients extension to mid-segments. In the HTN groups, the lesions were also located at the basal parts of the heart, but extended far more towards the mid and apical regions. As presented in Table 3, the (%) incidence of segments with abnormal relaxation increased progressively from base to apex in all groups. Hypertensive patients without global DD, based on conventional indices, had an increased per cent incidence of abnormal relaxation at the basal, mid, and apical segments compared with controls. However, patients with global DD appeared to have the highest per cent incidence of segments with abnormal relaxation at basal, mid, and apical territories, compared with both HTN-N and the control groups.

Myocardial topography of abnormal relaxation

In the control group, the segments with an abnormal relaxation pattern were mainly located basally, with progressive extension to mid-segments. In the HTN groups, the lesions were also located at the basal parts of the heart, but extended far more towards the mid and apical regions. As presented in Table 3, the (%) incidence of segments with abnormal relaxation increased progressively from base to apex in all groups. Hypertensive patients without global DD, based on conventional indices, had an increased per cent incidence of abnormal relaxation at the basal, mid, and apical segments compared with controls. However, patients with global DD appeared to have the highest per cent incidence of segments with abnormal relaxation at basal, mid, and apical territories, compared with both HTN-N and the control groups.

Table 2 Arterial stiffness and echocardiographic characteristics of the study groups

<table>
<thead>
<tr>
<th></th>
<th>Control, n: 30</th>
<th>HTN-N, n: 30</th>
<th>HTN-DD, n: 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial stiffness (PP/SVi) mmHg m²/mL</td>
<td>1.21 ± 0.31</td>
<td>1.45 ± 0.38*</td>
<td>1.79 ± 0.36**</td>
</tr>
<tr>
<td>Segmental DD (N)</td>
<td>4 ± 2</td>
<td>6 ± 3*</td>
<td>11 ± 3**</td>
</tr>
<tr>
<td>Mean longitudinal SR (1/s)</td>
<td>1.68 ± 0.24</td>
<td>2.02 ± 0.26*</td>
<td>1.72 ± 2.8**</td>
</tr>
<tr>
<td>Mean longitudinal strain (%)</td>
<td>21.2 ± 2.3</td>
<td>20.2 ± 2.5</td>
<td>17.0 ± 2.8**</td>
</tr>
<tr>
<td>LWS (Kdynes/cm²)</td>
<td>82.5 ± 11.4</td>
<td>82.2 ± 19.1</td>
<td>70.3 ± 26.5**</td>
</tr>
<tr>
<td>Mean mitral annulus (Ea), cm/s</td>
<td>10.9 ± 1.8*</td>
<td>8.1 ± 1.3*</td>
<td>5.8 ± 1.4**</td>
</tr>
<tr>
<td>Septal mitral annulus (Ea), cm/s</td>
<td>9.9 ± 2.2</td>
<td>7.8 ± 1.9*</td>
<td>9.2 ± 3.3**</td>
</tr>
<tr>
<td>Filling pressures E/Ea mean</td>
<td>6.1 ± 0.9</td>
<td>1.78 ± 0.9</td>
<td>1.57 ± 3.3**</td>
</tr>
</tbody>
</table>

HTN-DD, hypertensive with diastolic dysfunction; HTN-N, hypertensive without diastolic dysfunction; mean mitral annulus Ea = septal+lateral/2.

*P < 0.05: HTN-N or HTN-DD vs. control.

†P < 0.05: HTN-DD vs. HTN-N. Segmental DD = number (N) of segments with altered relaxation pattern.

Figure 1 Bar graphs representing arterial stiffness (PP/SVi) and segmental diastolic dysfunction (DD) (number of segments with strain rate SRE/SRA < 1.1) in the study groups.
with diastolic dysfunction compared with the control (Figure 1). Arterial stiffness was associated with parameters of segmental and global diastolic dysfunction [positive relation with segmental DD as well as with DT, IVRT and filling pressures (E/Ea) and negative relation with septal Ea, mean Ea and E/A] and was inversely associated with mean longitudinal systolic S and SR (Figure 2). Furthermore, AS was also positively related to indices of LV remodelling (WT, RWT, LVMI), as well as with ageing and obesity (BMI) (Table 4).

**Independent predictors**

In a multi-variate analysis, AS was found to be an independent predictor for abnormal segmental relaxation (segmental DD), mean Ea, and longitudinal systolic strain, irrespective of LV hypertrophy (LVMI), age, sex, and BMI (Table 4).

The relationship of the AS (PP/SVi) with the segmental DD and the longitudinal systolic strain remained significant even after the inclusion of a steady (non-pulsatile) component of BP (mean BP) in the regression model. An index of LV hypertrophy (LVMI) was also found to exert independent effects on diastolic (segmental DD, mean Ea) and systolic (longitudinal systolic strain) LV function (Table 4).

The intra-observer variability, based on the variability coefficient for strain and SR, was <10%, as reported previously in detail.\(^{11}\)

### Discussion

The key finding of the present study is that peripheral arterial stiffness is an independent predictor of segmental relaxation and longitudinal systolic deformation in hypertensive disease. It was also shown that hypertensive patients without global diastolic dysfunction based on conventional indices, but with higher AS compared with the control, appear to have significant segmental diastolic dysfunction detected by strain echocardiography and preserved global longitudinal deformation. With the progression of diastolic abnormalities (HTN-DD group), global longitudinal deformation appears also to become compromised compared with the control, along with the deterioration of peripheral AS. Finally, we also demonstrated that LV hypertrophy as expressed by LVMI is an independent predictor of abnormal segmental relaxation as well as of global longitudinal systolic deformation in systemic hypertension.

### Table 3

| Topography and per cent incidence of segments with abnormal relaxation |
|--------------------------|-----------------|-----------------|
|                         | Control,       | HTN-N,          | HTN-DD,         |
|                         | \(n:30\)       | \(n:30\)        | \(n:40\)        |
| Basal segments (%)      | 29.5           | 42.8*           | 80.5†           |
| Mid segments (%)        | 12.8           | 26.1*           | 61.1†           |
| Apical segments (%)     | 6.0            | 13.3*           | 41.6†           |

\(*P < 0.05: \text{compared with control}\); \(\hat{P} < 0.05: \text{compared with HTN-N}\).

### Figure 2

![Scatter diagrams and regression line with 95% confidence and 95% prediction lines of relations of arterial stiffness (PP/SVi) with segmental diastolic dysfunction, left ventricular mass index, global longitudinal strain, and mean mitral annulus Ea.](image)
Arterial stiffness and diastolic function

Previous studies have found a correlation of AS with global diastolic function using various methodological approaches, many suggesting that AS is independently related to diastolic dysfunction. The main causes of diastolic abnormalities in the presence of increased AS have also been described to be the result of increased loading, myocardial and vascular fibrosis, and decreased subendocardial perfusion.

This study further explores the effect of peripheral vascular stiffness on the LV diastolic function, associating changes of segmental relaxation based on strain echocardiography with a surrogate index of AS.

Our findings show that segmental diastolic dysfunction might initially be present in ‘healthy’ middle-aged individuals, probably due to the ageing process, even undetectable by the conventional indices of diastolic dysfunction. Apical myocardial territories seem to be the less-affected regions in that group (Table 3). With the deterioration of AS in hypertensive patients (HTN-H), after-loading increases, and abnormal segmental relaxation becomes more extensive compared with controls. Similarly in that group, there are more pronounced abnormalities at the base than at the apical LV regions. When AS becomes even more compromised (HTN-DD), abnormal relaxation becomes more extensive basally and further progresses towards the apical myocardial territories. In that stage, global LV diastolic dysfunction becomes detectable by conventional indices.

Topography of segmental diastolic dysfunction

The particular basal to apex distribution of segmental diastolic dysfunction reported in this study could be explained by the previously suggested higher regional wall stress/loading and/or wall thickness at the basal parts of the heart, compared with the apical territories of the LV.

In turn, the basally suggested higher wall stress could be the result of the higher radius of curvature of the basal myocardial regions compared with the apical part. Thus, increased regional wall stress and/or wall thickness, probably in combination with known hormonal substances such as the angiotensin-aldosterone components, may activate regional cascades of events that are more pronounced at the basal parts of the heart and may promote interstitial fibrosis, subendocardial ischaemia, and/or myocyte impairment. These pathological phenomena have been previously described as common causes of global diastolic dysfunction and could also be responsible for the presence of regional abnormal relaxation.

Arterial stiffness and longitudinal systolic deformation

Although previous studies have shown that longitudinal systolic function may be depressed in hypertensive patients, the present study further highlights that AS is inversely and independently related to global longitudinal deformation. It is well known that longitudinal fibres, due to their position in the subendocardial region of the myocardium, are more susceptible to increased loading/wall stress; a fact that predisposes them to microvascular ischaemia and fibrosis.

Arterial stiffening contributes to an increased afterload and systolic LV wall stress. Furthermore, it is associated with higher velocity transmission of the pulse wave generated by LV ejection, which results in an early return of reflected waves from the periphery, augmenting the central aortic pressure and decreasing the diastolic pressure and coronary perfusion. The combination of increased loading/afterload, LV hypertrophy, and compromised coronary perfusion may result in exacerbation of subendocardial and microvascular ischaemia, leading not only to diastolic dysfunction but also to subendocardial fibrosis and compromised longitudinal systolic deformation.

The role of left ventricular hypertrophy

Previous studies have shown the detrimental role of LV hypertrophy on diastolic and systolic LV function, as well as the patient’s prognosis. It is important to underline that in this study, hypertensive patients with global diastolic dysfunction (HTN-DD) also had evidence of LVH.
It seems that the hypertrophic state is responsible for significant intrinsic myocardial abnormalities, exerting a direct effect on LV diastolic and systolic function independent of the peripheral AS. Those abnormalities could be the result of inadequate blood supply to meet the demands of the thickened myocardium and consequent ischaemia, alteration of contractile proteins, or remodelling of the extracellular matrix and subsequent fibrosis.

Clinical significance

The implementation of strain echocardiography in the evaluation of hypertensive patients provides the advantage of earlier identification of functional abnormalities, which cannot be detected by conventional methods. This was particularly obvious in the present study in the control and the HTN-N groups, with important clinical implications for earlier risk stratification and proper therapeutic intervention.

The pathophysiological role of increased AS upon LV function was also highlighted in this study, and these findings may better explain common features of hypertensive heart disease.

Limitations

The independent effect of AS compared with systolic blood pressure could not be investigated in this study. This is because the formula PP/SVI is not entirely independent of systolic BP, as the latter is used for the estimation of the PP. As a consequence, the pathophysiological findings described in our study might also be attributed not only to pure AS and the elastic properties of conduit vessels, but also to the severity of arterial hypertension. Thus, further studies using direct measurement of central AS may be required to confirm our findings.

The PP method, based on peripheral BP measurements, is likely to be accurate for the estimation of AS only in patients with no or minor amplification of PP from the aorta to the peripheries; hence, it must be used cautiously with subjects exhibiting physiological pulse wave amplification. However, as physiological amplification is reduced in the elderly and in patients with decreased elasticity of central conduit arteries, the difference of central and peripheral PP becomes smaller.

The influence of vasoactive medical therapy on the study’s measurements could not be accurately analysed. Vasodilator drugs such as calcium-blocking agents and ACE inhibitors have little direct effect on elastic arteries, which are mainly affected by the increased AS, but can markedly lower systolic pressure by decreasing muscular artery stiffness.

Conclusion

Arterial stiffness and LVH are independently related to altered segmental relaxation pattern and longitudinal systolic deformation in hypertensive disease.

Strain echocardiography can detect early diastolic and systolic abnormalities in the LV function, which are not detectable by conventional methods.

Conflict of interest: none declared.

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