Heart

Arterioventricular Coupling and Ventricular Efficiency After Antihypertensive Therapy

A Noninvasive Prospective Study

Martin Osranek, John H. Eisenach, Bijoy K. Khandheria, Krishnaswamy Chandrasekaran, James B. Seward, Marek Belohlavek

Abstract—Patients with hypertension exhibit impaired energetic coupling between the ventricle and the arterial system, leading to reduced cardiac mechanic efficiency and exercise capacity. We tested whether blood pressure normalization with current antihypertensive therapy can improve arterioventricular coupling. Eighteen hypertensive patients without other cardiovascular disease were examined before and after antihypertensive therapy. Transthoracic echocardiography was performed. Central aortic pressure waveforms, including end-systolic pressure, were derived from radial artery applanation tonometry. Afterload was increased with isometric handgrip exercise. Central aortic end-systolic pressure and ventricular volumes at rest and handgrip were used to calculate ventricular elastance, effective arterial elastance, arterioventricular coupling (effective arterial elastance/ventricular elastance), and mechanical efficiency. After 142±67 days, systolic blood pressure decreased from 150.9±14.6 to 119.8±9.2 mm Hg (P<0.00001), diastolic blood pressure from 85.9±14.8 to 68.8±8.4 mm Hg (P=0.00002), and cardiac output from 5.8±1.7 to 4.9±1.8 L/min (P=0.03). Resting left ventricular end-systolic volume, ejection fraction, and septal thickness did not change. Ventricular elastance increased from 1.7±1.0 to 3.2±1.4 mm Hg/mL (P=0.00002), whereas effective arterial elastance decreased from 1.4±0.5 to 1.2±0.4 mm Hg/mL (P=0.02). Effective arterial elastance/ventricular elastance decreased in all patients, from 1.1±0.8 to 0.4±0.2 (P=0.0002). Efficiency improved at rest (72.9±5.8% versus 83.5±5.7%; P<0.00001) and during handgrip (63.5±7.8% versus 78.9±7.1%; P<0.00001). In hypertensive patients, optimal brachial and central blood pressure reduction shifts arterioventricular coupling from cardiac output maximization to ventricular mechanical efficiency optimization. This occurs before significant changes in ventricular geometry and may be responsible for early clinical improvements. (Hypertension. 2008;51:275-281.)

Key Words: arteriosclerosis ■ blood pressure ■ echocardiography ■ hemodynamics ■ hypertension

There is emerging evidence that systemic arterial hypertension is associated with the increasing prevalence of heart failure with preserved ejection fraction. The American College of Cardiology/American Heart Association guidelines for diagnosis and management of chronic heart failure, therefore, assign antihypertensive therapy a class I indication.

Even before the development of clinical heart failure or left ventricular hypertrophy, hypertension seems to accelerate the process of arterial and ventricular stiffening that usually occurs with aging, when reduced arterial compliance is matched by increased ventricular systolic contractility and diastolic stiffness. Consequently, blood pressure lability increases, whereas exercise capacity and left ventricular filling are impaired. These changes have been termed “coupling disease,” because coupling between the arterial system and the left ventricle is compromised. Therapeutic approaches to reverse this process by directly targeting arterial and ventricular wall stiffness are still under investigation. Meanwhile, control of hypertension with attention to the lowering of central aortic pressures and the use of drugs like angiotensin II receptor blockers have been demonstrated to improve outcome. The direct effects of this approach on the arterioventricular interaction are, however, not known.

In this prospective study, we assessed the effects of blood pressure lowering on arterioventricular coupling and cardiac mechanoenergetics according to a framework originally developed by Sunagawa et al, where left ventricular elastance (E\textsubscript{e}) and effective arterial elastance (E\textsubscript{a}) are expressed by the ventricular end-systolic pressure (ESP)-volume relationship and the ratio of ESP:stroke volume, respectively. This concept has been extensively validated by mathematical modeling, animal studies, and observational research in hu-
mans. In the present study we used an entirely noninvasive approach, relying on fewer assumptions than previous human studies.

**Methods**

**Patients**

After approval by the institutional review board, patients with isolated essential hypertension were consented. Clinic outpatients with no exclusion criteria in their medical charts and sufficiently elevated blood pressure at a recent nurse blood pressure check were invited for the baseline examination during a telephone interview.

Patients with ≥1 year of untreated or inadequately treated blood pressure of >140 mm Hg systolic during office visits confirmed by 1 week of daily home measurements were eligible. We focused on systolic blood pressure, as in patients >50 years of age, diastolic blood pressures can be lower because of arterial stiffness. Exclusion criteria were ejection fraction <50%, clinical symptoms of heart failure, confirmed or suspected coronary artery disease, wave motion abnormalities, conduction abnormalities, atrial fibrillation, more than trivial valvular regurgitation or stenosis, intracavitary obstruction or obliteration during systole, and diabetes mellitus.

**Antihypertensive Therapy**

All of the patients were started on approved antihypertensive medication, and the treatment goal was optimization, i.e., a weekly mean systolic home blood pressure ≤120 mm Hg. Patients were instructed how to measure blood pressure at home twice daily and report weekly over the telephone. Therapy was titrated according to a standardized scheme, first maximizing dosages before adding further medications. First-line treatment was an angiotensin II receptor blocker, followed by a thiazide diuretic and β-blocker. Second-line treatment included the addition of a calcium channel blocker and/or angiotensin-converting enzyme inhibitor. Patients who had already been taking atenolol were switched to metoprolol or a β-blocker and/or angiotensin-converting enzyme inhibitor. Patients with ≥1 year of untreated or inadequately treated blood pressure of >140 mm Hg systolic during office visits confirmed by 1 week of daily home measurements were eligible. We focused on systolic blood pressure, as in patients >50 years of age, diastolic blood pressures can be lower because of arterial stiffness. Exclusion criteria were ejection fraction <50%, clinical symptoms of heart failure, confirmed or suspected coronary artery disease, wave motion abnormalities, conduction abnormalities, atrial fibrillation, more than trivial valvular regurgitation or stenosis, intracavitary obstruction or obliteration during systole, and diabetes mellitus.

**Echocardiography**

Transthoracic echocardiography (Vivid7, GE Healthcare) was performed in the left lateral decubitus position before and after treatment. Echo-Doppler images were analyzed offline, blinded to sphygmomanometric and baseline/follow-up information. Left ventricular volumes were measured offline according to American Society of Echocardiography recommendations from apical 4- and 2-chamber views using the standard biplane Simpson’s method. Left ventricular dimensions and wall thickness were obtained from parasternal long axis views and used to calculate end-systolic wall stress. Pulsed-wave tissue Doppler imaging of the interventricular septum was used to measure early diastolic myocardial peak velocity.

**Central Aortic Pressure Waveform Analysis**

Blood pressure was assessed oscillometrically beat-to-beat with a finger plethysmograph (Finapres Medical Systems) on the right arm and confirmed with a standard brachial cuff on the same arm at rest. Continuous plethysmographic systolic and diastolic blood pressures were then used to calibrate pressure waveforms obtained by applanation tonometry (SphygmoCor, AtCor Medical) on the right radial artery. A validated generalized transfer function was used to generate a corresponding central aortic pressure waveform, which has been shown to differ <1 mm Hg from invasively measured pressures at the aortic root. ESP and the beginning of the diastolic period were identified by the incisure at aortic valve closure. Furthermore, the augmentation index was defined as the augmented pressure due to wave reflection divided by pulse pressure. The Buckberg subendocardial viability index (SVI) was obtained by dividing the central diastolic pressure-time integral by the systolic pressure-time integral.

**Study Protocol**

Patients underwent one examination before and after antihypertensive treatment. At both examinations, echocardiographic, plethysmographic, and tonometric data acquisition were performed after 10 minutes resting and during afterload increase induced by isometric handgrip. At the baseline visit, after the resting examination and ≥10 minutes before isometric exercise, each subject performed 3 maximal voluntary left forearm contractions with a Stoelting handgrip dynamometer (Stoelting). The force of contraction was averaged, and a submaximal target of 40% was used for both the baseline and the follow-up visit. During the isometric exercise, subjects squeezed with their left arm at the target force until fatigue. The last set of continuously recorded data were used as exercise values.

**Data Analysis**

The slope of the ESP-volume relationship (Ea) was obtained by connecting the 2 points at different loading conditions in the pressure-volume diagram. Together, Ea, ESP, and ventricular volumes allow for an estimation of total cardiac work, or pressure-volume area (PVA). The PVA correlates linearly with myocardial oxygen consumption (MVVO2) and consists of performed stroke work and potential energy (PE) stored in the ventricle at the end of ejection. PE is represented by the triangular area defined by Ees, ESP, and end-systolic volume to the left of the pressure-volume loop (Figure 1). Mechanical work efficiency was expressed as stroke work/PVA, according to Burkhoff and Sagawa.

E was calculated as ESP/stroke volume, reflecting the mean and pulsatile components of arterial load better than mean arterial resistance and similar to a more complex 3-element Windkessel model. E can be depicted in the pressure-volume diagram, allowing for a direct comparison (Figure 1). The ratio of E/E represents arterioventricular coupling.

Data are expressed as mean±SD or as a proportion (%) of patients. Paired comparisons of measurements before and after treatment or of rest and grip were performed using the paired t test or Wilcoxon signed-rank test. The statistical software package was SPSS 13.0 (SPSS Institute Inc).

**Results**

Twenty patients were enrolled in the study, and 18 completed the protocol. Two were not compliant and did not reach the treatment goal. The mean age was 61.0±10.1 years, and 11 patients (61%) were men. The mean body surface area was 2.2±0.2 m², and the mean body mass index was 30.6±3.0 kg/m². The mean duration of hypertension was 5.7±3.3 years, ranging from 2 to 10 years. The classes of antihypertensive drugs used are shown in Table 1. The mean duration of follow-up was 142±67 days.

**Resting Measurements**

Mean brachial systolic blood pressure decreased by 21% from 150.9±14.6 to 119.8±9.2 mm Hg (P<0.0001), diastolic blood pressure by 18% from 85.9±14.8 to 68.2±8.4 mm Hg (P=0.0002), and pulse pressure by 18% from 63.7±15.0 to 51.0±11.2 mm Hg (P=0.002). Central ESP was lowered by 20% (Table 2). Left ventricular ejection fraction and interventricular septal thickness (11.0±2.1 versus 10.3±1.8 mm; P=0.12) did not change. Although relative wall thickness did not change (0.46±0.13 versus 0.47±0.14; P=0.68), end-systolic meridional myocardial wall stress decreased (66.1±28.4 versus 48.7±21.8 kdyn/cm²; P=0.005). Mitral early diastolic peak velocity E was unchanged (69.9±17.3 versus 69.7±16.1 cm/s; P=0.95), yet early diastolic myocardial peak velocity increased (5.9±2.2
versus 6.7±2.4 cm/s; \( P=0.04 \), leading to an improved early diastolic myocardial peak velocity ratio (13.8±7.9 versus 11.5±4.3; \( P=0.03 \)). Deceleration time remained unchanged (239.6±61.4 versus 255.0±70.1 ms; \( P=0.23 \)), whereas isovolumic relaxation time showed a trend toward shortening (101.7±27.8 versus 90.8±34.9 ms; \( P=0.06 \)).

**Changes With Isometric Exercise**

The mean handgrip force used was 15.1±6.0 kg, and the time to fatigue did not change significantly from baseline to follow-up (146±77 versus 204±110 seconds; \( P=0.13 \)). The increase in ESP with grip was greater at follow-up with 48% (40.4 mm Hg) than at baseline with 31% (33.3 mm Hg; \( P=0.007 \)). The heart rate increase elicited by handgrip remained unchanged (14.1±9.1 versus 13.3±7.0 s\(^{-1} \); \( P=0.63 \)).

After therapy, cardiac output was lower at rest, yet it now increased significantly with grip. Left ventricular volumes increased significantly during grip (Table 2). At follow-up, there was no significant drop in ejection fraction during grip like before treatment.

Although augmentation index and central augmented pressure increased with grip, they were not significantly changed after treatment (Table 2). The relative diastolic period and SVI both decreased with grip. At follow-up, SVI improved compared with baseline, especially during grip.

**Arterioventricular Coupling**

\( E_{es} \) increased from baseline to follow-up, whereas arterial elastance (\( E_a \)) decreased at rest and during grip at follow-up (Figure 1). As a result, the arterioventricular coupling ratio \( E_a:E_{es} \) decreased in all patients at rest and during grip (Figure 2). The relative decrease in \( E_a:E_{es} \) was greater in patients with a shorter history of hypertension (\( R^2=0.62; \ P=0.0001 \), although baseline \( E_a:E_{es} \) was not associated with the duration of hypertension (\( R^2=0.09; \ P=0.24 \)). After therapy, left ventricular stroke work was reduced at rest but unchanged during grip. As PE decreased with therapy (Table 3), cardiac work efficiency improved at rest and during grip (Figure 3). Using 90% of the peripheral systolic blood pressure as a surrogate for central ESP in our patients, \( E_a:E_{es} \) and work efficiency showed comparable changes in the same direction and to a similar extent.

**Discussion**

We provide the initial description of the effects of contemporary antihypertensive therapy on arterioventricular coupling and the consequences for ventricular mechanic work efficiency. Before therapy, we found \( E_a \) and \( E_{es} \) to be approximately equal, indicating optimization for maximum cardiac output.\(^ {14,22}\) After achieving blood pressure optimization, \( E_{es} \) increased, whereas \( E_a \) decreased, resulting in an \( E_a:E_{es} \) ratio near 0.5, consistent with the optimization of mechanical work efficiency found in normal hearts as described by Starling and others.\(^ {8,14,23–25}\) Analyzed separately, few of the echocardiographic imaging and tonometric arterial waveform parameters changed significantly with treatment. Only when left ventricular volumes and central aortic pressures were analyzed in conjunction and under varying loading conditions did the direct mechanoenergetic effects of blood pressure control become apparent.
Combining Noninvasive Techniques to Assess Cardiovascular Hemodynamics

The use of $E_m$ has been limited by 2 factors: the need for invasive pressure measurements and for either pharmacological or mechanical alterations of preload or afterload. Using brachial cuff pressures as a direct surrogate for central pressures in hypertensive patients with the potential of arterial stiffening is not recommended, especially not to monitor the changes with antihypertensive treatment, which can have varying effects on central pressures. In our study, we used an oscillometric finger plethysmograph to continuously calibrate peripheral arterial pressure waveforms obtained by applanation tonometry and to subsequently generate the central waveform. Using a handgrip maneuver to increase afterload, we were able to noninvasively calculate $E_m$ from separate central ESPs and echocardiographic left ventricular volumes.

Several investigators have attempted to obviate the need for invasive pressure measurements and loading maneuvers by estimating $E_m$ noninvasively from a single beat. Although these techniques can approximate the mean $E_m$ of a large group of patients, they result in considerable scatter and fail to detect changes of contractility in individual patients.

Left Ventricular Contractility and Diastole

The significant and uniform change toward an $E_a:E_m$ coupling ratio of 0.5 was principally mediated by increases in $E_m$ and less by the reduction of $E_a$. Normalization of ESP itself has beneficial effects on contractility, because $E_m$ becomes nonlinear and plateaus at elevated pressures. Furthermore, improvements during diastole could be responsible for this increase in contractility. Subendocardial coronary flow to the myocardium occurs almost entirely during diastole and depends not only on the patency of epicardial arteries but also on diastolic duration and pressure in the aortic root and the opposing intramyocardial pressure. Accordingly, $E_m$ decreases with inadequate coronary artery pressures. A useful concept is that of supply and demand, expressed as SVI, first described by Buckberg et al, which compares the diastolic pressure-time integral to the systolic work generated by the ventricle measured as tension-time index. A low SVI can cause subendocardial ischemia in patients with normal coronary arteries. We speculate that, in our patients with mild myocardial hypertrophy, the improvement of SVI and the reduction of intramyocardial wall stress at end systole play roles in the increase of $E_m$. Interestingly, the rightward shift of

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Table 2. Echocardiographic Measurements and Central Aortic Pressure Waveform Analysis

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Rest</th>
<th>Grip</th>
<th>Rest</th>
<th>Grip</th>
<th>Before vs After, $P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, s$^{-1}$</td>
<td>67.4±10.3</td>
<td>81.6±12.8†</td>
<td>60.9±9.1</td>
<td>74.3±11.2†</td>
<td>0.006 0.005</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>5.8±1.7</td>
<td>6.4±2.2</td>
<td>4.9±1.8</td>
<td>6.3±1.9*</td>
<td>0.03 0.92</td>
</tr>
<tr>
<td>Left ventricular end-diastolic volume, mL</td>
<td>145.8±34.1</td>
<td>162.4±40.2*</td>
<td>143.2±37.9</td>
<td>162.4±35.3*</td>
<td>0.57 0.99</td>
</tr>
<tr>
<td>Left ventricular end-systolic volume, mL</td>
<td>60.9±22.0</td>
<td>84.2±25.5†</td>
<td>64.2±24.5</td>
<td>78.2±25.3†</td>
<td>0.30 0.03</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>84.9±20.9</td>
<td>78.2±24.6</td>
<td>79.0±21.60</td>
<td>84.2±18.8</td>
<td>0.21 0.34</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>38.7±8.6</td>
<td>47.9±8.7†</td>
<td>55.5±8.4</td>
<td>52.3±7.7</td>
<td>0.11 0.07</td>
</tr>
<tr>
<td>Left atrial volume, mL</td>
<td>81.9±21.4</td>
<td>73.1±16.9</td>
<td>74.5±20.1</td>
<td>71.1±10.1</td>
<td>0.12 0.62</td>
</tr>
<tr>
<td>Left atrial volume index, mL/m²</td>
<td>38.1±8.7</td>
<td>34.5±8.5</td>
<td>34.8±8.5</td>
<td>33.4±4.5</td>
<td>0.13 0.56</td>
</tr>
<tr>
<td>Central systolic blood pressure, mm Hg</td>
<td>127.8±20.6</td>
<td>170.0±29.1†</td>
<td>100.2±10.6</td>
<td>146.8±24.9†</td>
<td>0.00004 0.007</td>
</tr>
<tr>
<td>Central diastolic blood pressure, mm Hg</td>
<td>66.3±14.2</td>
<td>89.1±20.1†</td>
<td>51.7±9.5</td>
<td>78.2±15.9†</td>
<td>0.002 0.06</td>
</tr>
<tr>
<td>Central pulse pressure, mm Hg</td>
<td>61.6±17.6</td>
<td>80.8±18.3†</td>
<td>48.4±10.9</td>
<td>68.8±17.9†</td>
<td>0.003 0.01</td>
</tr>
<tr>
<td>Central ESP, mm Hg</td>
<td>108.9±18.2</td>
<td>142.2±26.1†</td>
<td>84.7±10.4</td>
<td>125.1±22.0†</td>
<td>0.00004 0.03</td>
</tr>
<tr>
<td>Central AP, mm Hg</td>
<td>15.8±10.8</td>
<td>27.1±14.1†</td>
<td>13.3±6.6</td>
<td>23.3±13.5*</td>
<td>0.22 0.32</td>
</tr>
<tr>
<td>Aix, %</td>
<td>23.4±12.2</td>
<td>31.8±12.9†</td>
<td>25.9±11.9</td>
<td>32.1±14.0*</td>
<td>0.19 0.94</td>
</tr>
<tr>
<td>Aix at 75 min$^{-1}$, %</td>
<td>19.9±10.0</td>
<td>34.9±11.4†</td>
<td>19.4±10.6</td>
<td>31.8±14.4*</td>
<td>0.74 0.38</td>
</tr>
<tr>
<td>Diastolic period, %</td>
<td>64.2±3.6</td>
<td>56.4±5.2†</td>
<td>65.8±3.8</td>
<td>58.4±5.1†</td>
<td>0.07 0.11</td>
</tr>
<tr>
<td>SVI, %</td>
<td>132.2±17.9</td>
<td>97.6±21.0†</td>
<td>142.4±27.0</td>
<td>107.8±21.1†</td>
<td>0.05 0.04</td>
</tr>
</tbody>
</table>

$AP$ indicates augmented pressure; Aix, augmentation index; Aix at 75 min$^{-1}$; Aix adjusted for a heart rate of 75 min$^{-1}$.

$*P<0.05$ and †$P<0.001$ for comparison between rest and grip.

Figure 2. Arterioventricular coupling. $E_a$ indicates effective arterial elastance; $E_m$, left ventricular elastance.
Ees that we observed with antihypertensive treatment, including angiotensin II receptor blockers, resembles the opposite change described in experimental studies after the infusion of angiotensin II.33

Arterioventricular Coupling and Cardiac Efficiency

Whether the arterioventricular coupling ratio $E_a:Ees$ in the normal heart is set at 1 for maximum cardiac output or at 0.5 for maximum mechanical work efficiency has been a topic of investigation.34 Several human studies have since confirmed mathematical models predicting that the normal coupling ratio in healthy individuals is closer to 0.5 than to 1.0.8,14,23–25 A change in $E_a:Ees$ from 1.0 to 0.5 improves mechanical efficiency and results only in a minor decrease of stroke volume and cardiac output,14,23 which are usually elevated in hypertension.35 During aerobic exercise in normal individuals, $E_a:Ees$ usually decreases to even less than 0.5.8 In this context, an elevated $E_a:Ees$ ratio at rest would be disadvantageous. A higher $Ees$ and, thus, lower $Ea:Ees$ ratio also cause the heart to experience a smaller loss of mechanical efficiency when afterload is increased.14 This is especially beneficial, because with elevated afterload, total PVA and $MV\dot{O}_2$ already inevitably increase for a given stroke volume.7 The linear relationship between PVA and $MV\dot{O}_2$ is subject to an upward shift with increasing $Ees$. For the same PVA, a ventricle with greater $Ees$ also requires greater $MV\dot{O}_2$.36 For example, this mechanism takes place in the opposite direction when failing hearts with moderately decreased $Ees$ maximize stroke work with an $E_a:Ees$ of 1 but disproportionately increase PE and, therefore, PVA. The expected increase in $MV\dot{O}_2$ is effectively blunted by a reduced oxygen demand for a lower $Ees$.24 We did not measure $MV\dot{O}_2$ in our study, and, therefore, cannot determine to what extent the energetic cost for an approximate doubling of $Ees$ was balanced by the reduction of PVA. However, even if the increased $MV\dot{O}_2$ because of a higher contractile state would completely negate the benefits of improved mechanical efficiency at rest, it seems to be more advantageous for the cardiovascular system to operate at an $E_a:Ees$ less susceptible to loading changes and more capable of responding to exercise demands.

Limitations

Because our treatment goal was complete blood pressure normalization in each patient, a uniform drug regimen was not possible. We instead aimed to represent current clinical practice, with attention to central blood pressure reduction. Unlike other hypertension treatment trials comparing blood pressure reductions or clinical events, our study did not involve randomization with control subjects, and the results can be affected by a regression to the mean, especially because we are studying patients at the right end of the normal distribution of blood pressures. Assessing the effects of individual drugs or of long-term changes, such as regres-

**Table 3. Cardiovascular Performance Parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before</th>
<th>After</th>
<th>Before vs After, P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular elastance $E_{es}$, mm Hg/mL</td>
<td>1.7±1.0</td>
<td>3.2±1.4</td>
<td>0.000002</td>
</tr>
<tr>
<td>Arterial elastance $E_{a}$, mm Hg/mL</td>
<td>1.4±0.5</td>
<td>1.2±0.4</td>
<td>0.02</td>
</tr>
<tr>
<td>$E_a/Ees$</td>
<td>1.1±0.8</td>
<td>0.4±0.2</td>
<td>0.0002</td>
</tr>
<tr>
<td>PVA, J</td>
<td>167.5±45.1</td>
<td>105.3±26.4</td>
<td>0.0003</td>
</tr>
<tr>
<td>Stroke work, J</td>
<td>122.0±33.8</td>
<td>88.3±24.5</td>
<td>0.0009</td>
</tr>
<tr>
<td>PE, J</td>
<td>45.4±15.8</td>
<td>17.0±6.3</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Mechanical efficiency, %</td>
<td>72.9±5.8</td>
<td>83.5±5.7</td>
<td>&lt;0.00001</td>
</tr>
</tbody>
</table>

$*P<0.05$ and $†P<0.0001$ for comparison between rest and grip.

![Figure 3. Cardiac mechanical work efficiency. Cardiac mechanical work efficiency expressed as (100 x stroke work / (stroke work + PE)). A, At rest. B, During peak handgrip.](http://hyper.ahajournals.org/Downloaded from http://hyper.ahajournals.org/)
sion of ventricular hypertrophy, was not our aim and should be the goal of future studies.

Along with previous studies, we estimated the pressure-volume loop as a simple square. In patients with increased afterload and impaired diastolic filling, pressure increases toward the end of systole and diastole lead to an overestimation of stroke work and mechanical efficiency with this method, especially before antihypertensive treatment. Calculations of $E_a$, $E_v$, and arteriovenous coupling are not affected by this assumption.

Conclusions
This study describes for the first time how blood pressure normalization in hypertensive patients restores ventricular mechanic efficiency, increases contractility, and normalizes arteriovenous coupling. These improvements occur early after successful blood pressure control, before significant changes in ventricular geometry. Combining entirely noninvasive technologies and a simple loading maneuver, our novel approach allowed for detection of hemodynamic changes that are not readily appreciated by either imaging or sphygmonanometric methods alone.

Perspectives
In hypertensive patients with mild left ventricular hypertrophy, we found alterations in arteriovenous coupling and ventricular efficiency similar to those described in moderate systolic dysfunction. Lowering of central blood pressures was essential to the normalization of these parameters. Our method, especially before antihypertensive treatment, could be important in echocardiography. The remaining authors report no conflicts.

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Disclosures
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