Exercise and Central Blood Pressure

Exercise Central (Aortic) Blood Pressure Is Predominantly Driven by Forward Traveling Waves, Not Wave Reflection

Martin G. Schultz, Justin E. Davies, Phillip Roberts-Thomson, J. Andrew Black, Alun D. Hughes, James E. Sharman

Abstract—Exercise hypertension independently predicts cardiovascular mortality, although little is known about exercise central hemodynamics. This study aimed to determine the contribution of arterial wave travel and aortic reservoir characteristics to central blood pressure (BP) during exercise. We hypothesized that exercise central BP would be principally related to forward wave travel and aortic reservoir function. After routine diagnostic coronary angiography, invasive pressure and flow velocity were recorded in the ascending aorta via sensor-tipped intra-arterial wires in 10 participants (age, 55±10 years; 70% men) free of coronary artery disease with normal left ventricular function. Measures were recorded at baseline and during supine cycle ergometry. Using wave intensity analysis, dominant wave types throughout the cardiac cycle were identified (forward and backward, compression, and decompression), and aortic reservoir and excess pressure were calculated. Central systolic BP increased significantly with exercise (Δ=19±12 mm Hg; P<0.001). This was associated with increases in systolic forward compression waves (Δ=12×10^6±17×10^6 W·m^−2·s^−1; P=0.045) and forward decompression waves in late systole (Δ=9×10^6±6×10^6 W·m^−2·s^−1; P<0.001). Despite significant augmentation in BP (Δ=9±6 mm Hg; P=0.002), reflected waves did not increase in magnitude (Δ=−1×10^6±3×10^6 W·m^−2·s^−1; P=0.2). Excess pressure rose significantly with exercise (Δ=16±9 mm Hg; P<0.001), and reservoir pressure integral fell (Δ=−5×10^5±5×10^5 Pa·s; P=0.010). Change in reflection coefficient negatively correlated with change in central systolic BP (r=−0.68; P=0.03). We conclude that elevation of exercise central BP is principally because of increases in aortic forward traveling waves generated by left ventricular ejection. These findings have relevance to understanding central BP waveform morphology and pathophysiology of exercise hypertension. (Hypertension. 2013;62:175-182.) ● Online Data Supplement

Key Words: aorta ■ blood pressure ■ exercise ■ pulse wave analysis ■ venous reservoirs ■ wave intensity ■ wave reflection

A hypertensive response to exercise independently predicts cardiovascular events and mortality.1 However, the physiological mechanisms contributing to elevation in blood pressure (BP) with exercise are poorly understood. Previous studies have focussed on changes to brachial BP during exercise, but little attention has been directed toward understanding central (aortic) BP (the pressure to which organs such as the heart are exposed). Because of variations in pulse pressure amplification, central systolic BP is usually lower than brachial systolic BP and may differ greatly between individuals with the same brachial systolic BP.2-5 Moreover, central to peripheral pressure amplification may be magnified during exercise,6,7 and we have also reported that individuals with increased cardiovascular risk because of hypercholesterolemia have significantly raised central systolic BP and augmentation index, but not brachial systolic BP, during light to moderate exercise.8 Thus, risk related to BP may be better assessed by central BP during light to moderate intensity exercise, rather than resting brachial BP. However, despite these observations, little is known of the contributing central hemodynamics.

At rest, with each heart beat a pressure wave generated by the left ventricle is propagated along the arteries and is reflected back toward the heart at sites of impedance mismatch. Return of this reflected pressure wave is proposed to be the sole contributor to augmentation (increase) in central BP.1 However, more recently it has been proposed that aortic pressure can be regarded as the sum of a reservoir pressure and an excess pressure, composed of discernibly discrete forward and backward propagating waves.9,10 Moreover, recent work has proposed that such discrete reflected waves make only a minor contribution to augmentation of the central BP under resting conditions.11 Whether the rise in central systolic BP with exercise can be attributed to increases in discrete forward or reflected waves, or the reservoir, has not been determined in humans. Given the large increase in systemic vasodilation that

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occurs during exercise, reduced augmentation of central BP during exercise might be expected. Therefore, we hypothesized that discernible wave reflection would be negligible with exercise and that the increase in central systolic BP would be predominantly driven by increased forward waves and possibly reduced aortic compliance. We aimed to determine this using wave intensity analysis and separation of invasively acquired aortic pressure into reservoir and wave components during exercise.

Methods

Study Participants

Twenty patients scheduled to undergo routine diagnostic coronary angiography at the Royal Hobart Hospital, Hobart, Australia were recruited for participation in this study. All patients had a clinical indication for diagnostic angiography (eg, chest pain or positive exercise stress test) and were consented to participate before the clinical procedure, if there was a reasonable likelihood of meeting the study inclusion criteria. Inclusion criteria were a normal coronary angiogram (<50% angiographic stenosis of any major coronary artery), preserved left ventricular function (ejection fraction >50%), and no aortic valve disease (<20 mm Hg aortic valve gradient). None of the participants had a clinical history of impaired sympathetic function. On the basis of our previous invasive exercise study,14 in which there was a 26±14 mm Hg increase in aortic systolic BP from rest to exercise, we determined that 10 participants were required to complete the study to detect a 211 mm Hg change in aortic systolic BP (α=0.05, β=0.20; ie, less than half the expected systolic BP change from rest to exercise seen previously). A total of 20 patients were recruited to allow for data loss because of failure to meet inclusion criteria or other reasons. Of the 20 patients who consented, 6 were identified as having clinically significant coronary artery disease and were excluded. A further 2 patients experienced radial artery spasm during the catheterization procedure, and it was deemed inappropriate to continue. From the remaining 12 participants, data from 2 individuals were excluded from the analysis because of poor-quality flow velocity recordings.

Study Protocol

After the standard coronary angiogram procedure (and confirmation of nonsignificant coronary vessel disease), hemodynamic measurement of ascending aortic pressure and flow velocity was made under baseline (resting) conditions and during supine cycle ergometry. Continuous measurements of hemodynamic data were made for ≥2 minutes during both resting and exercise conditions. Exercise was performed in the supine posture using a cycle ergometer (Monarch Rehab Trainer 881E, Sweden) which was placed on the catheter laboratory table. Load was set at 50 W, and patients were asked to cycle at a comfortable pace so that steady state heart rate at a light to moderate workload could be achieved, at which point all exercise hemodynamic measures were undertaken. Participant clinical characteristics were extracted from medical records. The study was approved by the University of Tasmania Human Research Ethics Committee, all participants provided written informed consent, and procedures were performed in accordance with the declaration of Helsinki.

Hemodynamic Data

Continuous simultaneous pressure and flow velocity were recorded by a single-use 0.014”, straight tip intra-arterial pressure, and Doppler flow wire (Combowire, Volcano Therapeutic Corp, Rancho Cordova, CA). Arterial access was made via standard radial puncture, and measurements were performed through a 100-cm 5F rim catheter (Cook Medical, Bloomington, IL). The catheter was positioned in the ascending aorta ≥5 cm distal to the valve leaflets and turned 180° with the tip facing away from the valve and flow direction. The Combowire was advanced ≥5 mm beyond the catheter tip, where it was stabilized by the catheter, away from the arterial wall and in the center of flow (confirmed by fluoroscopy). To obtain quality pressure and flow velocity, small rotational movements of the Combowire were made once it was positioned in the ascending aorta. Analogue outputs of the pressure and flow velocity signals were digitized (PowerLab ML870 8/30, AD Instruments, Bella Vista, Australia) and recorded using LabChart 7 software (AD Instruments). Data were acquired at a sampling rate of 1000 Hz, and a simultaneous 3-lead ECG recording was made to calculate heart rate. Pressure and flow velocity were calibrated offline using a 2-point calibration method. To obtain calibration values, 2 raw test signals of a known value were sent from the Combowire to acquisition software before measurement of hemodynamic data.

Aortic pressure and flow velocity captured during rest and exercise were ensemble averaged offline for ≤6 heart cycles. Aortic systolic BP was considered the maximum pressure point and the diastolic BP the minimum pressure point on the waveform. Aortic pulse pressure was defined as the difference between the systolic and diastolic BP. Aortic mean arterial pressure was calculated from integration of the waveform using custom written software. Aortic augmentation pressure (systolic BP−pressure at the first systolic shoulder or inflection point [P1]) was calculated using customized Matlab software to identify the inflection point on the aortic pressure wave (taken as P1) and calculated augmentation pressure in relation to maximal (systolic) pressure. Augmentation pressure as a percentage of the overall pulse pressure was calculated to derive the augmentation index (AIx). Aortic wave speed was calculated using the sum of squares method at the measurement site as previously described. Reproducibility of pressure and flow velocity measures was good (see online-only Data Supplement).

Wave Intensity Analysis

Identification of waves responsible for directing the flow of blood in an arterial segment was performed by wave intensity analysis. Waves were classified with respect to (1) their direction in relation to the direction of aortic flow (forward and backward) and the gradient of pressure change across the wavefront: waves with positive pressure gradients being termed compression waves, and waves with negative pressure gradient termed decompression waves. For example, in the proximal aorta, waves can originate from a proximal source (ie, the left ventricle) or from a distal source (eg, reflections from the peripheral vasculature). Acceleration of blood can result from compression waves of proximal origin or from decompression waves of distal origin, whereas deceleration of blood can result from compression waves of distal origin or decompression waves of proximal origin. Previous studies in the aorta have identified a consistent pattern of 3 dominant waves as shown in Table 1. In some recordings smaller waves were evident (typically with intensities <5% of the intensity of the initial compression wave) but not analyzed.

Wave intensity data for each individual, at rest and during exercise, were calculated from the ensemble averaged pressure and flow velocity data as previously described, and outlined in the online-only Data Supplement. Separation of pressure into forward and backward components was performed without (prereservoir subtraction) and after subtraction of the aortic reservoir pressure (postreservoir subtraction). Reflection coefficient was calculated as the ratio of peak backward to forward propagating pressure and multiplied by 100 to obtain percentage values. A wave reflection index was also calculated to determine the magnitude of wave reflection, using the ratio of backward compression wave integral to forward compression wave integral, and multiplied by 100 to obtain percentage values. Impedance analysis was also performed as described by Hughes and Parker, and is also described in the online-only Data Supplement.

Reservoir and Excess Pressure Separation

Ensemble averaged aortic pressure was separated into 2 components (reservoir and excess pressure; Figure 1). Reservoir pressure can be calculated using both pressure and flow velocity, or from pressure
Table 1. Origin and Nature of Waves in the Ascending Aorta as Defined by Wave Intensity Analysis

<table>
<thead>
<tr>
<th>Pressure</th>
<th>Flow Velocity</th>
<th>Wave Nature</th>
<th>Wave Origin</th>
<th>Proposed Cause of Wave</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase</td>
<td>Increase</td>
<td>Forward compression</td>
<td>Proximal</td>
<td>Left ventricular ejection</td>
</tr>
<tr>
<td>Increase</td>
<td>Decrease</td>
<td>Backward compression</td>
<td>Distal</td>
<td>Reflection of forward compression wave</td>
</tr>
<tr>
<td>Decrease</td>
<td>Decrease</td>
<td>Forward decompression</td>
<td>Proximal</td>
<td>Deceleration of left ventricular ejection before aortic valve closure</td>
</tr>
</tbody>
</table>

alone. Both methods produce quantitatively similar results, with only slight variation in shape of the initial upward inflection of reservoir pressure. As this did not alter the overall results (ie, the change in reservoir pressure from rest to exercise), and for simplicity, we present results from the pressure-only separation. This method of separation is outlined in the online-only Data Supplement. Excess pressure was calculated by subtracting the reservoir pressure from aortic pressure and represents pressure attributable to discrete forward and backward waves. Separated pressures are presented as peak or integral values.

Statistical Analysis
All statistical calculations were made using PASW 18.0 (SPSS Inc, Chicago, IL). Data were visually inspected for normality of distribution, and skewed data were log transformed if required. The change in all hemodynamic, wave intensity, and separated pressure wave parameters from rest to exercise were compared using paired Student t tests. Because of the shortening of the cardiac cycle, which occurs with exercise (increased heart rate), all integral data were additionally adjusted for heart rate, by dividing the integral values of wave intensity, reservoir, and excess pressure with heart rate (beats per minute). Pearson correlation coefficients (r) were calculated to assess relationships among hemodynamic, wave intensity, and wave separation variables at rest and during exercise. P<0.05 was considered statistically significant.

Results

Patient Characteristics
The clinical characteristics of study participants are outlined in Table 2. Participants were predominantly middle aged, men, and of elevated body mass. Most participants received treatment for hypertension and hyperlipidemia. Two participants had type 2 diabetes mellitus and 4 had a smoking history (current or former).

Hemodynamic Parameters: Changes From Rest to Exercise
Central systolic BP, mean arterial pressure, pulse pressure, P1, augmentation pressure, Aix, and heart rate increased significantly from rest to exercise (P<0.05 for all; Table 3). Aortic wave speed also increased significantly from rest to exercise, indicating a decrease in proximal aortic compliance. There were no significant changes in central diastolic BP and aortic flow velocity.

Wave Intensity: Changes From Rest to Exercise
Wave intensity data are presented in Table 4. Exercise caused significant increases in both the magnitude of the net forward compression and decompression waves. These remained significant after adjustment for heart rate for the forward compression waves (Δ=+19±24×10^4 W·m^−2·s^−1; P=0.03) and for the forward decompression waves (Δ=+14±19×10^4 W·m^−2·s^−1; P=0.001). The magnitude of the backward compression (reflected) wave was not significantly changed, before or after adjustment for heart rate (Δ=+2±5×10^4 W·m^−2·s^−1; P=0.2). The reflection coefficient decreased from rest to exercise, whether analyzed as peak (Table 4) or integral data (−9±28%; P=0.4) but these changes were not statistically significant. Figure 2 shows a representative example of wave intensity analysis of the response to exercise. In this example, from rest to exercise, heart rate and aortic systolic pressure increased significantly, along with large increases in both forward compression and decompression waves. Despite this, the backward compression (reflected) wave remained largely unchanged in magnitude.

Impedance and Forward and Backward Pressure (Without Reservoir Pressure Subtraction): Changes From Rest to Exercise
Pressure separation using impedance analysis was quantitatively similar to time-domain analysis, in that forward pressure increased significantly from rest to exercise, whereas backward pressure was not significantly changed (Table 4). Figure S1 in the online-only Data Supplement provides an example of wave separation at rest and during exercise using time-domain and frequency-domain approaches—the results are qualitatively indistinguishable. Analysis of impedance spectra plots was consistent with the findings of wave intensity analysis showing no evidence of increased wave reflection after exercise (Figure S2).

Forward and Backward Pressure (With Reservoir Pressure Subtraction): Changes From Rest to Exercise
Findings after subtraction of the aortic reservoir pressure were qualitatively similar to that of prereservoir extraction. Separated forward pressure increased significantly from rest to exercise and backward pressure remained unchanged. The reflection coefficient tended to be reduced from rest to
Table 2. Clinical Characteristics of the Study Population (n=10)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean±SD or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (men, %)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Age, y</td>
<td>55±10</td>
</tr>
<tr>
<td>Height, cm</td>
<td>173±11</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>93±17</td>
</tr>
<tr>
<td>Brachial systolic blood pressure, mmHg</td>
<td>126±15</td>
</tr>
<tr>
<td>Brachial diastolic blood pressure, mmHg</td>
<td>79±11</td>
</tr>
<tr>
<td>Body mass index, kg·m⁻²</td>
<td>32±5</td>
</tr>
<tr>
<td>Treated hypertension</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Antihypertensive medication</td>
<td></td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Angiotensin receptor blocker</td>
<td>1(10)</td>
</tr>
<tr>
<td>Non-dihydropyridine calcium channel blocker</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Diuretic</td>
<td>1 (10)</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus, %</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Smoking history, %</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Statin therapy, %</td>
<td>6 (60)</td>
</tr>
</tbody>
</table>

Smoking history is current or former. Blood pressure recorded at preprocedure examination.

Reservoir and Excess Pressure: Changes From Rest to Exercise

The integral of the excess pressure increased significantly from rest to exercise, before (Table 4) or after accounting for heart rate (Δ=+4±4×10³ Pa·s; P=0.008). Peak excess pressure increased significantly with exercise. From rest to exercise, the integral of the aortic reservoir pressure was significantly reduced (Table 4) and remained so after correcting for heart rate (Δ=−13±12×10³ Pa·s; P=0.008). Peak aortic reservoir pressure was unchanged with exercise. At rest, reservoir pressure comprised 68% of total pressure, and during exercise it dropped to 49% of total pressure. A typical example of the pressure waveform separated into forward and backward components at rest and during exercise in a 41-year-old male is depicted in Figure 3.

Associations Among Hemodynamic, Wave Intensity, and Separated Pressure Variables

Under both rest and exercise conditions, aortic systolic BP correlated closely with peak reservoir pressure (r=0.810; P=0.005 and r=−0.679; P=0.031, respectively). The change in central systolic BP was associated with the change in peak reservoir pressure (r=0.873; P=0.001). The change in aortic wave speed was associated with the change in backward compression and forward decompression waves (prereservoir subtraction: r=0.634; P=0.049 and r=0.681; P=0.030, respectively), as well as the change in the excess pressure integral (r=0.645; P=0.044). The change in the excess peak and excess integral pressure was strongly associated with the change in the integrated intensity of the forward compression wave (postreservoir subtraction: r=0.903; P<0.001 and r=0.633; P=0.050, respectively), but not the backward compression wave (postreservoir subtraction: r=0.224; P=0.535 and r=0.419; P=0.228, respectively). The change in the forward compression wave also positively correlated with the change in heart rate (postreservoir subtraction: r=0.672; P=0.033). There was also a significant negative (inverse) relationship between change in reflection coefficient (prereservoir subtraction integral values) and the change in central systolic BP (r=−0.682; P=0.030).

Discussion

This is the first study to demonstrate that elevation in exercise central BP is accounted for by major increases to forward propagating pressure waves, and not wave reflection. This finding is contrary to some previous studies which, on the basis of the elevated AIx, have attributed pressure augmentation during exercise to increases in wave reflection. This finding is of relevance to understanding central BP hemodynamic mechanisms and may have important clinical ramifications given the independent prognostic value of a hypertensive response to exercise for predicting adverse cardiovascular outcomes.1

Augmentation of central BP is widely believed to be mediated via wave reflection. With each contraction of the heart, a compression wave associated with a rise in pressure is propagated forward through the large arteries. Aortic systolic pressure separates into a wave heading forward in the large arteries and a wave of the same pressure returning back from the periphery to the aorta. This backward wave reflects at points along the arterial system and returns on itself in the wave speed is associated with the change in backward compression and forward decompression waves (Table 3). This finding is of relevance to understanding central BP hemodynamic mechanisms and may have important clinical ramifications given the independent prognostic value of a hypertensive response to exercise for predicting adverse cardiovascular outcomes.1

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Data are mean±SD.

Table 3. Aortic Hemodynamic Parameters at Rest and During Exercise (n=10)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rest</th>
<th>Exercise</th>
<th>Change</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic systolic pressure, mm Hg</td>
<td>121±8</td>
<td>140±11</td>
<td>19±12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aortic diastolic pressure, mm Hg</td>
<td>74±7</td>
<td>80±14</td>
<td>6±11</td>
<td>0.13</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>90±5</td>
<td>100±11</td>
<td>10±11</td>
<td>0.015</td>
</tr>
<tr>
<td>Aortic pulse pressure, mm Hg</td>
<td>47±11</td>
<td>60±13</td>
<td>14±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>P1, mm Hg</td>
<td>110±8</td>
<td>120±11</td>
<td>11±10</td>
<td>0.006</td>
</tr>
<tr>
<td>Augmentation pressure, mm Hg</td>
<td>12±8</td>
<td>21±10</td>
<td>9±6</td>
<td>0.002</td>
</tr>
<tr>
<td>Augmentation index, %</td>
<td>23±14</td>
<td>33±14</td>
<td>10±11</td>
<td>0.023</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>64±10</td>
<td>80±11</td>
<td>16±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak aortic flow velocity, cm·s⁻¹</td>
<td>73±18</td>
<td>80±15</td>
<td>7±12</td>
<td>0.100</td>
</tr>
<tr>
<td>Aortic wave speed, m·s⁻¹</td>
<td>6.5±2.2</td>
<td>7.9±2.2</td>
<td>1.4±1.1</td>
<td>0.004</td>
</tr>
</tbody>
</table>

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18 Hypertension July 2013
Exercise Hemodynamics: Forward and Reflected Waves in the Aorta

Exercise triggers several acute hemodynamic changes. Under normal circumstances, systemic vasodilation offsets the rise in cardiac contractility, heart rate, and left ventricular output, resulting in increased peripheral blood flow. Arterial pressure, both peripheral and central, rises in a graded fashion with increasing exercise intensity, but less is known about the underlying hemodynamic mechanisms of this increase. Murphy et al. measured invasive aortic pressure and flow velocity during exercise. They observed an exercise-induced increase in central systolic BP, coupled with a reduction in aortic compliance (as determined by an increase in aortic pulse wave velocity) and decreased peripheral vascular resistance. Although they reported a decrease in reflected wave transit time, the physiological stress of exercise was not sufficient to significantly alter the site or magnitude of wave reflections in the aorta. This observation is consistent with our finding of no appreciable changes in backward compression waves or reflection coefficient with exercise. In our studies, the magnitude of reflection at rest and during exercise ranged between 2% and 20%, and changes caused by exercise were on average around −6 to −3% (ie, reduction). Such minimal change in wave reflection, despite profound vasodilation on exercise, might be explained by poor retrograde transmission of reflected waves in the periphery resulting in a horizon effect on wave travel. This suggests that entrapment and dissipation of reflected pressure waves occurs within the periphery and that there is minimal backward transmission of discrete reflected waves. This notion is in keeping with our findings, where reflected wave components in the aorta seemed relatively unaffected by exercise-induced peripheral vasodilation, despite large increases in the magnitude of the incident pressure wave. Interestingly, Laskey et al. also found a reduction in the first harmonic of the reflection coefficient (suggesting diminished reflected wave magnitude) on initiation of exercise in healthy subjects. Adding to this observation, this current study found a strong and negative association between the change in magnitude of reflection and change in central systolic BP with exercise. Such results suggest that the cardiovascular system may be relatively close to an optimal design to maximize flow output by minimizing impedance to forward propagating waves, and that discrete reflections contribute only modestly to the morphology of the central BP waveform.

Contribution of Aortic Reservoir and Excess Pressure to Exercise Central BP

Accounting for the systolic radial expansion and diastolic recoil of the arteries in the separation of the pressure waveform into forward and backward components is the fundamental precept of the reservoir-excess pressure paradigm.

Table 4. Wave Intensity Analysis and Separated Pressure Wave Parameters at Rest and During Exercise (n=10)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rest</th>
<th>Exercise</th>
<th>Change</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prereservoir subtraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forward compression wave, Wm⁻²·s⁻¹</td>
<td>4×10⁸±18×10⁶</td>
<td>52×10⁸±22×10⁶</td>
<td>12×10⁸±17×10⁶</td>
<td>0.045</td>
</tr>
<tr>
<td>Backward compression wave, Wm⁻²·s⁻¹</td>
<td>−7×10⁶±4×10⁶</td>
<td>−8×10⁶±5×10⁶</td>
<td>−1×10⁶±3×10⁶</td>
<td>0.2</td>
</tr>
<tr>
<td>Forward decompression wave, Wm⁻²·s⁻¹</td>
<td>11×10⁶±5×10⁶</td>
<td>20×10⁶±6×10⁶</td>
<td>9×10⁶±6×10⁶</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peak forward pressure, mm Hg</td>
<td>69±16</td>
<td>79±14</td>
<td>10±9</td>
<td>0.009</td>
</tr>
<tr>
<td>Peak backward pressure, mm Hg</td>
<td>12±7</td>
<td>9±5</td>
<td>−3±6</td>
<td>0.2</td>
</tr>
<tr>
<td>Reflection coefficient, %</td>
<td>18±12</td>
<td>12±7</td>
<td>−6±9</td>
<td>0.06</td>
</tr>
<tr>
<td>Wave reflection index, %</td>
<td>20±11</td>
<td>17±10</td>
<td>−3±10</td>
<td>0.3</td>
</tr>
<tr>
<td>Postreservoir subtraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak forward pressure, mm Hg</td>
<td>61±15</td>
<td>74±14</td>
<td>13±9</td>
<td>0.009</td>
</tr>
<tr>
<td>Peak backward pressure, mm Hg</td>
<td>3±4</td>
<td>2±1</td>
<td>−2±4</td>
<td>0.2</td>
</tr>
<tr>
<td>Reflection coefficient, %</td>
<td>6±7</td>
<td>2±1</td>
<td>−4±7</td>
<td>0.2</td>
</tr>
<tr>
<td>Reservoir/excess pressure separation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak aortic reservoir pressure, mm Hg</td>
<td>110±5</td>
<td>114±17</td>
<td>4±16</td>
<td>0.5</td>
</tr>
<tr>
<td>Integral aortic reservoir pressure, Pa·s</td>
<td>18×10⁵±7×10⁵</td>
<td>13×10⁵±5×10⁵</td>
<td>−5×10⁵±5×10⁵</td>
<td>0.010</td>
</tr>
<tr>
<td>Peak aortic excess pressure, mm Hg</td>
<td>11±5</td>
<td>27±12</td>
<td>16±9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Integral aortic excess pressure, Pa·s</td>
<td>9×10⁵±3×10⁵</td>
<td>13×10⁵±4×10⁵</td>
<td>5×10⁵±3×10⁵</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are mean±SD. Wave intensity values are net integrals (area under the curve). A negative change in backward waves indicates greater intensity. Peak forward and backward pressures are above diastolic pressure. Reflection coefficient was calculated using the ratio peak backward/peak forward pressure. Wave reflection index was calculated using the ratio of backward compression wave integral/forward compression wave integral. Data presented are not adjusted for heart rate.
By definition, the aortic reservoir pressure is the result of both flow into and out of the proximal aorta and is dependent on the interaction between aortic compliance and downstream impedance. It, therefore, has been suggested to represent the theoretical minimum work that the left ventricle must perform to force blood into the proximal aorta. The excess pressure is, therefore, an indicator of the excess work required of the left ventricle above this minimum. The reservoir-excess pressure paradigm has never been assessed in humans in the context of exercise, but provides a novel way to describe changes to exercise central BP in the current study. With exercise, we observed an increase in central systolic BP and heart rate. Concurrently, there may be marked sympathetic activation to diminish blood flow to nonessential vascular beds, while skeletal muscle activity causes vasodilation of peripheral arterioles. Consequently, to meet the increased demand for blood flow during exercise, the heart must increase the excess pressure. The vasodilation of the peripheral vasculature and poor retrograde transmission would ensure the magnitude of wave reflections seen in the aorta is minor, and central BP is, therefore, augmented almost exclusively by incident pressure waves of myocardial origin. Indeed, in support of this view, we found that the change in both peak and integral of the excess pressure was positively associated with the change in the forward compression wave, but not reflected wave components.

Recent ex vivo modeled data criticized the reservoir-excess pressure paradigm, suggesting it introduces error
(overestimation of late systolic forward decompression waves) into hemodynamic analysis. It is important to note that the same pattern of wave intensity (large, significant increase to incident waves, and no change in reflected waves) emerged under both resting and exercise conditions. Irrespective of analysis technique, our data indicate only a minor role for wave reflection. Taken altogether, it seems plausible that the aortic reservoir-excess pressure paradigm provides a reasonable and physiologically sound explanation for the observed central BP changes with exercise that cannot be explained in terms of wave reflection alone.

Limitations

Study participants were older individuals with an indication for coronary angiography and, whilst all were free of significant coronary vessel disease, they cannot be considered truly healthy. Therefore, results may not be generalizable to healthy or younger individuals where augmentation pressure and augmentation index estimated by radial tonometry may reduce with exercise. This study was adequately powered on the basis of expected changes in central systolic BP from rest to exercise. However, larger variance in other hemodynamic factors may have increased the probability of a type 2 error because of a small study sample (despite the large hemodynamic perturbations induced with exercise and the consistency in the direction of responses). In addition, a mathematical model was used to derive aortic reservoir pressure and, because this is influenced by the compliance and buffering capacity of the aorta, future studies should directly measure the cyclic changes in aortic reservoir function and compliance.

Perspectives

To our knowledge, this is the first study to examine hemodynamic mechanisms related to elevations in central BP with exercise. The results demonstrate that augmentation of central BP during exercise is mainly because of increases in forward propagating waves generated by left ventricular ejection. These incident waves are the principal components of excess pressure load induced with exercise and, in contrast to current theory, there seems to be only a minor role for wave reflection in exercise central BP. These findings have relevance to understanding not only the physiology contributing to central BP waveform morphology, but also the pathophysiology of exercise hypertension.

Sources of Funding

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Disclosures

None.

References

Novelty and Significance

What Is New?
• Central pressure and flow were measured during exercise to determine the role of arterial wave travel on central blood pressure
• Central blood pressure rises during exercise because of increases in forward traveling waves generated by the heart.

What Is Relevant?
• Although never proven, popular opinion suggests that rises in central blood pressure during exercise are because of reflected waves from the periphery of the body. Our findings provide evidence to the contrary, and represent an important advance in understanding central blood pressure physiology.

Summary
Increased central blood pressure during exercise is caused mainly by forward propagating waves from the heart, whereas reflected waves play a minor role. These findings are significant with respect to understanding the physiology of central blood pressure and exercise hypertension.
Exercise Central (Aortic) Blood Pressure Is Predominantly Driven by Forward Traveling Waves, Not Wave Reflection

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Exercise central (aortic) blood pressure is predominantly driven by forward travelling waves, not wave reflection.

Supplementary Material

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Reproducibility of pressure and flow velocity measures. The within-subject standard deviation of the difference between replicate recordings in the proximal aorta was ± 3.0 mmHg (coefficient of variation [CV], 6.5%) and ± 6.1 mmHg (CV, 8.2%) for aortic systolic BP at rest and exercise respectively. For mean flow velocity, the standard deviation of the mean difference was ± 2.5 ms\(^{-1}\) (CV, 15.4%) and ± 2.7 ms\(^{-1}\) (CV, 14.1%) at rest and exercise respectively.

Wave intensity analysis. Utilising custom written software, the change in pressure was separated into forward (dP\(+\)) and backward components (dP\(\-\)),\(^1\) using equations 1 and 2 below, where \(\rho\) was the density of blood (taken as 1050 kg.m\(^{-3}\)), and \(c\) was the wave speed calculated using the single-point equation (equation 3), where dP was the incremental change in pressure, and dU the incremental change in blood velocity.

**Equation 1**

\[
dP_+ = \frac{1}{2}(dP + \rho cdU)
\]

**Equation 2**

\[
dP_- = \frac{1}{2}(dP - \rho cdU)
\]

**Equation 3**

\[
c = \frac{1}{\rho} \sqrt{\frac{\sum dP^2}{\sum dU^2}}
\]

Impedance analysis. Impedance analysis was performed as described by Hughes & Parker.\(^1\) The characteristic impedance (\(Z_0\)) was calculated using a time-domain based approach\(^1\) and separation of pressure into forward and backward components was undertaken using the modification of the technique of Westerhof et al.,\(^2\) described by Laxminarayan.\(^3\) This has been shown to give nearly identical results to pressure separation using the wave intensity approach.\(^4\)

Reservoir and excess pressure separation. Aortic reservoir pressure (\(P_{\text{reservoir}}\)) was calculated with Equation 6 below, where \(P_\infty\) is the pressure asymptote at which flow through the microcirculation would be expected to cease, \(P_\text{d}\) is the diastolic pressure at \(t = 0\), \(a\) is a constant of proportionality, \(b = 1/RC\) where \(R\) is the resistance and \(C\) is the compliance of the aortic reservoir.

**Equation 4.**

\[
P_{\text{reservoir}} - P_\infty = e^{-(a+b)t} \int_0^t [aP(t') + bP_\infty] e^{(a+b)t'} dt' + (P_\text{d} - P_\infty)e^{-(a+b)t}
\]
References

**Figure S1.** Example wave separation using time-domain (panels A and C) and frequency-domain (panels B and D) analysis under resting (baseline) and exercise conditions. The black line is the overall arterial pressure waveform, the blue line is the forward wave and the red line is the backward wave.
Figure S2. Example impedance spectra plots for an individual at rest (baseline) and during exercise.