Arterial Stiffness Gradient, Systemic Reflection Coefficient, and Pulsatile Pressure Wave Transmission in Essential Hypertension

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Abstract—Arterial stiffness and impedance gradients are known to influence pressure wave propagation and macrovascular-microvascular interactions. We studied the association between the carotid-femoral arterial stiffness gradient and the systemic reflection coefficient (N=393); of this population, 246 also underwent assessment of forward/backward pressure wave propagation and microvascular pulsatile pressure transmission (MPPT). Hemodynamic parameters were measured noninvasively. From peripheral vascular resistance and characteristic impedance, we estimated the systemic reflection coefficient and MPPT on peripheral and cardiac microcirculation in age-matched, sex-matched and body mass index-matched individuals with (n=147) or without (n=98) hypertension. The arterial stiffness gradient, systemic reflection coefficient, and correlations between the arterial stiffness gradient and age or blood pressure were similar in both populations. MPPT was higher in hypertension (P<0.0001), and the subendocardial viability (Buckberg) index lower (P<0.0001). In both populations, the systemic reflection coefficient and arterial stiffness gradient were significantly associated with changes in MPPT and the subendocardial viability index. Despite similar systemic reflection coefficients, the carotid reflected pressure and MPPT were higher in hypertension. Maintaining the systemic reflection coefficient within normal ranges was, therefore, insufficient to compensate for higher carotid forward pressure waves which, in hypertension, were associated with increased aortic stiffness (P<0.0001) and higher stroke volume (P=0.0365). Independently of cardiovascular risk, hypertension-induced changes have a weighted effect on MPPT, although insufficient to compensate for increased forward pressure waves. In hypertension, elevated aortic stiffness negatively affects the arterial stiffness gradient and systemic reflection coefficient but positively affects forward pressure. **(*Hypertension*. 2019;74:1366-1372. DOI: 10.1161/HYPERTENSIONAHA.119.13387.)** ● **Online Data Supplement**

Key Words: blood pressure ■ hypertension ■ microcirculation ■ risk ■ vascular resistance

Aortic and central large artery stiffness increases with age and is associated with a progressive decline in microvascular function. The concomitant occurrence of aortic stiffness and a deterioration in cerebral cognitive functions or decreased kidney function are classic examples.[1,2] These associations are frequently considered as the consequences of impaired cross-talk between macrovascular and microvascular circulations, which in turn results in the transmission of excessive pulsatile pressure to the microcirculation.[1,2]

Mean arterial pressure and pulse pressure vary along the arterial tree, falling to low levels within the capillaries.[3] The pressure exerted upon the capillary/microvascular network is practically the same in normotension and hypertension.[4] Arterial pressure wave reflections are essential in the control of pressure propagation and transmission along the arterial tree.[5] In this context, the Windkessel model can be used to evaluate the buffering function of large arteries.[6] However, this is not a propagative model of the arterial circulation and pulse wave velocity (PWV) has, therefore, been proposed as a reliable means to assess arterial stiffness in wave propagation.[3,5]

The arterial system is characterized by progressively increasing stiffness from the aorta and central arteries to the peripheral muscular conduit arteries, which produces a stiffness mismatch/gradient.[2,3] The stiffness gradient, together with the geometric pattern of systemic arteries,[7] generates a centrifugal impedance gradient.[2,3,7] Changes in the impedance gradient, in turn, produce partial and continuous local wave reflections, which are, therefore, a constant characteristic of this gradient.[3,5,8] The continuous partial reflections—and reflection at branching points and resistance arteries—summate to determine the systemic reflection coefficient,[3,8] which attenuates the transmission of pulsatile pressure into the microcirculation and affects macrovascular-microvascular cross-talk.[1–3,9]

Human studies have typically considered pressure transmission and its impact on the microcirculation in terms of

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forward/centrifugal propagation. However, reflected waves traveling in the backward/centripetal direction face a reverse impedance gradient with partial rereflections at the site of each impedance mismatch and progressive attenuation of the impact of backward-traveling waves on central arterial pressure.[10] This attenuation of the backward/centripetal traveling wave is expressed by the aortic reflection factor, which shows that only about 35% of the forward/incident pressure is reflected centrally.[9] The characteristics of forward/incident pressure propagation have an impact on peripheral pulsatile microvascular pressure transmission, whereas attenuation of the backward reflected pressure has a potential impact on heart function and structure.[1,2,7] Microvascular pulsatile pressure, therefore, plays a major role in maintaining end-organ blood flow. This is particularly noteworthy in several age-related clinical conditions.[11–14] Aging is associated with marked changes in the geometric pattern of the systemic arterial tree and mechanical arterial properties with a reduced arterial impedance gradient.[15] Until recently, factors influencing systemic reflections and microvascular pulsatile pressure transmission (MPPT) have been underestimated in individuals with uncomplicated hypertension. The aim of this study was to assess the impact of forward-traveling pressure waves on the microcirculation, and that of systemic retrograde pressure wave transmission on the common carotid artery augmented/reflected pressure, and cardiac microcirculation and function in untreated individuals. We investigated the determinants of the systemic reflection coefficient and the association of the latter with forward and backward pressure wave propagation in individuals with uncomplicated essential hypertension or normal blood pressure (BP) and analyzed the impact on peripheral and cardiac microcirculation.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design and Participant Profile

Design Protocol 1

We recruited 196 normotensive and 197 individuals with uncomplicated hypertension to study the correlation between age and mean BP (MBP) on the one hand, and aortic and brachial artery pulse wave velocities and arterial stiffness gradient on the other, as major factors affecting the propagation of arterial waves. Hypertension was defined as systolic BP >140 mm Hg, or diastolic BP >90 mm Hg. Hypertensive patients had no history of cardiovascular complications or other major risk factors.

Design Protocol 2

Macrovascular-microvascular cross-talk depends on arterial impedance mismatches but is also usually determined by other factors than the arterial stiffness gradient. To understand the role of these factors on the reflection coefficient and macrovascular-microvascular cross-talk, we examined the characteristics of 98 normotensive and 147 hypertensive subjects who underwent more thorough hemodynamic investigation.

Hemodynamic Protocol

Hemodynamic and echocardiographic parameters were measured noninvasively during the same procedure to determine pulsatile arterial hemodynamics using previously described techniques.[16] Hemodynamic assessments were undertaken with patients in fasting conditions in a temperature-controlled room, after 10 minutes in the supine position. Brachial artery BP was measured to the nearest 2 mm Hg using a mercury sphygmomanometer. The common carotid artery (CCA) pressure waveform was recorded by applanation tonometry (SphygmoCor, Sydney, Australia). The CCA pressure wave was calibrated from brachial diastolic BP and MBP. MBP was calculated by including the CCA pressure waveform using the SphygmoCor software. The calibrated CCA waveform was then used to evaluate the forward/incident pressure wave between the foot and the inflection point at the beginning of the upstroke of the reflected wave (Pi) of the CCA pressure curve. The reflected pressure wave (Pref) was determined as the difference between the CCA pulse pressure and the forward/incident pressure wave, expressed as augmented pressure in mm Hg or as a percentage of the CCA pulse pressure (augmentation index).[16,17] The carotid artery reflection factor is the ratio of Pref to the forward/incident pressure wave. The subendocardial viability index (SEVI)—previously known as the Buckberg index—was calculated from the mean CCA systolic BP and CCA diastolic BP and from left ventricular ejection and diastolic times measured by SphygmoCor. Arterial stiffness (PWV) was calculated from simultaneous pressure wave measurements from the CCA to the femoral arteries in the groin (carotid-femoral [central] or aortic PWV) and from the CCA to the radial artery (carotid-radial [peripheral] or brachial PWV; Complior; Colson, Les Lilas, France) as previously described.[15,17] Stiffness gradients were estimated from (brachial PWV/aortic PWV)$^{0.5}$.[15,16] The diameter of the ascending aorta was measured 2 cm above the root and at the aortic bifurcation by 2-dimensional directed M-mode echocardiogram (HP Sonos 100, Hewlett-Packard, Evry, France) as previously described.[16] Aortic tapering was, therefore, estimated as the ratio of the diameter of the ascending aorta/aortic bifurcation. Two-dimensional directed M-mode echocardiography was performed simultaneously with CCA tonometry (2.5- and 3.5-MHz transducers; HP Sonos 100; Hewlett-Packard). Aortic flow velocity was measured using a pulsed Doppler[16]: the sample volume was positioned at the tip of the aortic leaflets, and flow velocity was determined by spectral analysis of the digitized broadband audio signal. Peak flow (Q max) was calculated from the aortic annular cross-sectional area and maximum aortic flow velocity. Stroke volume was determined as the product of the aortic annular cross-sectional area and the velocity integral of left ventricular outflow, and cardiac output was calculated as stroke volume multiplied by heart rate. Total peripheral resistance (Zr) was estimated from cardiac output and MBP.[16] Characteristic impedance (Zc) was estimated in the time domain as described previously and computed as Z_c=Pi/Qmax.[16] The systemic/global reflection coefficient (Γ) was computed as the ratio $(1- Zc/Zr)/(1+Zc/Zr)$.[3,8] The systemic reflected pressure in mm Hg was estimated as (forward/incident pressure wave×Γ), which provides an estimation of the MPPT in mm Hg. The arterial Pref entrapment was estimated from 1-(carotid reflection factor/Γ).

Statistical Analysis

The Kolmogorov-Smirnov test was used to assess distribution. Data are expressed as means±standard error of the mean (SEM) and compared using *t* statistics. Sex (1, male; 0, female) and hypertension (1, yes; 0, no) were used as categorical variables. Pearson or Spearman regression analysis was used to assess correlations between the different parameters. Any predictor with a probability of $P<0.15$ was subsequently tested in a multivariable linear correlation analysis of variables associated with systemic reflection coefficients and estimated MPPT. The correlation slopes were expressed as β coefficients±SD. All comparisons were computed using NCSS 2011 software (J. Hintze, Kaysville, UT).

Results

Design Protocol 1

The results are shown in Figures 1, 2 and 3.. Aortic PWV increased with age in both groups ($P<0.0001$) with a more notable effect in individuals with hypertension (β coefficient 8.9±10.4 cm/y) than in the normotensive population (β

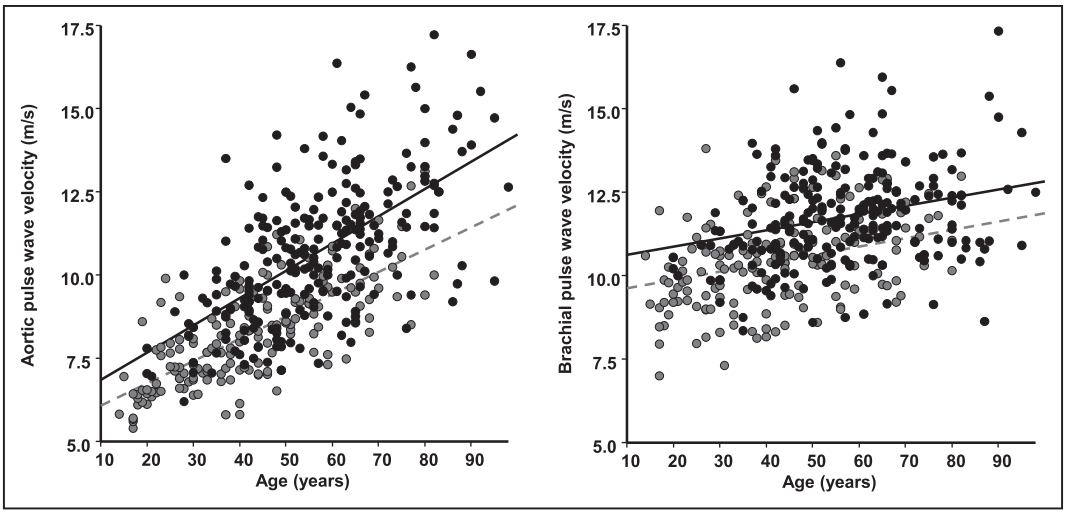

Figure 1. Correlations between age and aortic and brachial pulse wave velocities in normotensive (gray circles and dotted line) and hypertensive (black circles and full line) subjects. A significant association between age and aortic pulse wave velocity (PWV) was observed in both normotension (r=0.735; P<0.0001) and hypertension (r=0.648; P<0.0001), with a significantly steeper β coefficient in hypertension (8.8±10.7 cm/s/y) *vs* (6.6±6.1 cm/s/y) normotension. A significant association between age and brachial PWV was observed in the 2 groups (P<0.0001) with a significant reset in hypertension (intercept 10.27±5.54 m/s) vs normotension (9.27±3.39 m/s; P=0.032).

coefficient 6.6±6.0 cm/y; Figure 1). Brachial artery PWV also increased with age in both groups (P<0.0001) with similar β coefficients (normotensives 2.84±7.0 cm/y; hypertensives 2.95±9.6 cm/y), but with significant reset (intercept) in the hypertensive group (1.023±0.040 m/s versus 0.927±0.024 m/s; P=0.0328; Figure 1). Both aortic and brachial PWV increased with MBP (P<0.0001), with similar β coefficients (normotensives 5.9±14.3 cm/y; hypertensives 6.5±12.8 cm/y), and no significant reset in hypertensives (Figure 2). Significant inverse correlations between age and the arterial stiffness gradient were observed in both groups (P<0.0001) with similar β coefficient slopes (normotensives: −0.0023±0.0042 versus hypertensives: −0.0031±0.0056; P=0.164; Figure 3).

Design Protocol 2

Table 1 shows the statistical comparison between normotensive and hypertensive subjects in the population that underwent detailed hemodynamic analysis of factors associated with forward and backward pressure wave propagation and transmission. In a population that was closely matched in terms of sex, age, and body mass index, hypertensive individuals were characterized by significantly elevated brachial and carotid artery BP, with increased carotid forward and Pref amplitude and an increased carotid reflection factor (P<0.0001). Systolic (P<0.0001) and diastolic (P=0.0003) pressure time indexes were higher in hypertension with a lower SEVI (0.0194). Although aortic and brachial PWV were greater in hypertensive individuals (P<0.0001), the differences between the brachial and aortic stiffness gradients were not statistically significant. Peripheral resistance (P=0.0062) and characteristic impedance (P=0.0004) were higher in hypertension, but systemic reflection coefficients were not statistically different (P=0.0639). In multivariate correlation analyses, the systemic reflection coefficient was independently associated with the

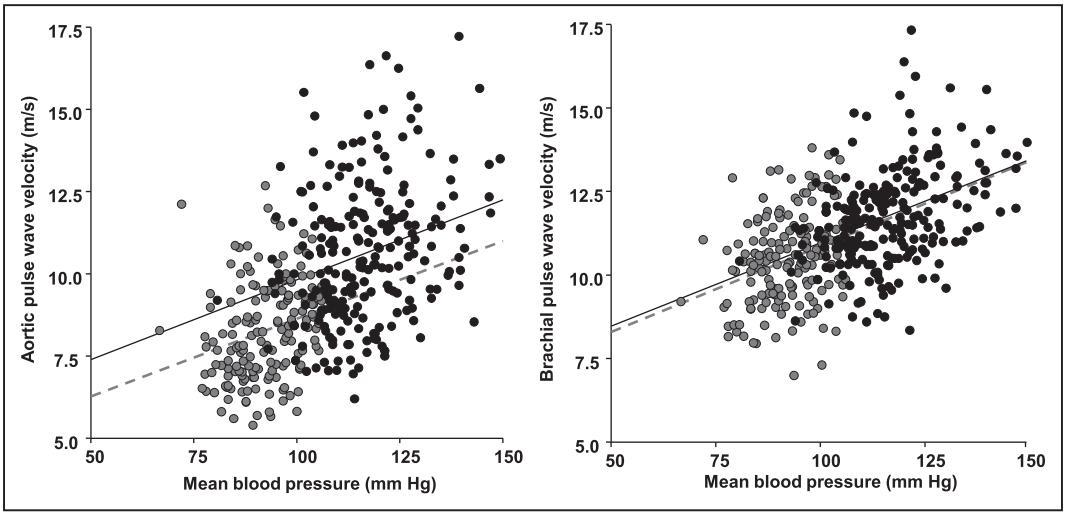

Figure 2. Correlations between mean blood pressure and brachial pulse wave velocity (PWV) in normotensive (gray circles and dotted line) and hypertensive (black circles and full line) subjects (P<0.0001 in both). β coefficients are similar in both groups, whereas the blood pressure/aortic PWV correlation reset observed in the hypertensive group is not significant (P=0.0876).

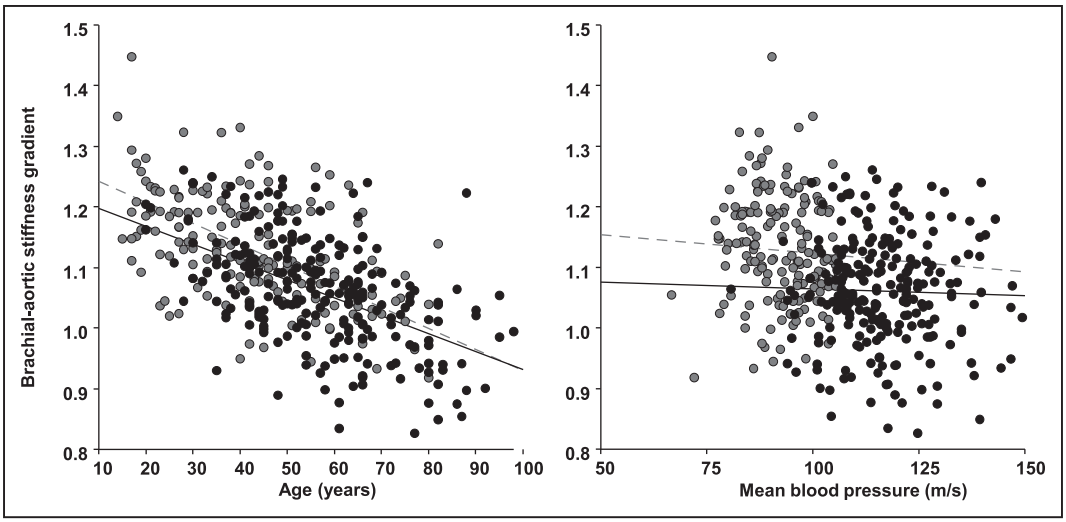

Figure 3. Correlations between age and the arterial stiffness gradient (**left**), and mean blood pressure and the arterial stiffness gradient (**right**) in normotension (gray circles and dotted line), and hypertension (black circles and full line). An inverse correlation between age and arterial stiffness gradient is observed in both groups (P<0.0001), with intercept values and β coefficients that are not significantly different (normotensives 1.252±0.015–0.0023±0.0003×age vs hypertensives 1.24±0.022–0.0031±0.0004×age; values are means and SEM). A significant inverse correlation between mean blood pressure and the stiffness gradient is observed in normotensive subjects (R=–0.182; P=0.0107) but not in the hypertensive group (R=–0.118; nonsignificant).

arterial stiffness gradient, heart period, and body mass index, whereas age had the opposite effect (Table 2). There was a significant correlation between the arterial stiffness gradient and the systemic reflection coefficient in both groups, with similar intercepts and slopes. In the control population, the systemic reflection coefficient showed that 84% of forward pressure waves were reflected versus 83.1% in hypertensive patients (nonsignificant). This contrasted with observations of the carotid reflection factor where only 24% (controls) and 41% (hypertension) of forward pressure waves affected common carotid pressure augmentation, suggesting considerable systemic reflected-pressure entrapment (Table 1). Estimated microvascular pressure transmission was significantly higher in hypertensive individuals (P<0.0001; Table 1). A higher systemic reflection coefficient reduced not only forward-traveling pressure transmission to the microcirculation but also the rereflection of backward-traveling reflected waves thus limiting the transmission of the latter towards the central arteries and modulating the carotid systolic pressure time index and changes in the SEVI. Figure 4 shows the positive correlation between the systemic reflection coefficient and SEVI, with similar intercepts and slopes in both groups. These observations highlight the influence of the systemic reflection coefficient on the propagation of both forward- and backward-traveling pressure.

Discussion

In the present study, we investigated the factors affecting the systemic arterial wave reflection coefficient and more particularly how it influences forward wave propagation to the peripheral microcirculation and backward wave propagation to the central arteries in normotension and in individuals with uncomplicated mild hypertension. Our results show that despite the different effects of age and BP on the aorta and peripheral arteries (Figures 1 and 2), the associations between the arterial stiffness gradient, age, and BP are similar in individuals with uncomplicated hypertension and in those with normal BP levels (Figure 3). Indeed, earlier aortic aging in hypertension is counter-balanced by a significant BP-related upward reset of peripheral muscular artery PWV (Figure 1). Moreover, our results show that the arterial stiffness gradient, body shape, and heart rate are all significant correlates of the systemic reflection coefficient (Table 2) irrespective of the presence of hypertension. These findings highlight the roles of capacitive and conduit artery structure and function in macrovascular-microvascular cross-talk in both normotensive and hypertensive subjects. The systemic reflection coefficient substantially reduced forward pressure wave transmission to the microcirculation in both subgroups. The impedance mismatches also created rereflections of the backward-traveling pressure, with pressure entrapment attenuating the impact of wave reflections on aortic and central artery pressure. Vascular reflected-pressure entrapment increases with systemic reflection coefficients. However, despite similar systemic reflection coefficients, the impact of both forward and backward pressure is greater in hypertension (higher MPPT, increased Pref, and lower SEVI). Nevertheless, microvascular pulsatile transmission and SEVI values are close to physiological levels.[18,19]

Although the arterial stiffness gradient is an important determinant of the systemic reflection coefficient, other factors likely to influence macrovascular-microvascular cross-talk also play a role. In line with theoretical, experimental, and comparative physiological observations, differences in impedance patterns can be explained by differences in body size and shape.[20,21] Body shape and height influence the extent of dispersion of reflecting sites and the intensity of reflections, as well as the frequencies of impedance minima and heart rate.[1,3,20,21] Our results are consistent with these observations and highlight the role of body shape (body mass index) or heart period as associated variables that influence systemic pressure reflections. Continuous partial

Table 1. Clinical and Central Hemodynamic Characteristics of the Populations in Design Protocol 2

Variable	Normotensive (n=98)	Hypertensive (n=147)	*P* Value
Age, y	54.4±1.56	53.7±1.28	NS
Sex ratio (0-male; 1-female)	1.40±0.05	1.35±0.05	NS
Body weight, kg	70.6±1.88	69.5±1.23	NS
Body height, m	1.66±0.01	1.67±0.01	NS
Body mass index, kg/m^2	25.4±0.01	24.7±4.4	NS
Brachial systolic blood pressure, mm Hg	121.9±1.37	162.8±1.67	<0.0001
Brachial diastolic blood pressure, mm Hg	72.4±1.06	90.4±1.15	<0.0001
Mean blood pressure, mm Hg	88.8±1.01	113.5±1.09	<0.0001
Carotid systolic blood pressure, mm Hg	115.7±1.40	155.4±1.69	<0.0001
Carotid pulse pressure, mm Hg	43.1±1.33	66.3±1.76	<0.0001
Pfrw, carotid Pfrw, mm Hg	34.3±0.93	46.5±1.01	<0.0001
Pref, carotid backward/Pref, mm Hg	8.8±0.67	19.5±0.97	<0.0001
Carotid reflection factor (Pref/Pfrw)	0.26±0.02	0.41±0.20	<0.0001
Carotid augmentation index, %	19.3±1.08	28.2±0.94	<0.0001
Heart period, ms	920±15.3	927±11.7	NS
Left ventricular ejection time, ms	306±3.0	311±2.6	NS
Diastolic time, ms	614±13.6	607±10.3	NS
Systolic pressure time index, mm Hg·s/m	3108±53.1	3997±60.9	<0.0001
Diastolic pressure time index, mm Hg·s/m	5262±130	6073±131	0.0003
Subendocardial viability (Buckberg) index, %	167±2.9	155±2.7	0.0194
Aortic pulse wave velocity, m/s	9.57±0.22	10.94±0.20	<0.0001
Brachial pulse wave velocity, m/s	10.50±0.17	11.73±0.12	<0.0001
Brachial/aortic stiffness gradient (ratio)	1.056±0.011	1.048±0.01	NS
Peripheral resistances, dynes·s·cm^{-5}	2014±72	2284±58	0.0071
Characteristic impedance, dynes·s·cm^{-5}	172±10	228±8.0	0.0002
Systemic reflection coefficient	0.837±0.003	0.831±0.004	NS
Estimated microvascular pressure transmission, mm Hg	5.7±0.03	7.7±0.03	<0.0001
Estimated arterial tree reflected-pressure entrapment, %	0.69±2.1	0.51±2.0	<0.0001
AoD, cm	28.2±0.38	28±0.30	NS
Abif diameter, cm	16.7±0.26	17.2±0.21	NS
AoD/Abif ratio (aortic taper)	1.69±0.02	1.64±0.02	NS

Values are ±SEM. Abif indicates aortic bifurcation; AoD, diameter of the ascending aorta; NS, nonsignificant; Pfrw, forward/incident pressure wave; and Pref, reflected pressure wave.

reflections regulate the contribution of the systemic reflection coefficient to energy dissipation and BP reductions along the arterial tree, thus providing a protective mechanism to control intraluminal pressure in the distal precapillary microcirculation.[1–3,5,8] Clinical studies typically consider pressure transmission and its impact on the microcirculation in the forward/centrifugal direction, but backward-traveling reflected waves are confronted with opposing stiffness and impedance gradients, both of which affect the impact of reflected waves on central arterial pressure and the heart. As shown in the present study, the arterial stiffness gradient and systemic reflection coefficient are preserved in essential uncomplicated hypertension and have an effect on MPPT and SEVI. Despite similar systemic reflection coefficients and stiffness gradients in both normotensive and hypertensive subjects (Table 1), entrapment of the systemic reflected pressure was less notable, and the carotid Pref was higher in the hypertensive group. Furthermore, factors that influence the systemic reflection coefficient do not have the capacity to normalize the forward pressure wave generated in the aorta and central arteries. One possible explanation is the fact that while aortic stiffening significantly increases forward pressure, it also has a tendency to reduce the systemic reflection coefficient. The determinants of the forward pressure wave are influenced not only by arterial stiffness and the stiffness gradient but also by stroke volume and the characteristics of

Table 2. Multiple Regression Analyses of Variables Associated With the Systemic Reflection Coefficient

Variable	*T* Statistics	*P* Value
Aortic PWV, m/s	5.503	<0.0001
Brachial PWV, m/s	3.071	0.0024
Ascending aortic diameter, cm	2.578	0.0106
Aortic bifurcation diameter, cm	−3.807	0.0002
Diastolic time, ms	6.287	<0.0001
Body mass index, kg/m^2	2.461	0.0042
Age, y	1.887	0.0602
R^2=0.4253; P<0.0001		

PWV indicates pulse wave velocity.

left ventricular ejection, including heart rate (left ventricular ejection time, and diastolic time). As shown in Table S1 in the online-only Data Supplement, stroke volume and cardiac output were higher in hypertensive subjects (in line with previous observations in borderline and uncomplicated essential hypertension).[22] The relationships between these parameters and the systemic reflection coefficient require further investigation and in particular the links with microvascular pressure transmission that are more notable in individuals with essential hypertension (Table S2). Myogenic vasoconstriction—modulated by local factors acting on the endothelium or smooth muscle cells—exerts the ultimate level of control on microvascular/capillary pressure transmission, and this is influenced by microvascular systolic and pulsatile pressures.[12] In clinical situations, such as renal disease, severe hypertension, or aging, where microvascular autoregulation is thwarted, transmission of pressure to the microcirculation can be more pronounced, with a resulting decline in renal or cognitive functions associated with aortic stiffening, hypertension, and age.[9–14]

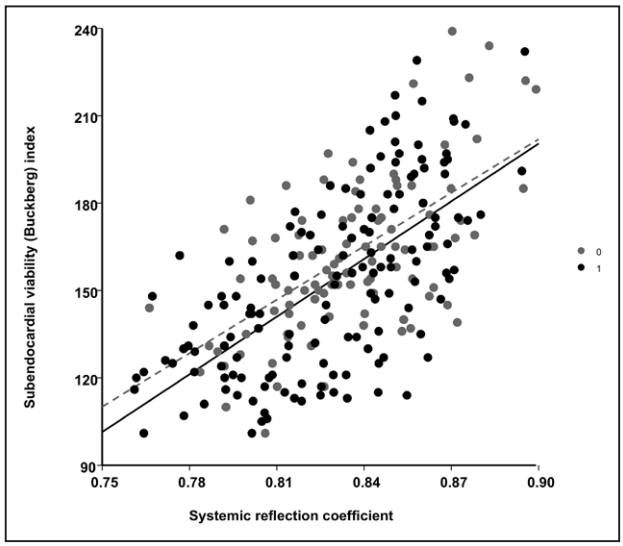

Figure 4. Positive correlation between systemic reflection coefficient and the subendocardial viability (Buckberg) index in normotension (gray circles and dotted gray regression line; P<0.0001)and hypertension (black circles and full black line; P<0.0001). The intercepts and slopes (β coefficients) are not statistically different. Hypertensive patients, R=0.6457, P<0.00001. Control patients, R=0.5983, P<0.00001

Study Limitations

Our study does have several limitations, including the limited number of participants, and the fact that those with elevated BP only had uncomplicated mild hypertension. Our findings can, therefore, not be extrapolated to other clinical conditions, such as severe or treatment-resistant hypertension. Another limitation is the fact that the formula used to calculate the systemic reflection coefficient is based on the model of a uniform elastic tube with characteristic terminal impedance (tube ending in 2 branches). The vascular tree is, however, not a uniform longitudinal model but a complex network of branches with progressively increasing stiffness and changes in arterial dimensions that generate continuous reflections. In vivo studies in males have shown that pressure is amplified along the aorta and that the major reflection site lies close to the aorta—where impedance mismatch occurs—or distal to the terminal bifurcation.[3,7,8,23] Despite the limitations, multivariable regression analysis (Table 2) showed that for the assessment of the systemic reflection coefficient, this formula is significantly associated with factors known to influence wave propagation, such as the stiffness gradient, aortic taper, and body shape. Moreover, this approach shows that our estimation of MPPT was very close to the actual pressure levels measured.[20] Another limitation of our study is the fact that the single distal termination point described suggests that wave reflections chiefly arise from the arterial tree of the lower body and does not account for the reflection from upper-body arteries.[23] Multiple correlation analyses (Table 2) of aortic and brachial PWV and aortic dimensions and taper possibly suggest that wave reflections arise mainly from the lower parts of the body. However, this approach does not allow for the fact that wave reflections are continuous throughout the arterial trees. It has been shown that the upper part of the body is also affected by arterial wave transmission and reflections.[3,23] Several studies have shown that pressure wave propagation affects the functions and structure of the brain and the cerebral microcirculation. Aortic PWV has been shown to be associated with silent cerebral small-vessel disease, the extent of brain white matter,[24,25] and reduced cognitive function.[26] Moreover, a reduced carotid reflection coefficient is associated with increased cerebral pulsatile transmission, and vascular damage within the brain.[9] Lastly, this is a purely mechanistic observational study. The potential physiological or clinical impact of MPPT in uncomplicated mild hypertension should be interpreted with caution, thus highlighting the need for further investigations to confirm our findings.

Perspectives

Studies on hypertension to date have focused primarily on increased cardiovascular risk and treatments effects. The Windkessel model was the primary emphasis of hemodynamic studies and investigations. More recent reports have drawn attention to the role of arterial stiffness and the impedance gradient as key contributors to the properties of systemic arterial wave reflections and macrovascular-microvascular interactions. Data from these studies have provided clearer insight into the clinical and physiological consequences of power dissipation and BP reductions along the arterial tree. The results of our study suggest that elevated BP affects not only cardiovascular risk but also macrovascular changes whereby a stable stiffness gradient exerts a stabilizing effect against pulsatile microvascular pressure transmission.

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Disclosures

None.

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Novelty and Significance

What Is New?

- Recently, arterial stiffness and the impedance gradient have been identified as key contributors to the properties of systemic arterial wave reflections and macrovascular-microvascular interactions.

What Is Relevant?

- Our findings suggest that elevated blood pressure affects not only cardiovascular risk but also macrovascular changes whereby a stable stiffness gradient exerts a stabilizing-protective effect against pulsatile microvascular pressure transmission.

Summary

Aortic and central large artery stiffness increases with age and is associated with a progressive decline in stiffness gradient and systemic reflection coefficient and microvascular function, as frequently demonstrated by concomitant aortic stiffness and cognitive decline or decreased kidney function. These associations are likely consequences of impaired cross-talk between macrovascular and microvascular circulations, which in turn results in the transmission of excessive pulsatile pressure to the microcirculation. Pulsatile microvascular pressure is crucial in maintaining end-organ blood flow, and yet factors influencing systemic reflections and microvascular pulse pressure transmission have to date been underestimated.