Acute Systemic Inflammation Increases Arterial Stiffness and Decreases Wave Reflections in Healthy Individuals

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Background—Aortic stiffness is a marker of cardiovascular disease and an independent predictor of cardiovascular risk. Although an association between inflammatory markers and increased arterial stiffness has been suggested, the causative relationship between inflammation and arterial stiffness has not been investigated.

Methods and Results—One hundred healthy individuals were studied according to a randomized, double-blind, sham procedure–controlled design. Each substudy consisted of 2 treatment arms, 1 with Salmonella typhi vaccination and 1 with sham vaccination. Vaccination produced a significant (P<0.01) increase in pulse wave velocity (at 8 hours by 0.43 m/s), denoting an increase in aortic stiffness. Wave reflections were reduced significantly (P<0.01) by vaccination (decrease in augmentation index of 5.0% at 8 hours and 2.5% at 32 hours) as a result of peripheral vasodilatation. These effects were associated with significant increases in inflammatory markers such as high-sensitivity C-reactive protein (P<0.001), high-sensitivity interleukin-6 (P<0.001), and matrix metalloproteinase-9 (P<0.01). With aspirin pretreatment (1200 mg PO), neither pulse wave velocity nor augmentation index changed significantly after vaccination (increase of 0.11 m/s and 0.4%, respectively; P=NS for both).

Conclusions—This is the first study to show through a cause-and-effect relationship that acute systemic inflammation leads to deterioration of large-artery stiffness and to a decrease in wave reflections. These findings have important implications, given the importance of arterial stiffness for cardiovascular function and risk and the potential of therapeutic interventions with antiinflammatory properties. (Circulation. 2005;112:2193-2200.)

Key Words: arterial stiffness ■ atherosclerosis ■ endothelium ■ inflammation ■ wave reflections

Recent studies suggest an association between inflammation and increased cardiovascular risk. Besides the link between chronic, low-grade inflammation and the slow process of atherogenesis, a significant body of evidence suggests that even acute inflammatory or infectious stimuli may transiently increase the risk of a cardiovascular event. Furthermore, unstable angina is associated with inflammation, which might precede the onset of the syndrome.

Arterial stiffness and enhanced wave reflections are markers of cardiovascular disease and independent predictors of cardiovascular risk. Stiffening of the large arteries and enhanced wave reflections lead to increased left ventricular (LV) afterload, disturbed coronary perfusion, and mechanical fatigue of the arterial wall.

Recent studies suggest that chronic subclinical inflammation is associated with impaired arterial elastic properties. However, these observational studies regarding arterial stiffness have not addressed the issue of causality, ie, whether inflammation in itself causes the deterioration of arterial stiffness or whether the relation is merely an epiphenomenon. Previous studies using a model of mild systemic inflammatory response generated by the administration of a vaccine have shown that acute systemic inflammation impairs endothelium-dependent dilatation in humans and that aspirin prevents this effect. Extending these studies and using this model of acute inflammation, we sought to evaluate in the present randomized, double-blind, sham procedure–controlled study the acute effect of systemic inflammation on arterial stiffness and wave reflections (a composite measure of arterial stiffness and peripheral vasodilatation) in humans. Furthermore, we sought to investigate the effect of pretreatment with aspirin and to explore whether any changes would be associated with changes in specific inflammatory markers, mediators, and enzymes.

Methods

Study Population
We studied 100 healthy individuals (55 men) recruited from among hospital staff (doctors, nurses, and their families). All subjects were nonsmokers and nonobese (body mass index <27 kg/m²) and did not have diabetes, hyperlipidemia, or a family history of premature vascular disease. They were clinically well and took no regular cardiovascular medications or antioxidant vitamin supplementation. They had not had any bacterial or viral infection for the last 2 months. They did not report regular use of antiinflammatory or steroid substances during the past 2 months, and they had not
received any typhoid vaccination in the previous 6 months. No female participant was on oral contraceptives. Subjects abstained from caffeine, ethanol, and flavonoid-containing beverages for at least 12 hours before the first session and up to the end of the study. The study protocol was approved by our Institutional Review Board.

Study Design
The study, which consisted of 2 separate substudies, was carried out using a randomized, double-blind, sham procedure-controlled design. Each substudy consisted of 2 treatment arms: 1 with vaccination with Salmonella typhi capsular polysaccharide vaccine (0.025 mg, Typhim Vi, Pasteur Merieux MSD) and 1 with sham vaccination (normal saline). Vaccine or sham vaccine was injected into the deltoid muscle of the subjects’ dominant arm. Subjects were studied in a quiet, temperature-controlled room at 23°C; they had fasted for at least 6 hours before each session. Baseline measurements for evaluation of arterial elastic properties, wave reflections, cardiac function, and peripheral resistance were taken in the morning after a 20-minute rest period in the supine position. Body temperature was measured by mercury thermometer, and venous blood for assessment of white blood cell (WBC) count and inflammatory markers was drawn into Vacutainer tubes.

Study 1
The effect of vaccination on aortic stiffness and wave reflections was studied in 48 subjects. Each treatment arm included 24 age- and sex-matched subjects. Measurements were made at baseline and at 8 and 32 hours after injection.

Echocardiographic Study
The effect of vaccination on cardiac function and total peripheral resistance was studied in a subpopulation (22 subjects, 11 age- and sex-matched subjects at each treatment arm) of the total population of study 1. Measurements were made at baseline and 8 hours after injection. Inflammatory markers were measured at baseline and at 8 and 32 hours after injection in all but the subjects of the echocardiographic study (n=26).

Study 2
The effect of an antiinflammatory agent such as aspirin on the impact of vaccination on arterial function indexes was studied in 52 subjects; in 24 of these subjects, the effect on inflammatory markers was also assessed. Each treatment arm was made up of 26 age- and sex-matched subjects. After baseline measurements, subjects received aspirin (1200 mg PO), and measurements were repeated 8 hours after injection.

Evaluation of Aortic Elastic Properties
Pulse travels at a higher velocity in stiffer aorta. Carotid-femoral pulse wave velocity (PWV), an established index of aortic stiffness,12,14–16,24–27 was calculated from measurements of pulse transit time and the distance traveled between 2 recording sites (PWV equals distance in meters divided by transit time in seconds) with a validated noninvasive device (Complior, Artech). Carotid-femoral PWV was measured with a validated, commercially available device (SphygmoCor, Atcor Medical) that uses the principle of applanation tonometry and appropriate acquisition and analysis software for noninvasive recording and analysis of the arterial pulse. The technique has been described in detail previously.16,29–31 In brief, from radial artery recordings, the central (aortic) arterial pressure was derived with the use of a generalized transfer function shown to give an accurate estimate of the central arterial pressure waveform and its characteristics.16,29,31 Waveforms of radial pressure were calibrated according to sphygmomanometric systolic and diastolic pressures measured in the brachial artery because there is practically negligible pressure pulse amplification between the brachial and radial arteries.16

Evaluation of Cardiac Function and Total Peripheral Resistance
The subjects underwent a complete echocardiographic study using a phased-array ultrasound system (Hewlett-Packard, Sonos 5500). A 1.8-MHz duplex transducer for combined cross-sectional imaging and Doppler echocardiography was used, and second harmonic imaging for optimal visualization of the endocardial border was applied.

LV stroke volume was calculated in all subjects from the Doppler velocity-time integral of the LV outflow tract flow and the corresponding area.34 We calculated LV outflow tract area after measuring LV outflow tract diameter from the parasternal cross-sectional image of the LV. All scans were obtained and analyzed offline by a single experienced operator who was blinded to the randomization of the subjects. Three cardiac cycles were averaged for each measurement. Total peripheral resistance was calculated as follows: mean blood pressure times 80 divided by cardiac output.

Measurement of Inflammatory Markers
Immediately after acquisition of venous blood, plasma or serum was separated by centrifugation (3000g at 4°C for 15 minutes), placed in aliquots, and stored at −70°C for the measurement of inflammatory markers. High-sensitivity C-reactive protein (hsCRP) was measured by immunonephelometry (Dade Behring). High-sensitivity interleukin-6 (hsIL-6) and total matrix metalloproteinase-9 (MMP-9) were measured with specific ELISAs (R&D Systems). Soluble CD-14 (sCD-14) was determined through the use of an enzyme-amplified sensitivity immunoassay (Biosource). WBC count was determined with an automated Advia Hematology analyzer (Bayer Advia 120, Diamond Diagnostics Inc).

Statistical Analysis
Because of the relatively small sample sizes in our substudies and the skewness of some variables, logarithmic transformation was performed before analysis (except for AP and AIx because they may occasionally have a negative value and because their values had a remarkably good fit to the normal distribution).

Values are expressed as the antilogs of the mean log values (geometric means) and their 95% CIs. At baseline, numerical parameters among the study subgroups were compared by 1-way ANOVA, followed by the Bonferroni correction if appropriate; contingency tables and the χ2 test were applied for categorical
parameters. An unpaired t test or χ2 test was used to compare baseline values in the echocardiographic substudy. The effect of vaccination versus control in each substudy was evaluated with paired t test or unpaired t test, followed by the Bonferroni correction for multiple comparisons. Correlation matrixes for arterial stiffness and inflammatory markers were done by Spearman’s rank test. Data analysis was performed with SPSS software, version 10.1.

Sample size calculations were based on data from our unit, which showed that the standard deviations of PWV and AIx for apparently healthy subjects with characteristics similar to those of our study population were 0.75 m/s and 7%, respectively. Therefore, we estimated that 26 subjects per group (52 in total) would provide 80% power at the 5% level of significance to detect a difference of 0.6 m/s in PWV in a parallel-design study, which is the case for the present study. Similarly, 23 subjects per group would provide 80% power to detect an absolute difference of 6% in AIx.

Results

There were no significant differences in all baseline characteristics between study groups (Tables 1 and 2). The effect of vaccination versus control is better described by reporting response, defined as net active intervention effect minus control procedure effect at each time point. Response was calculated as follows: (geometric mean at a time point for the vaccine group−geometric mean at baseline for the vaccine group)/baseline geometric mean.

TABLE 1. Baseline Characteristics of the Study Sessions in Studies 1 and 2

<table>
<thead>
<tr>
<th></th>
<th>Vaccination</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>34.4 (30.9–38.1)</td>
<td>33.9 (30.6–37.5)</td>
</tr>
<tr>
<td>Men/women</td>
<td>13/11</td>
<td>13/11</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>64.8 (61.2–68.5)</td>
<td>64.6 (61.6–67.6)</td>
</tr>
<tr>
<td>Central SP, mm Hg</td>
<td>98.0 (92.4–103.9)</td>
<td>97.8 (93.6–102.2)</td>
</tr>
<tr>
<td>Central DP, mm Hg</td>
<td>69.9 (65.5–74.6)</td>
<td>70.5 (67.3–73.7)</td>
</tr>
<tr>
<td>Central PP, mm Hg</td>
<td>27.1 (24.8–29.6)</td>
<td>26.9 (24.6–29.4)</td>
</tr>
<tr>
<td>Central MP, mm Hg</td>
<td>82.2 (77.2–87.5)</td>
<td>83.1 (79.7–86.7)</td>
</tr>
<tr>
<td>Peripheral SP, mm Hg</td>
<td>107.1 (101.2–113.4)</td>
<td>107.8 (104.0–111.8)</td>
</tr>
<tr>
<td>Peripheral DP, mm Hg</td>
<td>68.5 (63.8–73.4)</td>
<td>69.7 (66.6–72.9)</td>
</tr>
<tr>
<td>Peripheral PP, mm Hg</td>
<td>38.2 (35.4–41.1)</td>
<td>37.7 (35.4–40.3)</td>
</tr>
<tr>
<td>Peripheral MP, mm Hg</td>
<td>81.4 (76.4–86.7)</td>
<td>82.4 (79.3–85.7)</td>
</tr>
<tr>
<td>PWV, m/s</td>
<td>5.53 (5.05–6.04)</td>
<td>5.92 (5.48–6.39)</td>
</tr>
<tr>
<td>AP, mm Hg</td>
<td>5.35 (3.07–7.63)</td>
<td>5.12 (3.26–6.98)</td>
</tr>
<tr>
<td>Alx, %</td>
<td>17.4 (11.1–23.7)</td>
<td>16.9 (11.9–21.9)</td>
</tr>
<tr>
<td>Pi, mm Hg</td>
<td>21.9 (20.3–23.6)</td>
<td>22.1 (20.6–23.8)</td>
</tr>
<tr>
<td>Body temperature, °C</td>
<td>36.5 (36.3–36.6)</td>
<td>36.4 (36.3–36.6)</td>
</tr>
<tr>
<td>WBC count, 10^9/L</td>
<td>6.18 (5.22–7.32)</td>
<td>5.25 (4.51–6.12)</td>
</tr>
<tr>
<td>hsCRP, mg/mL</td>
<td>0.47 (0.28–0.80)</td>
<td>0.60 (0.33–1.08)</td>
</tr>
<tr>
<td>sCD-14, ng/mL</td>
<td>4.13 (3.79–4.49)</td>
<td>4.19 (3.97–4.41)</td>
</tr>
<tr>
<td>MMP-9, ng/mL</td>
<td>73.8 (41.2–132.3)</td>
<td>99.2 (61.6–159.8)</td>
</tr>
</tbody>
</table>

HR indicates heart rate; SP, systolic pressure; DP, diastolic pressure; PP, pulse pressure; and MP, mean pressure. Categorical variables are presented as absolute frequencies; continuous variables, as geometric mean (95% CI). Probability values derived from 1-way ANOVA of log-transformed values across the 4 subgroups.

*Probability value derived from χ2 test examining the association between gender and the 4 subgroups.
†For inflammatory markers of study 1, total n = 26. For inflammatory markers of study 2, total n = 24.

TABLE 2. Baseline Characteristics of the Study Sessions in the Echocardiographic Substudy of Study 1

<table>
<thead>
<tr>
<th></th>
<th>Vaccination</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>32.3 (26.8–39.0)</td>
<td>33.7 (29.4–38.8)</td>
</tr>
<tr>
<td>Men/women</td>
<td>6/5</td>
<td>6/5</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>65.8 (63.0–68.7)</td>
<td>65.3 (61.6–69.3)</td>
</tr>
<tr>
<td>Peripheral SP, mm Hg</td>
<td>119.3 (113.9–124.9)</td>
<td>113.9 (107.5–120.7)</td>
</tr>
<tr>
<td>Peripheral DP, mm Hg</td>
<td>76.7 (71.4–82.4)</td>
<td>73.1 (68.5–78.1)</td>
</tr>
<tr>
<td>Peripheral PP, mm Hg</td>
<td>41.6 (36.0–46.0)</td>
<td>40.3 (36.0–45.1)</td>
</tr>
<tr>
<td>Peripheral MP, mm Hg</td>
<td>91.0 (86.5–95.7)</td>
<td>86.8 (81.9–92.0)</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>52.6 (44.3–61.7)</td>
<td>59.8 (52.4–68.3)</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>3.46 (2.96–4.04)</td>
<td>3.91 (3.41–4.49)</td>
</tr>
<tr>
<td>Total peripheral resistance, dyne/cm · s⁻³</td>
<td>2106 (1746–2541)</td>
<td>1776 (1359–2050)</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1. Categorical variables are presented as absolute frequencies; continuous variables, as geometric mean (95% CI). Probability values derived from Student’s t test for unpaired measures of log-transformed values or χ2 test (gender).
Inflammatory Markers, Mediators, and Enzymes

Study 1

Vaccination led to a significant increase in body temperature at 8 hours (0.27°C; \( P < 0.05 \)). Similarly, WBC count increased (\( P < 0.001 \)) after vaccination (3.09 \( \times 10^9 \)/L at 8 hours; \( P < 0.001 \)).

Systemic inflammation produced a significant increase in hsCRP (\( P < 0.001 \)), hsIL-6 (\( P < 0.001 \)), and MMP-9 (\( P < 0.01 \)). hsCRP increased compared with control at both 8 hours (by 0.16 mg/L; \( P < 0.05 \)) and 32 hours (by 1.77 mg/L; \( P < 0.001 \); Figure 1). hsIL-6 increased at 8 hours (by 2.91 pg/mL; \( P < 0.001 \)) but not at 32 hours (0.30 pg/mL increase; \( P = NS \)). MMP-9 increased at 8 hours after vaccination (increase of 135 ng/mL; \( P < 0.01 \)), whereas sCD-14 did not change significantly (\( P = NS \); Figure 1).

Study 2

Vaccination led to a nonsignificant increase in body temperature (of 0.11°C) and to a significant increase in WBC count (by 1.80 \( \times 10^9 \)/L; \( P < 0.01 \)) at 8 hours.

Despite aspirin administration, vaccination produced a significant increase in inflammatory markers. hsCRP increased by 0.10 mg/L (\( P < 0.05 \)), hsIL-6 by 1.78 pg/mL, (\( P < 0.001 \)), and MMP-9 by 64 ng/mL (\( P < 0.05 \)) at 8 hours (Figure 2). sCD-14 did not change significantly.

Response of Arterial Stiffness and Wave Reflections to Inflammation

Study 1

Vaccination produced a significant (\( P < 0.01 \)) increase in PWV (increase at 8 hours by 0.43 m/s; \( P < 0.001 \)), denoting an increase in aortic stiffness. PWV values returned toward but did not completely reach baseline values at 32 hours (increase by 0.21 m/s; \( P = NS \); Figure 1). PWV was significantly correlated with hsCRP (\( r = 0.40, P < 0.001 \)) and hsIL-6 (\( r = 0.30, P < 0.01 \); Figure 4).

AIx was reduced significantly (\( P < 0.01 \)) by vaccination (at 8 hours, decrease of 5% [absolute value]; \( P < 0.001 \); at 32 hours, marginal decrease of 2.5%; \( P = 0.06 \); Figure 1), indicating a decrease in wave reflections. AIx corrected for changes in heart rate was significantly (\( P < 0.01 \)) decreased (by 4% at 8 hours, \( P < 0.001 \); by 2.8% at 32 hours, \( P < 0.05 \)). AP did not change significantly with vaccination.

Pi did not change significantly with vaccination, indicating no significant change in the force of cardiac ejection.

Study 2

Aspirin abrogated the effect of vaccination on aortic stiffness: PWV increased by 0.11 m/s, but this increase was not
statistically significant ($P=\text{NS}$; Figure 2). PWV was significantly correlated with hsCRP ($r=0.57$, $P<0.01$) but not with hsIL-6 ($r=0.04$, $P=\text{NS}$; Figure 4). Furthermore, the effect of vaccination on wave reflections was completely abrogated by aspirin (increase in AIx of 0.4%; $P=\text{NS}$; Figure 2).

**Discussion**

To the best of our knowledge, this is the first study to show through a cause-and-effect relationship that acute systemic inflammation leads to deterioration of large-artery stiffness. Furthermore, acute systemic inflammation leads to decrease
in wave reflections that apparently is caused by peripheral vasodilation. Aspirin pretreatment abrogates the effect of inflammation on arterial stiffness and wave reflections.

Clinical Implications

Our study has important clinical implications. Indeed, a growing body of evidence focuses on the potential of inflammation to increase cardiovascular risk.1–9 Although chronic, low-grade inflammation promotes atherosclerosis,1 accumulating data also suggest an association between acute systemic inflammatory responses such those in infections or after surgery and a short-term increased risk of a cardiovascular event.4–8 A recent study showed a transiently increased risk of myocardial infarction or stroke during the first 3 days after the onset of an acute respiratory or urinary tract infection.9 Furthermore, unstable angina is associated with inflammation,3,10 which might precede the onset of the syndrome. Our findings provide a mechanism through which acute inflammation may exert an unfavorable effect on the cardiovascular system. Indeed, elastic properties of large arteries are independent predictors of cardiovascular morbidity and mortality.12,14,15 A stiff aorta increases LV load and myocardial oxygen demands and impairs ventricular function while compromising coronary blood flow and predisposing to ischemia.16 Furthermore, a stiff aorta increases pulsatile stretch of the arteries, which leads to mechanical fatigue of their elastic components and renders them more prone to dissection and rupture.16

Mechanisms

Aortic Stiffness

Our study corroborates previous observational studies showing an association between arterial stiffness and inflammatory markers17–20 and provides an explanatory causative link for these associations.

Given the regulatory role of endothelium on arterial stiffness,35 the increase in aortic stiffness observed in this study could be attributed to an unfavorable effect of inflammation on nitric oxide (NO) bioavailability. The group of investigators who developed the model of inflammation that we used in this study have demonstrated that acute inflammation impairs normal endothelial performance and reduces NO bioavailability, possibly through the cytokine cascade.4,21–23 Interestingly, proinflammatory cytokines such as IL-6 have a direct adverse effect on NO-dependent vasorelaxation of experimental aortas.36 However, it is not possible to define precisely a substance responsible for the changes observed in our study. The positive correlation of PWV and CRP cannot substantiate an etiological role of the latter because trends of these parameters during the study were opposite (Figure 1), and recent data suggest that increase in CRP coincides with the restoration rather than the development of endothelial dysfunction.37 Undoubtedly, the contribution of other cytokines that we did not measure such as TNFα and IL-1β cannot be excluded and should be investigated.

Inflammation can also provoke structural and/or functional changes in the extracellular matrix of the aortic wall by increasing the levels of MMPs.39 Recent studies have shown that MMP-9 levels are associated with aortic stiffness in both healthy subjects and patients with isolated systolic hypertension.40

Wave Reflections

PWV and wave reflection indexes often change in parallel because the PWV affects the timing of the merging of incident and reflected waves. Despite the increase in PWV by inflammation, however, wave reflections were decreased in the present study. This decrease is apparently due to a decrease in the amount of the incident wave reflected at peripheral sites, not to the delayed return of this reflected wave, because there was no decrease but rather an increase in PWV. Thus, the predominant mechanism appears to be dilatation of medium and small peripheral muscular arteries and arterioles, as suggested by the decrease in peripheral resistance observed in our study.

Previous studies have shown that exogenously administered cytokines (specifically IL-1β) cause an NO-mediated
basal vasodilation in human veins by inducing the constitutively expressed endothelial NO synthase. Such an effect could account, at least in part, for the peripheral vasodilation observed in our study, given that the vaccine model we used results in significant activation of the IL-1 system. This hypothesis is further supported by our finding that aspirin, an agent that prevents the release of IL-1, fully abrogated the inflammation-induced decrease of wave reflection in our study. Vasodilating prostanoids may also contribute to vasodilation, as suggested by the reversal of wave reflection decrease with aspirin. This is also in line with the finding that the vaccination model does not appear to increase vasoconstricting prostanoids. Finally, the systemic hyperemia and vasorelaxation observed in inflammation might be mediated by vascular adrenoreceptor hyperreactivity induced by functional modification of potassium channels or even direct catecholamine inactivation driven by increased oxidant stress.

Our study was not designed to fully elucidate the mechanisms and mediators responsible for these changes. Undoubtedly, further studies are warranted, especially for clarifying the differential effect of inflammation on the aorta and peripheral arteries. Possibilities include differential effect of mediators on different vascular beds related to either the type of regulation (IL-1β increases basal but impairs agonist-induced NO production) or the nature of the artery (the elastic-type aorta may be affected more by extracellular matrix enzymes such as MMP-9).

Specific Comments and Study Limitations
Aortic stiffness can change passively as a result of an increase in blood pressure. However, in our study, neither peripheral nor central blood pressure changed, indicating that the increase in aortic stiffness was due to a direct effect of inflammation on the intrinsic properties of the aortic wall.

Changes in PWV are not likely to be related to changes in cardiac ejection because neither stroke volume nor Pi changed with inflammation.

Whether our findings can be extended to a chronic situation is a matter of discussion. Observational studies suggest that although inflammation may increase chronic aortic stiffness, decreases in wave reflections may be attenuated to some extent. Interestingly, in a recent study, which is in line with our results, a positive association was found between subclinical inflammation and aortic stiffness, whereas no such association was found with wave reflection indexes. In another study, a positive association was found between AIx and subclinical inflammation. Still, in this particular study, an increase in wave reflections can be attributed largely to the increase in aortic stiffness as indicated by the decreased time for the reflected wave to meet the incident wave (Δt).

Conclusions
This is the first study to demonstrate through a causative link that, in healthy individuals, acute systemic inflammation has a differential impact on different vascular beds: It increases stiffness of large, elastic-type arteries such as the aorta but decreases wave reflections by peripheral vasodilatation. Furthermore, aspirin pretreatment abrogates the effect of inflammation on arterial stiffness and wave reflections. These findings have important implications given the importance of aortic stiffness for cardiovascular function and the risk and potential of therapeutic interventions with antiinflammatory properties.

References
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