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Brachial Arterial Dynamics during Staged Lower Extremity Exercise: Utility and Comparison in Physically Active versus Sedentary Subjects

Alexander J. Muster, M.D.^{*}, Bonnie Kane, B.S.^{*}, Hyunggun Kim, Ph.D.[†], and David D. McPherson, M.D.[†]

^{*}Feinberg Cardiovascular Research Institute, Feinberg School of Medicine, Northwestern University, Chicago, Illinois

[†]University of Texas-Houston, Houston, Texas

Abstract

Constriction and relaxation of peripheral conduit arteries in response to exercise and recovery are amenable to noninvasive imaging. Diameter changes in the brachial artery during stationary bicycle pedaling are paradoxical to those in the lower extremities. When exercise is confined to the legs, arteries in the upper extremities constrict while leg arteries dilate. The magnitude of vasoconstriction in the upper extremities reflects the integrity of exercise mediated vascular responses. In the current study, young and old men with various levels of physical activity and cardiovascular histories exercised on a stationary bicycle while brachial artery diameter and flow velocity were continuously obtained. Results suggest that normal aging blunts arterial reactivity in seniors even if they exercise regularly. However, arterial dysfunction is greater when associated with sedentary lifestyle. This methodology of imaging brachial artery diameter changes during bicycle pedaling appears to be an effective tool for assessing the physiologic integrity of the vascular bed.

Keywords

exercise; vascular imaging; elderly

Determining vascular responses during exercise to assess vascular integrity is difficult. The extremities in motion make direct arterial evaluation unfeasible. However, arteries remote from muscular activity are amenable to evaluation. While cross-sectional area of arteries in the active muscle groups dilate to accommodate the increased blood flow,¹ the conduit arteries in the inactive upper extremities react to remote leg exercise in a paradoxical manner.

During muscular activity, oxygen and energy nutrients are channeled preferentially to active muscles. Conduit arteries participate actively in regulating blood supply to exercising muscles.² Arteries in inactive body regions constrict to exclude the added cardiac output dedicated to muscular activity.

What occurs in a conduit artery in a nonexercising extremity? Figure 1 illustrates diameter and velocity changes in the brachial artery. Physical activity with sudden onset is executed before a true increase in cardiac output takes effect. Blood flow for such muscle activity is shifted from inactive body regions that can temporarily tolerate reduced arterial flow.² As much as 20% of the resting blood volume is stored in skeletal muscle. At the start of pedaling, a portion of resting cardiac output is routed into the lower circulation from the upper extremities. The early constriction is depicted graphically as the first descending limb of the “W” pattern.

As pedaling effort progresses, cardiac output increases in proportion to energy requirements. Stored blood from the liver, kidneys, skin, and other organs is recruited into arterial circulation. A moderate pedaling effort (steady state) can be maintained without continuous shifting from inactive musculature. Arterial diameter is either fixed or slightly relaxed during exercise equilibrium (ascending limb of the “W” pattern).

As pedaling becomes strenuous, cardiac output reaches its upper limit. To continue pedaling beyond exhaustion, maximal blood volume is recruited into the vascular bed.

Vasoconstriction reaches its peak, represented as the second descending limb of the W. At this stage, cardiac output can reach five times its resting value and as much as 84% of this increase is distributed to active muscles.³ For example, blood flow in the kidneys can drop from 22% to 1% and in the liver from 27% to 2%. When muscle energy supplies are exhausted, pedaling comes to a stop.

In recovery, flow velocity drops and artery diameter increases. This stage is shown as the second ascending limb of the W. The time to reach baseline varies and reflects physical fitness and arterial wall integrity. Pooled blood becomes gradually redistributed to organs that store blood.

This study was aimed at determining the applicability of imaging changes in the conduit arteries occurring during remote exercise in young and old athletes (OA), sedentary subjects, and subjects with cardiovascular disease. We evaluated changes in brachial artery diameter that occurred while test subjects exercised on an upright stationary bicycle against progressive pedaling resistance.

Methods

Test Population

The study was approved by the Institutional Review Board of Northwestern University. Following informed consent, subjects were enrolled. Males only were evaluated, as a unique population of elderly elite male athletes was available for recruitment from a sister protocol. These elderly elite athletes had agreed to long-term cardiovascular evaluation.

Data were collected during two testing periods. In 1999, six young athletic men (mean age: 27 years), six young healthy sedentary men (mean age: 27 years), six older athletic men (mean age: 72 years), six old healthy sedentary men (mean age: 69 years), and six seniors with cardiovascular disease (mean age: 69 years) were tested. In 2005, five of the original athletes had follow-up bicycle stress test (6-year interval).

No sedentary or athletic participant was receiving cardioactive prescription medications. The six seniors with cardiovascular disease were all receiving medical management. Cardiovascular history and lifestyle were evaluated to determine suitability and safety for participation.

Exercise Protocol

We have previously reported on this method to evaluate vascular reactivity.^{4,5} All subjects underwent a baseline 12 lead electrocardiogram (ECG) and right arm blood pressure. The left upper extremity was immobilized on a board, elevated to shoulder height, extended laterally, and rested on a cushioned pad. A segment of the brachial artery proximal to the antecubital fossa was marked to ensure the identical transducer position throughout the test. The ECG was continuously recorded. Opposite (right) arm cuff blood pressure and heart rate were obtained before pedaling and every 3 minutes after pedaling resistance was increased.

Subjects rested sitting on an upright stationary bicycle for at least 5 minutes prior to initiation of exercise. Baseline image and velocity data were obtained at rest using a Siemens Sequoia ultrasound unit with an 8L5 linear transducer (Siemens Inc., Mountain View, CA, USA). Pedaling began at 40 W with turnover (pedaling) rate of 60 revolutions per minute. Resistance to pedaling increased stepwise by 10 W every 3 minutes until subjects declared inability to continue exercise (usually 120 W). The effort was self-graded by subjects as light, moderate, or hard. Subjects were then imaged through 3 and 6 minutes of recovery.

In 1999, data were recorded onto videocassette recorder (VCR) tape and arterial diameter and flow velocity were measured manually. In 2005, data were recorded digitally and quantitated on a dedicated workstation.

The variability of the measurement technique was assessed with repeat measurements taken and measurements reanalyzed. Repeat variability was 1.1% and measurement variability was 3.7%.

Statistical Analysis

Measured diameter of the brachial artery at each exercise protocol stage was normalized with respect to the resting baseline (stage 1) of each group. Comparison among the four groups was performed by determining percent diameter changes. True and normalized means and standard deviations at each stage for all the groups are tabulated ($\bar{x} \pm SD$), whereas normalized means are only graphed for clearer comparison between groups. SigmaStat (Version 3.1, Systat Software Inc., Point Richmond, CA, USA) was utilized for statistical analysis with the use of the Mann–Whitney rank sum test with $P < 0.05$ value to access differences in diameter changes.

Results

Figure 2 illustrates the composite changes for all groups including those with cardiovascular disease. It is clearly observed that arterial diameter changes show a fluctuating pattern of the letter of “W.”

Table I provides means and standard deviations of brachial artery diameters for the four groups (excluding the group with cardiovascular disease). To better illustrate diameter changes in these four groups, normalized means and standard deviations of the brachial arterial diameters for each stage compared to baseline are tabularized in Table II.

Figure 3 illustrates comparisons of the graphic patterns that characterize each group (excluding the group with cardiovascular disease). Diameter changes are expressed as percent of baseline. Whether plotted individually for each subject or summarized as group means (Fig. 2), the artery diameter of each group represents as variation of the characteristic “W” pattern. The least variation among groups occurs during early vasoconstriction (first descending limb of “W”), whereas the greatest variation among groups is in the total

amplitude during maximal pedaling effort and recovery stages. Table III provides the normalized mean changes of the brachial arterial diameters.

Young athletes (YA) have greater total arterial constriction (10% YA vs 7.5% OA between stage 1 and 4) and the greater capacity for recovery at 3 minutes (10% YA vs 5% OA between stage 4 and 5, $P < 0.05$) compared to old athletes. A similar tendency is observed between young athletes and young sedentary (YS) controls. Although young controls have preserved vasoconstrictive capacity (10% YA vs 8% YS), arterial relaxation is reduced during recovery (10% YA vs 5% YS, $P < 0.05$). The largest difference in early arterial relaxation is observed between young athletes and old sedentary (OS) groups. Vasoconstrictive capacity in the older sedentary controls is similar (10% YA vs 8% OS); however, arterial relaxation is reduced (10% YA vs 2.5% OS, $P < 0.05$).

When we compare old athletes with sedentary controls, the old athletes have similar vasoconstrictive and vasodilatory capacity to the young sedentary controls (vasoconstriction 7.5% OA vs 8% YS; vasodilation 5% OA vs 5% YS). Old sedentary controls have relatively preserved vasoconstriction (7.5% OA vs 8% OS), but their capacity to vasodilate is reduced in both groups (5% OA vs 2.5% OS).

To evaluate vasoreactive changes in the presence of cardiovascular disease, elderly sedentary controls were compared to elderly cardiovascular controls (Fig. 4). Vasoconstriction is reduced with pathologic cardiovascular disease (8% OS vs 3% OC, $P < 0.05$). Relaxation during the recovery stage is comparably low in both groups (2.5% OS vs 3% OC).

We also performed 6-year follow-up for the elderly athletes to assess the influence of aging on vasoconstriction and vasodilation (Fig. 5). As aging progresses, arterial response to exercise is blunted (vasoconstriction 8% vs 3%, age 72–77 years, $P < 0.05$; vasodilation 5% vs 3%, age 72–77 years).

Discussion

These data demonstrate that the vascular bed in an extremity excluded from direct exercise can be used to evaluate vascular integrity across population groups. As well, they demonstrate better preservation of vascular integrity in subjects who exercise in later years and are free of cardiovascular disease. Our discussion focuses on potential mechanisms of these changes, implications of these, and factors influencing our results.

The evaluation of the brachial artery traditionally assesses resting flow mediated dilatation (FMD) as a measure of endothelial function.^{6,7} However, the pathophysiologic effects of exercise on the total vascular system cannot be evaluated using FMD. In this study, we recorded brachial arterial diameter changes that result from exercise physiology taking place concurrently in the legs.

The sequence of brachial arterial constriction and relaxation increases in a stepwise form with increasing pedaling resistance and recovery following a characteristic pattern that implies the status of vasoreactivity. The brachial artery constricts at the start of exercise and remains variably constricted through all active stages of the leg pedaling. While arterial flow velocity increases continuously in proportion to the pedaling effort, the arterial diameter fluctuates. The amplitude of fluctuation appears to be affected by age, physical fitness, and vascular wall integrity.

Paradoxical brachial arterial constriction in the face of high arterial flow velocity implies that this response is not flow mediated. Similarly, arterial dilatation occurs paradoxically

while arterial flow velocity is slowing. These vascular responses may be initiated by central neuroregulators.⁸

Our results demonstrated some interesting findings.

We designated arterial response to remote exercise in young athletes as optimal arterial reactivity. Senior athletes were found to have arterial function closest to that of healthy young men. Cardiovascular disease and sedentary lifestyle have an impact on vascular reactivity. As this study was based on an imaging methodology to assess vasoreactivity, the physiologic mechanisms that mediate these responses and the effect of exercise on vascular responses were not investigated. Other studies have evaluated cardiac functional changes with aging.^{9,10} They have found that, although ventricular diastolic function decreases with aging, exercise tends to preserve and lessen the age related decline in ventricular diastolic function. Our study demonstrates that the arterial dynamics, especially relaxation, are relatively preserved with aging, although it declines as seniors reach their ninth decade.

As the study centered on evaluating a small group of elderly elite athletes and a similar number of elderly control subjects, the number of subjects in the other groups for comparison was by definition small and significance was not found except when comparing data to the young athletes. Similarly, the absolute change in the artery dimensions was small. Nevertheless, when changes were normalized, variations appear characteristic and reflect age and arterial wall integrity. As our principal group was elite elderly athletes, there were not enough women in the Chicago metropolitan area who met our entry criteria and so unfortunately women were not evaluated. The findings in women at all ages, athletic level, and disease level remain to be determined. Future studies will be necessary with larger population groups to better quantify the changes with aging, physical activity, and cardiovascular pathology.

The noninvasive stress protocol used in this study appears practical as a tool to evaluate vascular integrity during exercise. It allows comparison of arterial wall responses to exercise for different age groups and lifestyles.

Conclusion

This study confirms the feasibility of measuring brachial artery vasoreactivity directly as leg exercise takes place. Although resting brachial artery dynamics is opposite to those that occur in physically active musculature, they nevertheless reflect the status of arterial wall reactivity. This imaging method promises to be a practical modality for assessment of the effects of cardiovascular fitness and age on arterial vasoreactivity.

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Figure 1.

This figure demonstrates brachial arterial flow velocity (above baseline) and arterial constriction (below baseline) of nonexercising conduit arteries with remote exercise. Velocity rises and falls in a linear fashion during pedaling. Arterial constriction (negative values below baseline) takes place in a nonlinear manner as the degree of constriction intensifies or relaxes. Values represent percent deviation from baseline. Percent velocity is 1/10 of true velocity.

Figure 2.

Composite changes for all five groups displaying fluctuation in artery diameter during remote exercise resembles the letter “W.” Each data point is the average of the means of all groups tested including those with cardiovascular disease ($\bar{x} \pm SD$).

Changes in Brachial Artery Vasodynamic Response

Figure 3.

Changes in brachial artery response to pedaling for the four groups (without cardiovascular disease) shown as percent deviation from baseline. Young athletes demonstrate maximal vasoreactivity. Vasoreactivity in older athletes is blunted compared to young athletes, but similar to young sedentary males. The effect of sedentary lifestyle is most evident in the low rate of arterial relaxation in recovery.

Figure 4.

Effects of cardiovascular disease on vasoreactivity in the elderly groups. Sedentary seniors with cardiovascular disease show a reduction of contractile response to exercise and delayed relaxation during recovery compared to control elderly males.

Figure 5.
Six-year follow-up of the elderly athletes illustrating the effects of aging. Arterial vasoreactivity decreases as aging progresses.

TABLE I
Means and Standard Deviations ($\bar{x} \pm \text{SD}$) of the Brachial Arterial Diameters (cm) for Each Group

Group	Exercise Stage				
	1 (Baseline)	2	3	4	5/6 (Recovery)
Young athletes	0.40 $\pm$ 0.039	0.38 $\pm$ 0.036	0.38 $\pm$ 0.029	0.36 $\pm$ 0.036	0.40 $\pm$ 0.049
Old athletes	0.37 $\pm$ 0.041	0.36 $\pm$ 0.044	0.37 $\pm$ 0.034	0.34 $\pm$ 0.040	0.36 $\pm$ 0.042
Young sedentary	0.36 $\pm$ 0.028	0.34 $\pm$ 0.028	0.34 $\pm$ 0.029	0.33 $\pm$ 0.028	0.36 $\pm$ 0.033
Old sedentary	0.38 $\pm$ 0.052	0.36 $\pm$ 0.041	0.36 $\pm$ 0.058	0.34 $\pm$ 0.059	0.35 $\pm$ 0.056

TABLE II
Normalized Means and Standard Deviations ($\bar{x} \pm \text{SD}$) of the Brachial Arterial Diameters Compared to Baseline

Group	Exercise Stage				
	1 (Baseline)	2	3	4	5/6 (Recovery)
Young athletes	1.00 $\pm$ 0.000	0.95 $\pm$ 0.022	0.95 $\pm$ 0.045	0.90 $\pm$ 0.094	1.00 $\pm$ 0.082
Old athletes	1.00 $\pm$ 0.000	0.95 $\pm$ 0.025	0.98 $\pm$ 0.042	0.93 $\pm$ 0.041	0.98 $\pm$ 0.052
Young sedentary	1.00 $\pm$ 0.000	0.94 $\pm$ 0.016	0.94 $\pm$ 0.045	0.92 $\pm$ 0.021	0.97 $\pm$ 0.033
Old sedentary	1.00 $\pm$ 0.000	0.95 $\pm$ 0.086	0.95 $\pm$ 0.042	0.92 $\pm$ 0.038	0.95 $\pm$ 0.049

TABLE III

Normalized Percent Means of the Brachial Arterial Diameter Changes Between Exercise Stages

Group	Δ Exercise Stages			
	1-2	2-3	3-4	4-5/6
Young athletes	-5.0	+0.0	-5.0	+10.0*
Old athletes	-5.0	+2.5	-5.0	+5.0**
Young sedentary	-6.0	+0.0	-2.0	+5.0**
Old sedentary	-5.5	+0.0	-2.5	+2.5

* YA have greater vasodilation from peak exercise to recovery compared to all other groups ($P < 0.05$).

** OA and YS are not different in vasodilation from peak exercise to recovery ($P = NS$).