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Low Flow-Mediated Constriction: Prevalence, Impact and Physiological Determinants

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Low Flow-Mediated Constriction: Prevalence, Impact and Physiological Determinants

by

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Abstract

Low Flow-Mediated Constriction: Prevalence, Impact and Physiological Determinants

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Flow-mediated dilation (FMD) is used as a surrogate marker for endothelial function, a subclinical indicator of coronary artery disease (CAD) and for that reason; FMD is commonly used to compare endothelial function across groups differing in age and number and/or type of CAD risk factors. The traditional calculation of FMD involves arterial diameter prior to cuff inflation and then peak arterial diameter following cuff release. Generally, arterial response during cuff inflation is not taken into consideration. The aims of the present study were to determine 1) if there were differences in brachial artery response, more specifically vasoconstriction, during cuff inflation in a diverse population of subjects, 2) if variability existed, the resulting impact on the calculation of traditional FMD, and 3) if arterial stiffness was a physiological determinant in this

process. A total of 84 subjects, varying in age (18-62 years) and CAD risk factor profiles were studied. Low flow-mediated constriction (L-FMC), during cuff inflation, traditional FMD, and modified FMD, which accounts for L-FMC, were calculated to investigate brachial artery response during all three stages of the FMD measurement. Subjects ≥ 50 years old had lower FMD response compared with those ≤ 35 years old but only the modified FMD was statistically significant. The same effect was seen when comparing healthy subjects to those with multiple risk factors for CAD; there was an attenuated FMD response that only reached statistical significance with modified FMD. L-FMC was modestly but significantly associated with FMD. L-FMC was weakly but positively correlated with brachial pulse wave velocity (PWV). Our results indicate that modified FMD, which takes into consideration brachial response to cuff inflation, may be a more sensitive indicator of endothelial dysfunction and that arterial stiffening may be a physiological determinant in this process.

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Introduction

Cardiovascular disease is the primary cause of mortality in the United States, and many of these deaths can be attributed to coronary artery disease (CAD). Endothelial dysfunction is believed to be the initial pathological process that gives rise to CAD. Flow-mediated dilation (FMD) is a common, non-invasive technique that is used as a surrogate marker for endothelial function (2).

FMD is dependent on vessel response to the increase in blood flow that follows the release of a cuff. The calculation of FMD involves arterial diameter prior to cuff inflation and then peak arterial diameter following cuff release. Generally, arterial response to cuff inflation is not taken into consideration. Currently, there is discrepancy in the literature as to what actually happens to the artery during cuff inflation. There are some studies reporting vasoconstriction during cuff inflation and termed this response as low flow-mediated constriction (L-FMC) (5, 6). However, some studies show vasodilation and some show no response at all (8, 14, 15). The first aim of this study was to determine if there were differences in brachial artery response during cuff inflation in a diverse population of subjects.

Currently, most FMD measurements only quantify the percent change in vessel diameter compared with baseline and do not take into account changes occurring during cuff inflation. However, the actual state of the vessel when it responded to the hyperemic blood flow upon cuff release could be important so the second aim of our study was to determine the impact of accounting for the changes in vasoactive state during cuff inflation on the subsequent calculation of FMD. We used the term "modified FMD" to represent the effect of using the inflation diameter versus the baseline diameter for the

FMD calculation. This was assessed in young versus older groups and in individuals with 0 versus 2+ CAD risk factors.

If arterial diameter changes during cuff inflation, arterial stiffness or the structural changes in the arterial wall may be a possible mechanism for the varied vessel response during cuff inflation. However, this question has yet to be studied. Therefore, the third aim of our study was to compare arterial stiffness with L-FMC as a possible physiological determinant for the varied brachial artery response.

Methods

SUBJECTS

A total of 84 adults (46 male/38 female) with a varied profile of CAD risk factors were studied (Table 1). 13% of subjects were hypertensive (systolic BP ≥140mmHg and/or diastolic BP ≥90mmHg), 39% obese (BMI ≥30kg/m^2), 22% diabetic (fasting blood glucose ≥126 mg/dL), and 27% dyslipidemic (HDL ≤35 mg/dL and/or LDL ≥130 mg/dL). Participants with overt symptoms of cardiovascular disease were excluded from the current study. All subjects provided written informed consent prior to participation. The study was reviewed and approved by the Institutional Review Board.

MEASUREMENTS

Following a 12 hour overnight fast, a blood sample was collected from the antecubital vein by venipuncture. Plasma concentrations of low-density lipoprotein, high-density lipoprotein, triglycerides, and glucose were determined by enzymatic methods. Brachial blood pressure was measured in triplicate from the contralateral arm in a supine position with an automated oscillometric device (HEM-907XL, OMRON Healthcare, Vernon Hills, Illinois).

FMD MEASUREMENT

Brachial FMD measurements were taken in accordance with previously defined protocol (3). Briefly, participants were asked to avoid exercise and alcohol for ≥24 hours before measurement. All measurements were performed after fasting and abstaining from caffeine for ≥4 hours. Subjects were studied in a supine position after ≥15 minutes of rest in a temperature-controlled (22-24°C) laboratory setting.

A longitudinal image of the brachial artery was obtained using a B-mode Doppler ultrasound machine equipped with a compact high-resolution linear-array transducer (iE 33 ultrasound System, Phllips, Bothel, WA). A customized transducer-holding device held the transducer in place 5 to 10 cm proximal to the antecubital fossa. A rapid inflation cuff was placed on the ipsilateral forearm distal to the elbow (E20, Hokanson, Bellevue, WA). Following the baseline recording, a blood flow occlusion cuff was inflated to 100 mmHg above baseline systolic blood pressure for 5 minutes. 60 seconds of diameter measurements were made at baseline, prior to cuff inflation, and then at 3 minutes 30 seconds after cuff inflation. The timing of the occluded artery diameter measurement was made in accordance with previous work (5). Peak reactive hyperemia diameter measurements were made continuously for 90 seconds, beginning 10 seconds prior to cuff deflation in order to ensure that peak diameter would be captured.

All ultrasound-derived images were transferred and analyzed using image analysis software (Vascular Research Tool Brachial Analyzer, Medical Imaging Applications, Coralville, Iowa). All of the images were taken and analyzed by the same investigator who was blinded to physical and physiological characteristics of the subjects.

L-FMC, FMD AND MODIFIED FMD CALCULATIONS

$$\text{L-FMC} = \frac{D_{\text{infl}} - D_{base}}{D_{base}} \times 100\%$$

$$FMD = \frac{D_{rep} - D_{base}}{D_{base}} \times 100\%$$

$$\text{Modified FMD} = \frac{D_{rep} - D_{\text{infl}}}{D_{\text{infl}}} \times 100\%$$

where D_{base} is the average of 10 consecutive end-diastolic brachial artery diameters before cuff-inflation, D_{infl} is the average of the 3 consecutively lowest end-diastolic diameters during cuff-inflation, and D_{rep} is the average of the 3 consecutively highest peak end-diastolic diameters during reperfusion, all expressed in mm.

Brachial pulse wave velocity (PWV) was calculated as previously described (1) using the following equations:

$$PWV = \frac{1}{\sqrt{DCp}}$$

$$DC = \frac{2D_{base}\Delta D + \Delta D^2}{\Delta P {D_{base}}^2}$$

where DC = distensibility coefficient expressed in 10-3/kPa, p is the density of blood (assumed to be 1,060 kg/m3), ΔD is difference between the average of 10 consecutive end-systolic brachial artery diameters before cuff-inflation and Dbase, and ΔP is pulse pressure in kPa. PWV is expressed in m/s.

STATISTICAL ANALYSIS

In order to determine the impact of age and CAD risk factors on L-FMC, subjects were divided according to age (≤35 and ≥50 years) and number of CAD risk factors (0 and 2+ risk factors). One-way analysis of variance determined differences between L-FMC, FMD, and modified FMD measures in all group comparisons. Pearson correlation analysis determined relations between L-FMC vs. FMD and L-FMC vs. brachial PWV. Significance was set a priori at $p<0.05$. All data expressed as mean±SEM.

Results

PREVALENCE

In our subject sample, as displayed in Figure 1, the prevalence of L-FMC was 67%; 33% displayed vasodilation during blood pressure cuff inflation.

IMPACT OF FMC

The subjects were divided into young (≤35 years old) and older (≥50 years old) age groups. There was a significant difference between baseline brachial diameter and inflation diameter in the young (3.94±0.11 mm vs. 3.86±0.10 mm; $p<0.001$) but not in the old (4.20±0.19 mm vs. 4.19±0.20 mm; $p=0.90$). These age-associated differences were attributed to differences in L-FMC (upper panel in Figure 2). FMD tended to be lower in older than in young subjects but the difference did not reach statistical significance ($p = 0.06$). After accounting for L-FMC, the modified FMD was significantly higher than FMD in young subjects (5.13±.48 % vs. 7.41±0.56 %; $p<0.001$). However, such a trend was not observed in older subjects (3.76±0.52 % vs. 3.92±0.60 %; $p=0.78$).

In order to assess the impact of CAD risk factors, the subjects were divided into healthy (i.e. no risk factors) and multiple risk factor (2+) groups (n=34). In an attempt to isolate the impact of CAD risk factors, these 2 groups were age-matched. As depicted in Figure 3, L-FMC and FMD were not different between the risk factor groups. When brachial response during cuff inflation was accounted for, the modified FMD was significantly lower in the multiple risk factor group than in the healthy group.

PHYSIOLOGICAL DETERMINANTS

L-FMC was modestly but significantly correlated with FMD (r=0.26) (Figure 4). L-FMC was positively and significantly associated with brachial PWV (r=0.30) (Figure 5).

Discussion

PREVALENCE

This study assessed brachial artery response to cuff inflation in a diverse population of subjects. As seen in Figure 1, about two thirds of the subjects vasoconstricted during cuff inflation compared with one third that vasodilated. Gori et al. initially introduced the term, L-FMC, to describe this response and suggested that it could also be used as a compliment to FMD in the assessment of vascular function (5, 6). Interestingly, FMD was assessed in the radial rather than the brachial artery and all of the subjects vasoconstricted during cuff inflation, in spite of a subject population diverse in both age and CAD risk factors. Using the brachial artery for the measurement of FMD has been proven to be both accurate and reproducible (10), and endothelial function in the brachial artery has been shown to be well correlated with endothelial function in the coronary arteries (13). Weissgerber et al examined differences in L-FMC between the radial and brachial arteries and concluded that vasoconstriction occurred in the radial but not in the brachial artery (15). Our diverse group of subjects showed a variable brachial arterial response to inflation of the cuff.

IMPACT OF FMC

When comparing baseline brachial diameter and diameter during cuff inflation among the subjects, there was a difference in vessel response between the young and the older group. The young showed significant vasoconstriction ($p<0.001$) that was not seen with the older group, who showed no significant change ($p=0.90$). These results differ from those presented by Parker et al. who found no age group differences between brachial artery baseline and inflation diameters in young (22±1 yrs) or old (70±2 yrs)

subjects (8) as well as from Thijssen et al, who found significant vasodilation in children (10±1 yrs) and adults (28±6 yrs) but no significant change in the older adults (58±5 yrs) (14). These diverse results demonstrate that brachial response to cuff inflation does vary widely among a diverse population of subjects.

The differences in L-FMC became important when considering which diameter (D_{base} vs. D_{infl}) to use for calculating FMD. In the present study, there was a statistically significant difference in the FMD of the young group when their inflation diameter (D_{infl}) was used in place of their baseline diameter (D_{base}) ($p<0.001$) but no significant difference was seen between the two in the older group ($p=0.78$). Thijssen et al. also demonstrated a significant effect on the resulting FMD depending on which diameter was used for the calculation (14). Figure 2 further demonstrates the effect of taking into consideration brachial artery response by comparing L-FMC, FMD and modified FMD across the two age groups. Again, statistical significance was found only with the modified FMD ($p<0.001$).

This is the first study to attempt to isolate the effect of overall CAD risk on brachial artery response to cuff inflation. Two groups were age-matched, separated into 0 vs. 2+ risk factors, and then L-FMC, FMD, and modified FMD across the two groups were compared; shown in Figure 3. Statistical significance was achieved only with the modified FMD ($p<0.05$). This implies that brachial response to cuff inflation is not only affected by age but also by an increasing number of CAD risk factors. Other studies have demonstrated a variable brachial arterial response when comparing healthy subjects to those with specific CAD risk factors such as smoking and hypercholesterolemia (4, 12).

FMD is routinely used in research settings as a surrogate marker for endothelial function and, as such, is often the tool used to compare endothelial function across groups differing in age, fitness level, number of CAD risk factors, etc. Using modified FMD may

make comparisons across groups more accurate as it represents the actual state of the vessel when it responds to the hyperemic blood flow following cuff release. As such, this measure may be a better indicator of endothelial function.

PHYSIOLOGICAL DETERMINANTS

Figure 4 demonstrates a weakly positive correlation between L-FMC and FMD ($p<0.05$). This relation suggests that the greater the vasoconstriction during cuff inflation, the lower the calculated FMD. This may provide some insight as to the interplay between these two responses. Weissgerber et al. also saw a weak positive correlation between the two and suggested that the endothelial mediators that control L-FMC are still active and could interfere with the mediators responsible for the FMD reperfusion response (15) . The reactivity of the brachial artery is influenced by a number of chemical mediators that control vasoconstriction and vasodilation in response to environmental change. A disruption in the balance of these, an excess of one or a deficit of another, could influence the response of the artery to its environment. One study used a selective ET_A receptor specific antagonist and concluded that endothelin-1 mediated radial artery constriction during a low flow state (11).

Thijssen et al. speculated that L-FMC brachial response might be related to the age-related increase in arterial stiffness (14). A possible explanation is that as arterial stiffness increases, the ability of the brachial artery to vasoconstrict during cuff inflation decreases; as a result of a less compliant, stiffer vessel. We also found a modest positive correlation between L-FMC and brachial PWV ($p<0.05$).

Limitations to the current study include the relatively small sample size. This number of subjects did not allow for the investigation of specific CAD risk factors such as hypertension, diabetes, obesity and dyslipidemia on their own so we assessed them as an element of overall CAD risk. Further exploration is warranted to determine if there is a

characteristic brachial artery response specific to any one of these risk factors. This would perhaps provide further insight into the mechanisms involved. Second, we did not have blood samples on our entire population of subjects. The missing blood measures on these subjects were glucose and lipids so responses to a health research questionnaire were the criteria used to classify about one quarter of the subjects into the 0 risk factor group. These were all believed to be healthy subjects that had never been told by a doctor that they had either of these the risk factors so we do believe they were classified appropriately.

Conclusion

Over the past decade, guidelines have been put forth to try and standardize the FMD procedure (3, 7, 9) thereby decreasing variability between studies. Up to now, these guidelines stop short of suggesting which diameter, D_{base} vs. D_{infl}, to use for the FMD calculation, but the evidence presented here suggests that this facet of FMD measurement may warrant such standardization.

Table 1: Selected Subject Characteristics

Variable	Mean±SEM
Male/Female	46/38
Age, yrs	41±1
Height, cm	167±1
Body Mass, kg	83±3
BMI, kg/m^2	30±1
Systolic BP, mmHg	122±2
Diastolic BP, mmHg	71±1

BMI = Body Mass Index, BP = Blood Pressure

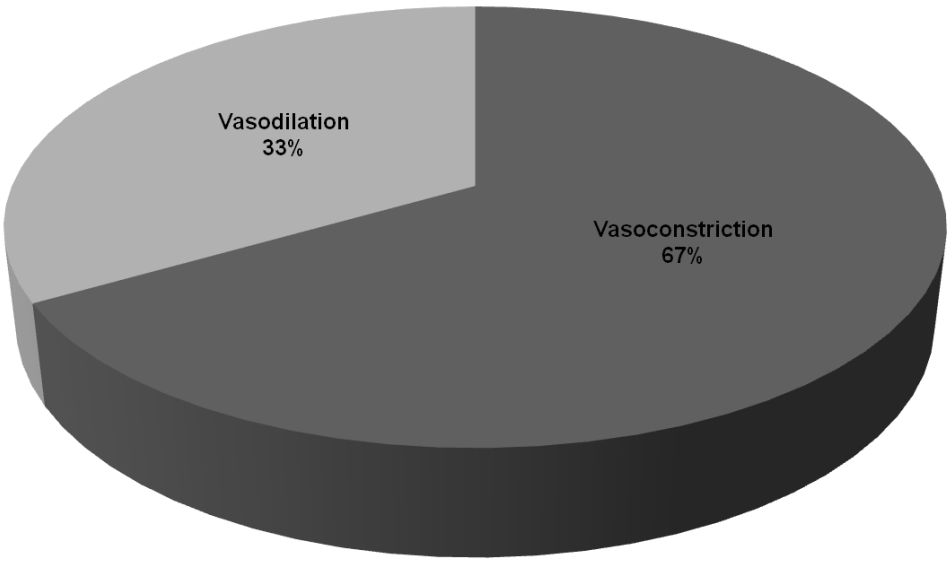

Figure 1: Brachial artery response to blood pressure cuff-induced ischemia.

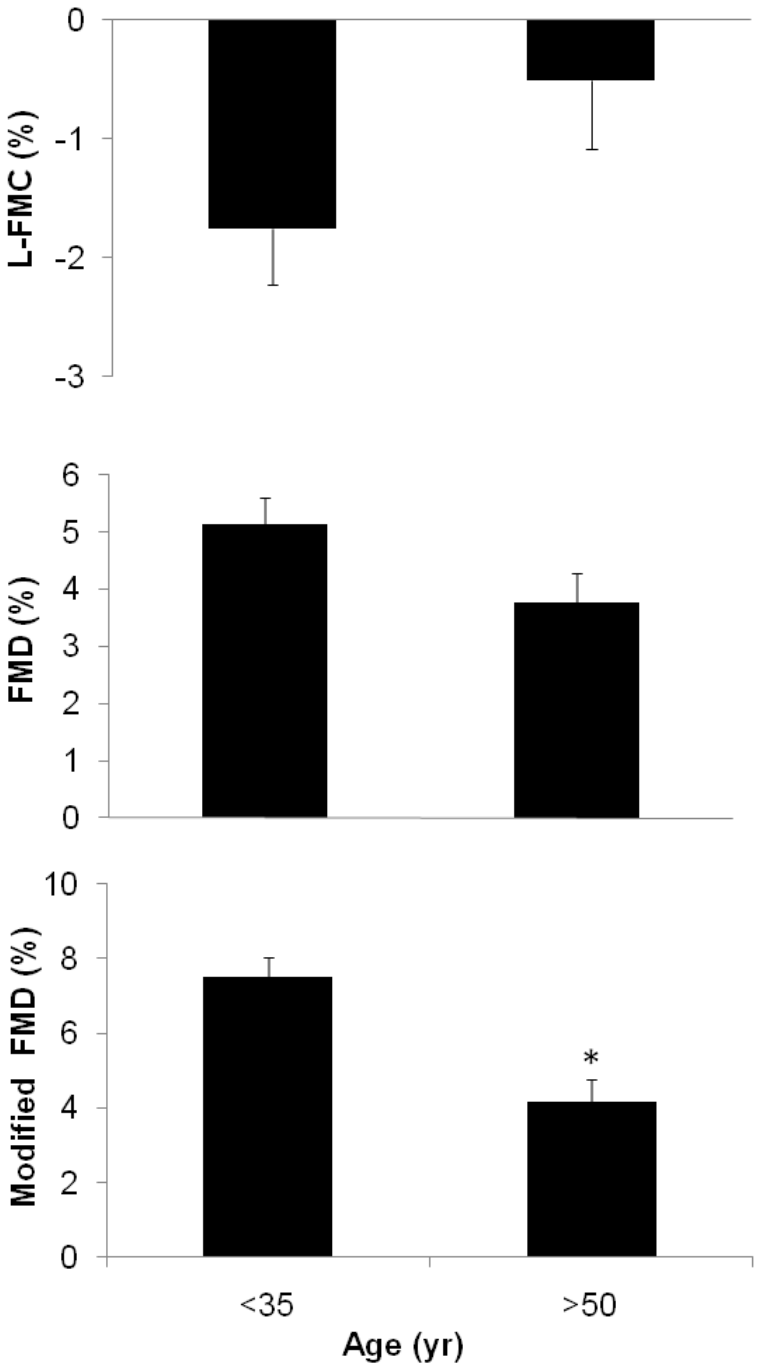

Figure 2: Age-associated differences in low flow-mediated constriction (L-FMC) and flow-mediated dilation (FMD) [n=60].
*p<0.001 vs. <35 yr.

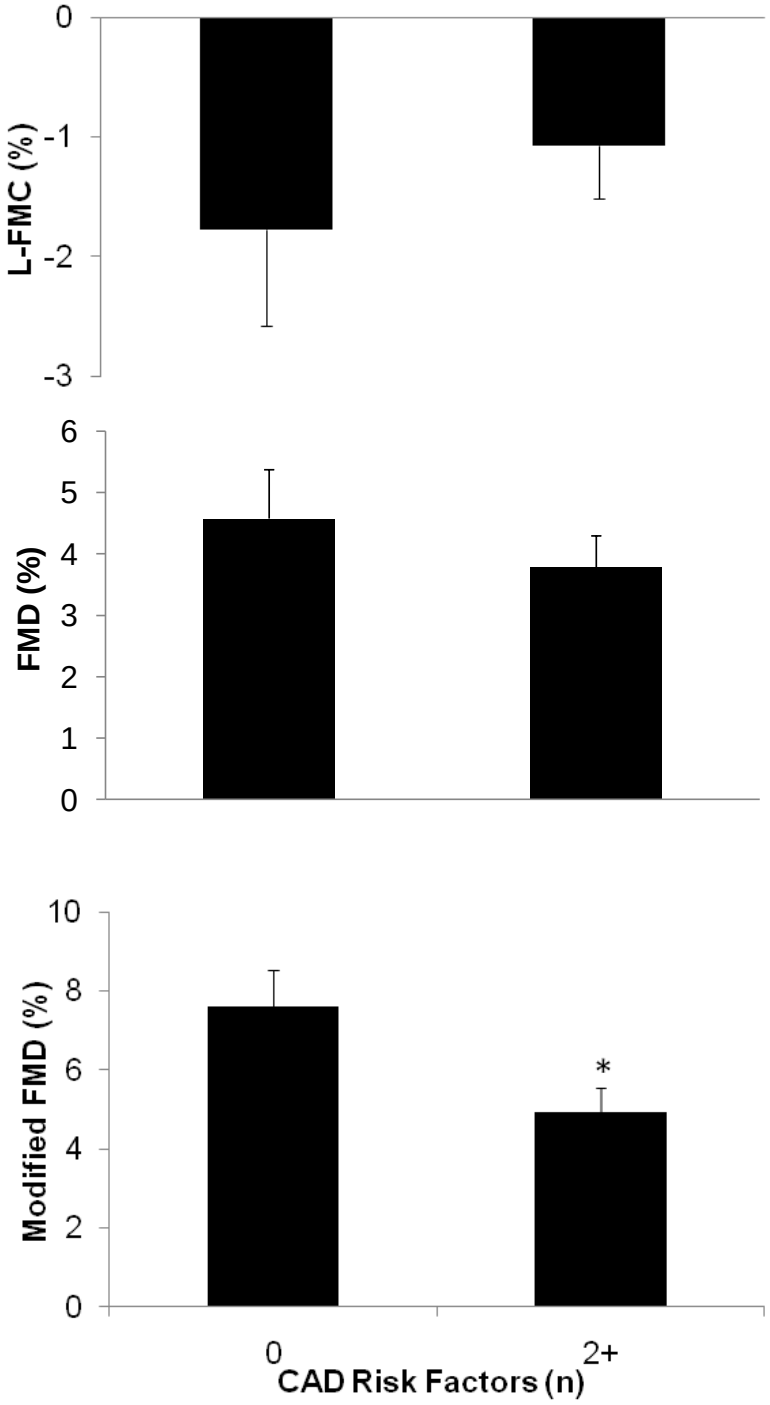

Figure 3: Low flow-mediated constriction (L-FMC) and flow-mediated dilation (FMD) as a function of the number of risk factors for coronary artery disease [n=34]. *p<0.05 vs. 0 CAD risk factors

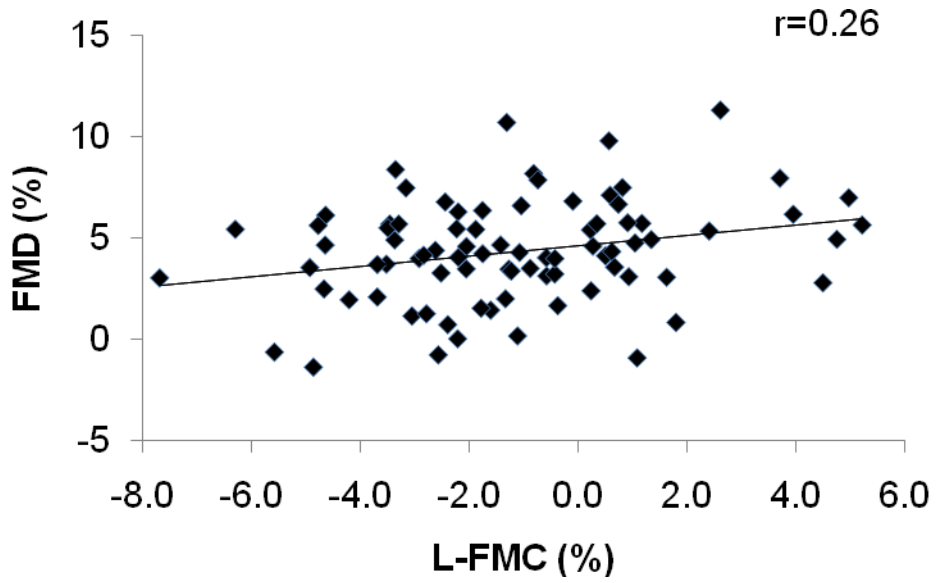

Figure 4: Association between low flow-mediated constriction (L-FMC) and flow-mediated dilation (FMD).

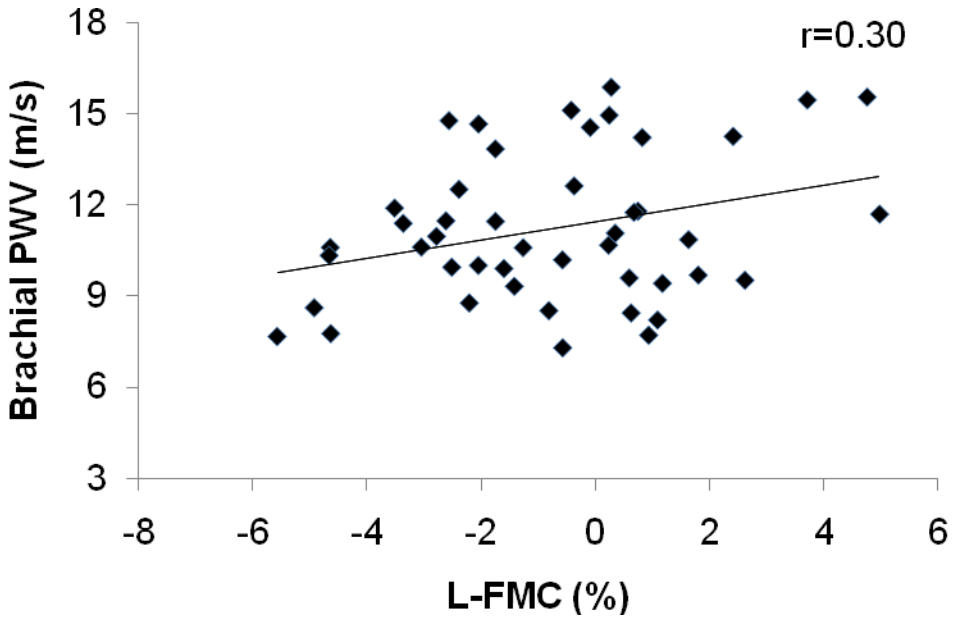

Figure 5: Association between low flow-mediated constriction (L-FMC) and brachial artery pulse wave velocity (PWV).

Appendix

Research Health Questionnaire

Cardiovascular Aging Research Laboratory

Personal Information

Today's Date _____ Subject ID _____

Date of Birth _____ Age _____ Sex ☐ Male
☐ Female: Date of Last Menstrual Period:_____

Please circle the highest grade in school you have completed:

Elementary school	1	2	3	4	5	6	7	8
High school	9	10	11	12				
College/Post Grad	13	14	15	16	17	18	19	20+

What is your marital status? ☐ Never Married ☐ Married ☐ Widowed ☐ Divorced; Separated

Ethnic Background: ☐ Hispanic or Latino ☐ Not Hispanic or Latino

Race:
☐ White ☐ American Indian/Alaskan Native ☐ Pacific Islander
☐ Black or African American ☐ Asian ☐ Other: _____

Symptoms or Signs Suggestive of Disease

Check appropriate box:

Yes	No		
☐	☐	1.	Have you experienced unusual pain or discomfort in your chest, neck, jaw, arms or other areas that may be due to heart problems?
☐	☐	2.	Have you experienced unusual fatigue or shortness of breath at rest, during usual activities, or during mild-to-moderate exercise (e.g., climbing stairs, carrying groceries, brisk walking, cycling)?
☐	☐	3.	When you stand up, or sometimes during the night while you are sleeping, do you have difficulty breathing?
☐	☐	4.	Do you lose your balance because of dizziness or do you ever lose consciousness?
☐	☐	5.	Do you suffer from swelling of the ankles (ankle edema)?
☐	☐	6.	Have you experienced an unusual and rapid throbbing or fluttering of the heart?
☐	☐	7.	Have you experienced severe pain in your leg muscles during walking?
☐	☐	8.	Has a doctor told you that you have a heart murmur?

Chronic Disease Risk Factors

Check appropriate box:

Yes	No		
☐	☐	9a.	Are you a male over age 45 years or a female over age 55 years?
☐	☐		b. Are you a female who has experienced premature menopause?
☐	☐		c. If you answered "yes" to 9b, are you on estrogen replacement therapy?
☐	☐	10.	Has your father or brother had a heart attack or died suddenly of heart disease before the age of 55; has your mother or sister experienced these heart problems before the age of 65?
☐	☐	11.	Are you a current cigarette smoker? If quit smoking, when? Date:

Yes	No		
☐	☐	12.	Has a doctor told you that you have high blood pressure (more than 140/90 mm Hg) or a heart condition?
☐	☐	13.	Is your total serum cholesterol greater than 200 mg/dl, or has a doctor told you that your cholesterol is at a high risk-level?
☐	☐	14.	Do you have diabetes mellitus?
☐	☐	15.	Are you physically inactive and sedentary (little physical activity on the job or during leisure time)?
☐	☐	16.	Do you have a bone or joint problem that could be made worse by a change in your physical activity?
☐	☐	17.	During the past year, would you say that you have experienced enough stress, strain, and pressure to have a significant effect on your health?
☐	☐	18.	Do you eat foods nearly every day that are high in fat and cholesterol such as fatty meats, cheese, fried foods, butter, whole milk, or eggs?
☐	☐	19.	Do you weigh 30 or more pounds than you should?
☐	☐	20.	Do you know of any other reason you should not do physical activity?

Medical History

21. *Please check which of the following conditions you have had or now have. Also check medical conditions in your family (father, mother, brother(s), or sister(s)). Check as many as apply.*

Self	Family	Medical Condition	Self	Family	Medical Condition
☐	☐	Coronary heart disease, heart attack; by-pass surgery	☐	☐	Major injury/fracture to foot, leg, knee
☐	☐	Arrhythmias	☐	☐	Major injury to back or neck
☐	☐	Angina	☐	☐	Major injury/fracture to hip or shoulder
☐	☐	Marfan's syndrome			
☐	☐	High blood pressure	☐	☐	Recent leg trauma/injury
☐	☐	Peripheral vascular disease	☐	☐	Rheumatoid arthritis
☐	☐	Phlebitis or emboli	☐	☐	Osteoarthritis
☐	☐	Other heart problems	☐	☐	Osteoporosis
☐	☐	Stroke	☐	☐	Fibromyalgia
☐	☐	Asthma	☐	☐	Chronic fatigue syndrome
☐	☐	Bronchitis	☐	☐	Systemic lupus erythematosus
☐	☐	C.O.P.D. (emphysema)	☐	☐	Anemia (low iron)
☐	☐	Pulmonary embolism (blood clots in lungs)	☐	☐	Thyroid problems
			☐	☐	Gout
☐	☐	Deep vein thrombosis (blood clots in legs)	☐	☐	Kidney disease
			☐	☐	Nephrotic syndrome
☐	☐	Antithrombin III deficiency	☐	☐	Gallstones/gallbladder disease
☐	☐	Inherited hypercoaguability	☐	☐	Liver disease (cirrhosis)
☐	☐	Acquired hypercoaguability	☐	☐	Hepatitis
☐	☐	Factor V leiden mutations	☐	☐	Diabetes mellitus
☐	☐	Protein C deficiency	☐	☐	Raynaud's disease
☐	☐	Protein S deficiency	☐	☐	Crohn's disease
☐	☐	Stomach/duodenal ulcer	☐	☐	Hysterectomy
☐	☐	Rectal growth or bleeding	☐	☐	Problems with menstruation

Self	Family	Medical Condition	Self	Family	Medical Condition
☐	☐	Irritable bowel syndrome	☐	☐	Post-menopausal
☐	☐	Lung cancer			Date:
☐	☐	Breast cancer	☐	☐	Allergies
☐	☐	Prostate cancer	☐	☐	Depression
☐	☐	Skin cancer	☐	☐	Anxiety, phobias
☐	☐	Colorectal cancer	☐	☐	Eating disorders
☐	☐	Other cancer Specify:	☐	☐	Substance abuse problems (alcohol, other drugs, etc.)
☐	☐	Hearing loss	☐	☐	Sleeping problems
☐	☐	Cataracts	☐	☐	Other
☐	☐	Glaucoma			Specify:

Please specify and include information on any recent illnesses, hospitalizations, surgical procedures, or other health problems.

_____

_____

22a. Are you currently pregnant, think you may be pregnant, or are currently trying to get pregnant?

☐ Yes ☐ No ☐ Not sure ☐ Not applicable (male or post-menopausal)

b. If you answered "yes" or "not sure" to 22a, do you need a pregnancy test? ☐ Yes ☐ No

23. In the past two weeks, have you had a barium test, a nuclear medicine scan, or x-rays with a dye injection?

☐ **Yes** ☐ **No**

24. *Please check any of the following medications you take regularly and give the name and dose of the medication.*

Medication	Name of Medication
☐ Heart medicine	_____
☐ Blood pressure medicine	_____
☐ Blood cholesterol medicine	_____
☐ Thromboembolic disease medicine	_____
☐ Hypercoaguability medicine	_____
☐ Steroids	_____
☐ Hormones/HRT	_____
☐ Birth control medicine	_____
☐ Medicine for breathing/lungs	_____
☐ Insulin	_____
☐ Other medicine for diabetes	_____
☐ Arthritis medicine	_____
☐ Medicine for depression	_____
☐ Medicine for anxiety	_____
☐ Thyroid medicine	_____
☐ Medicine for ulcers	_____
☐ Painkiller medicine	_____
☐ Allergy medicine	_____
☐ Dietary supplements (herbs, vitamins, etc)	_____

☐ Other (please specify) _____

25. Do you have any known drug allergies? _____

Body Weight

26. What is the most you have ever weighed? _____
27. Are you now trying to:

☐ Lose weight ☐ Gain weight ☐ Stay about the same ☐ Not trying to do anything

Stress

28. During the past month, how would you rate your overall level of stress?

☐ Very high ☐ High ☐ Moderate ☐ Low

29. In the past year, how much effect has stress had on your health?

☐ A lot ☐ Some ☐ Hardly any or none

30. On average, how many hours of sleep do you get in a 24-hour period?

☐ Less than 5 ☐ 5-6 ☐ 7-9 ☐ More than 9

Substance Use

31. How would you describe your cigarette smoking habits?

☐ Never smoked

☐ Used to smoke. How many years has it been since you smoked? _____ years

☐ Still smoke. How many cigarettes a day do you smoke on average? _____ cigarettes/day

32. How many alcoholic drinks do you consume? (A "drink" is a glass of wine, a wine cooler, a 16oz bottle/12oz can of beer, a shot glass of liquor, or a mixed drink).

☐ Never use alcohol ☐ Less than 1 per week ☐ 1-6 per week
☐ 1 per day ☐ 2-3 per day ☐ More than 3 per day

33. In one sitting, how many drinks do you typically consume? _____
34. How many cups (8 ounces) of coffee do you drink per day? _____
35. How many ounces of sodas containing caffeine do you drink per day? _____

Physical Fitness, Physical Activity/Exercise

36. Considering a **7-Day period** (a week), how many times on the average do you do the following kinds of exercise for **more than 15 minutes** during your **free time** (write on each line the appropriate number).

	Times Per Week
a) **STRENUOUS EXERCISE (HEART BEATS RAPIDLY)** (i.e. running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling)	_____
b) **MODERATE EXERCISE (NOT EXHAUSTING)** (i.e. fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing)	_____
c) **MILD EXERCISE (MINIMAL EFFORT)** (i.e. yoga, archery, fishing from river bank, bowling, horseshoes, golf, snow-mobiling, easy walking)	_____

37. Considering a 7-Day period (a week), during your leisure-time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?

☐ OFTEN ☐ SOMETIMES ☐ NEVER/RARELY

38. How long have you exercised or played sports regularly?

☐ I do not exercise regularly ☐ Less than 1 year ☐ 1-2 years
☐ 2-5 years ☐ 5-10 years ☐ More than 10 years

39. Please describe your regular physical activity during a typical week. Please include the intensity, duration, and type of activity. If you do not exercise, write "none".

	Activity	Duration (time)	Intensity
Monday			
Tuesday			
Wednesday			
Thursday			
Friday			
Saturday			
Sunday			

Occupational Health

40. Please describe your main job title and duties.

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41. How much hard physical work is required on your job?

☐ A great deal ☐ A moderate amount ☐ A little ☐ None

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Vitae

Michelle Harrison was born in Dryden, ON, Canada on January 25, 1969, the daughter of Paulette and Paul Bujold. After graduating high school from Port Arthur Collegiate Institute in Thunder Bay, ON in 1987, she entered the Thunder Bay Institute of Medical Technology and received her certification as a Medical Laboratory Technologist. She obtained her Bachelor of Medical Laboratory Science degree from the University of British Columbia in 2004. In September 2008, she entered The Graduate School at The University of Texas at Austin to pursue a Master's of Arts in Kinesiology.

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This thesis was typed by Michelle Harrison.