EFFECTS OF EXERCISE INDUCED BRACHIAL AND CAROTID ARTERY VASCULAR RESPONSES IN NORMAL SUBJECTS

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ABSTRACT

Background: Brachial artery reactivity in response to ischemia hyperemia reflects endothelial health. Responses of brachial artery and carotid artery to a physiologic stimulus of exercise may be a novel method to assess vascular heatlh.

Purpose: To compare brachial artery (BA) endothelium-dependent vasodilation to exercise induced vasodilation and to evaluate carotid artery (CA) responses to exercise in normal subjects.

Methods: We evaluated BA vasodilation in response to arm ischemia induced by blood pressure cuff as well as supine bicycle exercise stress induced BA and CA responses in 13 healthy volunteers aged 30±8 years.

Results: There was a 10%+4% BA vasodilation in response to ischemia. This was associated with a decrease in forearm resistance and an increase in forearm blood flow. Exercise produced 6±6% and 8±5% vasodilation of BA and CA respectively. No significant change in brachial artery blood flow measured by PW Doppler (98±55 to 78±38 ml/min, baseline vs. peak p=0.06, delta=-12±29%) or in CA blood flow (472±125 to 496±237 ml/min, baseline vs. peak p=0.7, delta=-6±21%) occurred.

Conclusion: Supine bicycle exercise produces BA and CA vasodilation, Assessment of BA and CA reactivity by ultrasound is a novel method for assessing vascular endothelial function.

Key Words: brachial artery, carotid artery, ultrasound, exercise, blood flow.

INTRODUCTION

Nitric oxide (NO) release from arterial endothelium causes vasodilation in response to physical stress[1], mental stress[2-3], and acetylcholine[3] in healthy subjects. Aging[4], hypercholesterolemia[5], hypertension[6-7], smoking[8], diabetes mellitus[9], and hyperhomocystenemia[10] are associated with an impaired endothelium dependent vasodilation. Brachial artery reactivity (BART) in response to ischemia induced shear stress assesses endothelial function by measuring arterial dilation[11,12], and is abnormal in patients with coronary artery disease[13,14,15] and its risk factors.[4,5,6,7,8,9,10,11,12] This test also assesses forearm arteriolar resistance and blood flow reserve by measuring Doppler velocity shifts before and during hyperemia. BA responses to rhythmic hand grip exercise has been evaluated[16,17], Ultrasound evaluation of shear induced vasodilation in response to exercise has not been used in the forearm or cerebral vascular beds. Cerebrovascular endothelial derived NO mediates local increase in cerebral blood flow during increase in cerebral metabolism in health[15,17] and disease[18]. Carotid artery (CA) increasing wall thickness (IMT) is a marker of atherosclerosis[19] and correlates with coronary risk factors.[20,21] Hypertension is associated with accelerated atherosclerosis and increased CA IMT as well as reduced endothelium-dependent vasodilation

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in peripheral arteries.[22] Since common CA supplies 80% blood flow to internal CA and only 20% to external CA, and since it is an ideal site to measure atherosclerotic burden via IMT, it may be ideally suited to investigate the effect of atherosclerosis on cerebrovascular blood flow reserve and CA endothelium dependent responses. To investigate the normal responses to a physiologic stimulus such as exercise that is likely to produce increased local shear stress within CA. on CA and BA arteries, we examined the effects supine bicycle exercise on brachial artery (BA) and CA. We hypothesized that BA and CA will demonstrate vasodilation in healthy subjects and that this vasodilation is measurable by ultrasound. Since the conventional ischemia induced BART technique cannot be applied to the cerebral circulation. CA reactivity in response to exercise may be a useful adjunctive tool for assessment of cerebrovascular endothelial function in health and disease.

METHODS

Thirteen healthy subjects participated in BA and CA reactivity during exercise. We performed BA reactivity to compare CA responses against this previously validated technique that measures endothelial function as well as to compare our lab results on BART with the published results. All studies were performed in the morning hours (between 8 and 11 AM) after an overnight fast. Informed consent was obtained and the protocol was approved by the Institutional Review Board for Human Subjects.

Study Recruitment and Eligibility

Subjects older than 18 years, right-handed, normotensive in normal sinus rhythm and able to give informed consent were included. Subjects with history of hypercholesterolemia (total cholesterol >240 and/or LDL cholesterol ≥160 mg/dl), coronary artery disease, congestive heart failure, cerebrovascular disease, diabetes mellitus, smoking during the previous 1 year, know systemic disease or malignancy, plaque in the common CA or its branches or IMT > 1.4 mm in the common CA, use of hormone replacement therapy or oral contraceptives within the last 3 months were excluded. Vitamin C, vitamin E, folic acid were withheld for 24 hours prior to the study participation.

Study Protocol

Demographic information was obtained prior to a 15-minute rest period in a quiet room. Arm blood pressure was measured by an automated machine. Heart rate was measured by ECG leads placed on the chest wall and displayed on the ultrasound system.

Ultrasound Studies. Ultrasound studies were performed using ATL 3000 ultrasound systems equipped with a linear array 5-12 MHz variable frequency scan head. The depth of field, gain, transmit focus and resolution mode settings were adjusted in each patient to give the image of maximum clarity with clear definition of intima and kept constant throughout the study. BA imaging was performed approximately 1-2 inches above medial anticubital fossa. CA imaging was performed to obtain a straight 5-7 cm segment of the CA below the carotid bulb. Ultrasound probe position was marked on the skin with a marker and position as well as baseline orientation of the probe was mimicked during peak hyperemia for BA and exercise for BA and CA. All procedures were recorded on videotape and select loops were digitized. DICOM images for PW Doppler measurements and cine loop recording for BA and CA diameter were stored in the hard as well as in magneto-optical discs.

Ultrasound Measurements. BA and CA diameter was measured at the onset of QRS complex from the cine loop recording as an average of 10 measurements from 2 separate digitized images, as the line identifying the media-adventitia interface in the near to the far wall using calipers in the ultrasound system. CA diameter measurements were made over 3 cm of a straight segment below the CA bulb. PW Doppler measurements included: velocity time integral (VTI), peak systolic (PSV), end diastolic velocity (EDV), pulsatility index (PI = (PSV-EDV)/VTI, resistive index (RI=PSV-EDV)/PSV) and blood flow (ml/min=3.14x $(r)^2$ x VTI x 60). All PW Doppler data was acquired using a 60° angle.

Five averaged Doppler measurements over atleast 10 cardiac and 2 respiratory cycles were measured.

Quantification was performed on the ATL 3000 ultrasound system.

Protocol 1: Exercise stress. Before the start of exercise, standard BART with hyperemic response to ischemia by blood pressure cuff was performed in the left arm. This was followed by ultrasound examination of right CA and right BA before and during peak exercise.

a) Brachial Artery Reactivity (BART)

This was performed using standard methods as described by Stradler et al. Briefly left BA diameter and flow were measured before and 60 and 90 seconds after cuff deflation that was placed around the proximal arm above the elbow and inflated to 50 mm Hg above systolic BP pressure for 5 minutes. We observed maximum hyperemia 1.5 minutes after cuff release, hence data for 1.5 minute post cuff deflation is shown. After 15 minutes of rest, 0.4 mg sublingual nitroglycerin (NTG) was given and BA and CA measurements repeated after 5 minutes.

b) Exercise Test

We performed baseline ultrasound examination of the right BA and right CA. Subjects then performed maximum tolerated bicycle ergometry exercise in a supine echo bed (Echo™ Bed, Amercian Echo, USA). Heart rate was monitored continuously throughout the study and BP was measured at every minute. Exercise data was obtained at peak exercise and within 60 seconds post exercise by repeat ultrasound examination of the CA and BA.

Stastical Analysis. Continuous variables are presented as mean ± standard deviation, and categorical variables as counts and percentages. Differences between baseline and post-hyperemia and peak exercise stress variables within each group were compared by Student's paired t-test. A p value of <0.05 was considered statistically significant.

Inter-and Intra-observer Variability. All measurements were made in a blinded fashion. At the onset of our studies, we first tested 3 different methods for measurement of BA diameter: 1) averaged diameter of 10 measurements by caliper, 2) determination of area by manual trace and 3) determination of area by point-by-point method – all 3 available on the ultrasound system. Inter-observer variability was tested in 33 randomly sets of digitized images for baseline, peak hyperemia and NTG images for BART under the same conditions. For CA diameter, 29 randomly selected peak exercise images were measured by the same observer twice and by 2 observers 1 week apart. The intra and inter-observer variability was expressed as a percent error for each measurement and were determined as the difference between the 2 observations divided by the mean value of the two observations (x1-x2/(x1+x2)/2*100. Inter-observer variability was 3.4±4% (0.06±0.21 mm), 3.6±4.2% (0.14±0.2 mm) and 2.3±4% (0.09±0.17 mm) for BA diameter measurements by caliper, area by manual trace and by point-by-point methods respectively. We chose to use caliper method of measurement, because of it ease and because of no significant differences from other relatively more cumbersome methods. Intra-observer variability (for combined 66 measurements by observer 1 and 2 was 1.0±2% (0.02±0.02 mm) for measurements for BA. Interobserver variability for CA diameter was 1.1±1.2% (0.01±0.01 mm). These intra-observer and inter-observer variability are comparable to results published earlier.[10,24,25]

RESULTS

Brachial Artery Reactivity (BART):

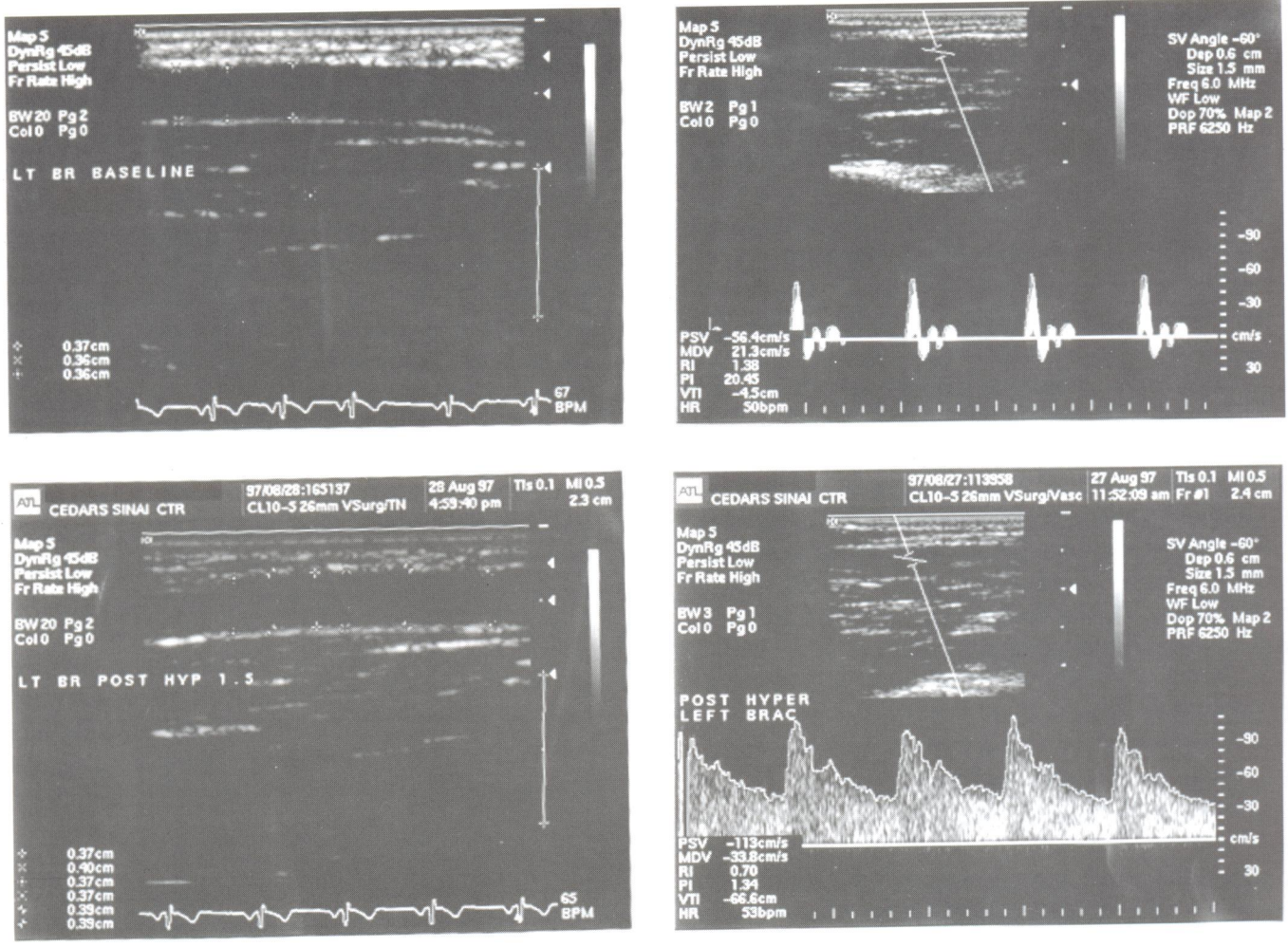
We studied 13 healthy volunteers, mean age 30±8 years, which included 4 females for both standard BART and BA and CA reactivity exercise protocols. Results are summarized in Table 1 and Figure 1 is a representative example. There was a 10%±4% BA vasodilation in response to ischemia induced

Table-1 : Brachial Artery Reactivity Test (BART) in Healthy Volunteer Subjects (n=13)

	Baseline	Post Hyperemia
Diam (cm)	0.38±0.06	0.42±0.07*
PSV (cm/s)	72±25	126±35*
PI	8.35±7	2.6±2.7*
RI	1.1±0.2	0.9±0.2*
VTI (cm/sec)	14±9	61±29
Flow (ml/min)	96±62	550±280*

Values are mean±SD. n=13, *p<0.05 vs. baseline. There was a 9.8±4% increase in brachial artery diameter in response to hyperemia. Flow = 3.14 x 60 x (radius)^2 x VTI. RI (resistive index) = PSV – EDV/PSV) & PI (pulsatility index) = PSV – EDV/VTI) denote resistance to blood flow, VTI = velocity time integral, PSV = Peak systolic velocity.

Figure-1 : Ischemia induced BA reactivity test in a normal subject. Brachial artery diameter responses are shown in left panels and PW Doppler velocity responses in the right panels. Note an increase in BA diameter (white arrow) in post hyperemia phase (B) compared to baseline (A) and an increase in flow and decrease in resistance during hyperemia phase (D) compared to baseline (C).



hyperemia. This was associated with a decrease in resistance (PI and RI) and an increase in VTI. Volume flow increased by 800%±540%.

Carotid Artery Reactivity:

Carotid Artery Reactivity to Exercise.

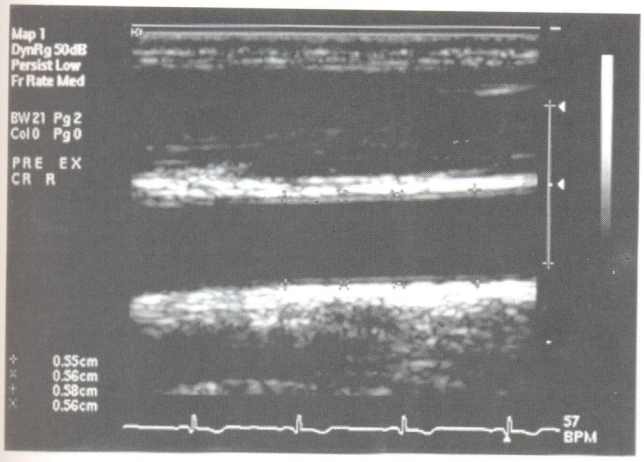
Results of exercise study are shown in Table 2. Subjects attained 75%±7% of maximum age predicted heart rate and hence our results represent

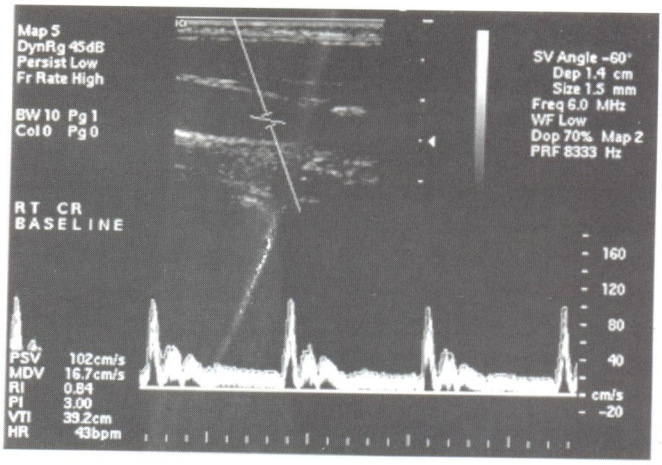
Table-2 : Effects of Exercise on Brachial and Carotid Artery Responses in Healthy Subjects (n=13)

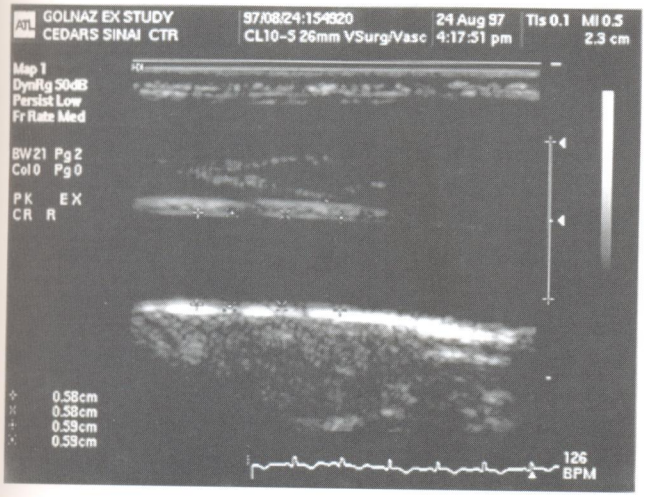
	Brachial Artery		Carotid Artery	
	Baseline	Post Exercise	Baseline	Peak Exercise
Diam (cm)	0.39±0.05	0.42 ±0.05*	0.62±0.05	0.66±0.05*
PSV (cm/s)	78±26	104±19*	78±26	129±34*
PI	9.1±7	9.3±7	2.68±0.5	4.2±0.6*
RI	1±0.2	1.3±0.1*	0.9±0.2	1.1±0.1*
VTI (cm)	14±8	10±5*	27 ± 8	24±9*
Flow (ml/min)	98±55	78±38	472±125†	496±237

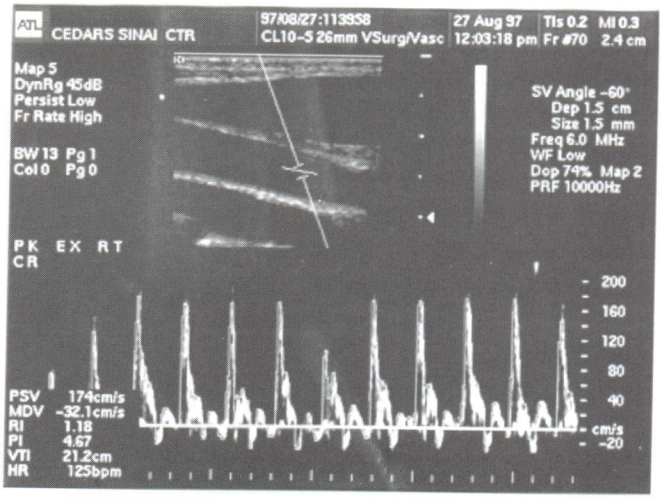
Values are mean±SD, n=13, *p<0.03 vs. baseline. †p<0.0001 vs. brachial artery. Flow = 3.14x60x(radius)²xVTI. PSV=peak systolic velocity, EDV=end-diastolic velocity, Diam=diameter, VTI= velocity times integral, RI=resistive index, PI=pulsatility index.

Figure-2 : Effect of supine bicycle exercise in a normal subject. Carotid artery diameter responses are shown in left panels and PW Doppler velocity responses in the right panels An increase in CA diameter (white arrow) at peak exercise (B) compared to baseline (A) is shown. There is an increase in resistance (RI and PI) and a decrease in flow (VTI) at peak exercise (D) compared to baseline (C)









the results of moderate exercise. Figure 2 is a representative case example from an exercise study. Systolic BP pressure increased from 120±9 to 168±27 mm Hg, ($p<0.001$ vs. baseline), diastolic BP from 76±10 to 81±15 mm Hg, (p=NS), mean BP from 91±9 to 110±117 mm Hg, $p<0.001$ vs baseline) and heart rate from 62±12 to 140±10 bpm, $p<0.001$ vs. baseline. Exercise produced 8±5% vasodilation of CA and 6±6% vasodilation of BA. There was a trend towards a decrease in BA (p=0.060) and no significant change in CA flow. Correlation between the change in the product of heart rate and systolic BP during exercise and change in CA and BA diameter was 0.59 (p=0.03) and 0.53 (p=0.05) respectively.

Vascular Reactivity to Nitroglycerin:

NTG responses were assessed in 8 normal subjects. NTG administration increased the BA diameter from 0.39±0.05 cm to 0.43±0.06 cm ($p<0.01$) at 5 minutes, representing a 13±5% vasodilation from baseline. Increase in CA diameter in response to NTG was 5±3% (0.67±0.03 to 0.70±0.04 cm, $p<0.01$). NTG decreased mean BP by 3±4%.

DISCUSSION

The main findings of our study are that in healthy subjects supine bicycle exercise produced CA and BA vasodilation proportional to the hemodynamic effects of exercise, a net increase in resistance in both forearm and cerebral circulation, and no significant no significant change in the BA and CA blood flow. Similar to physical exercise, NTG also produced BA and CA vasodilation. These differences in blood flow reserve and vasodilation in normal subjects as measured from the CA and BA are similar, albeit

smaller, to the differences observed using BART in subjects with HTN and other risk factors for coronary artery disease[6-11,16] and in coronary arteries in response to exercise.[27,28,29]

Exercise leads to forearm vasodilation, which is blocked by NO inhibitor N-monomethyl-L-arginine (L-NMMA),1 suggesting it is nitric oxide mediated. The effects of exercise that we observed on BA are consistent with those of other investigators[16,17] which showed BA vasodilation with physical stress. Previous work suggests that moderate upright exercise induces an increase in cerebral blood flow as measured from CA Doppler velocity, whereas a decrease in CA flow velocities were observed as the work increased beyond moderate levels.[30] This increased resistance and decrease blood flow that we observed in the BA and CA and others[31,32] observed in the CA likely reflects intense cerebrovascular and peripheral autoregulation and vasoconstriction and is partly secondary to catecholamine release,[31] thus altering the balance between adrenergic vasoconstriction and endothelial NO-induced vasodilation during exercise.[27,33]

Earlier venous plethysmographic studies suggest that mental stress produces vasodilation of forearm vasculature and that this vasodilation is NO mediated2 and not catecholamine mediated.[34] Unlike exercise responses and similar to BART responses to ischemia-hyperemia in the forearm, mental stress-induced forearm responses included vasodilation of BA, a decrease in resistance, and a net increase in blood flow. Thus mental stress induced BA responses appear to be predominantly NO mediated and may provide better assessment of endothelial function, than exercise-induced responses.

Use of physical stress to assess CA and BA endothelial function is a novel non-invasive technique of assessment of vascular endothelial function. Inappropriate vasoconstriction, or lack of dilation in BA and CA in response to exercise may suggest endothelial dysfunction and needs to be further studied in subjects with risk factors for or those with established coronary, peripheral and cerebrovascular disease.

Limitations

These are preliminary findings in a small group of subjects. We did not perform continuous imaging of the CA and BA during exercise. This was due to motion artifact during exercise. The exercise protocol exercised leg muscles, hence evaluation of femoral arteries may have provided a better assessment of physiologic effects of exercise. The purpose of our exercise protocol was however to see if a stimulus, i.e. increased shear stress from increased heart rate and blood pressure will cause local vasodilation. In addition, imaging femoral arteries is not feasible on the supine bicycle during exercise. Finally we did not evaluate the effects of nitric oxide antagonists on BA and CA responses to evaluate the exact role of NO in causing BA and CA vasodilation.

REFERENCES

1. Gilligan DM, Panza JA, Kilcoyne CM, Waclawiw MA, Casino PR, Quyyumi AA. Contribution of endothelium-derived nitric oxide to exercise-induced vasodilation. Circulation 1994;90;2853-58.

2. Dietz NM, Rivera JM, Eggener SE, Fix RT, Warner DO, Joyner MJ. Nitric oxide contributes to the rise in forearm blood flow during mental stress in humans. Jour of Physiology; 1994; 480.2; 361-67.

3. Harris CW, Edwards JL, Baruch A, Riley WA, Pusser BE, Rejeski WJ, Herrington DM. Effects of mental stress on brachial artery flow-mediated vasodilation in healthy normal individuals. Am Heart J. 2000;139:405-11.

4. Gerhard M, Roddy MA, Creager Shelly J, Creager Mark A: Aging Progressively Impairs endothelium-dependent vasodilation in forearm resistance vessels of humans. Hypertension; 1996;27:849-53.

5. Vogel RA. Corretti MC. Plotnick GD. Changes in flow-mediated brachial artery vasoactivity with lowering of desirable cholesterol levels in healthy middle-aged men. Am J Cardiol. 1996;77:37-40.

6. Iiyama K, Nagano M, Yo Y, Nagano N, Kamide K, Higaki J, Mikami H, Ogihara T. Impaired endothelial function with essential hypertension assessed by ultrasonography. Am Heart J. 1996, 132:779-82 .

7. Taddei S, Virdis A, Mattei P, Ghiadoni L, Gennari A, Fasolo CB, Sudano I, Salvetti A, Aging and endothelial function in normotensive subjects and patients with essential hypertension. Circulation 1995;91:1981-87.

8. Celermajer DS, Sorensen KE, Georgakopoulos D, Bull C, Thomas O, Robinson J, Deanfield JE. Cigarette smoking is associated with dose-related and potentially reversible impairment of endothelium-dependent dilation in healthy young adults. Circulation 1993;88(part 1):2149-55.

9. McNally P G, Watt Pamela AC, Rimmer T, Burden AC, Hearnshaw John R, Thurston H. Impaired contraction and endothelium-dependent relaxation in isolated resistance vessels from patients with insulin-dependent diabetes mellitus; Clinical Science 1994; 87; 31-36.

10. Tawakol A., Rorbjorn O, Gerhard M, Wu JT, Creager MA. Hyperhomocyst(e)inemia is associated with impaired endothelium-dependent vasodilation in human. Circulation; 1997;95:1119-21.

11. Celermajer DS, Sorensen KE, Bull C, Robinson J, Deanfield JE. Endothelium-dependent dilation in the systemic arteries of asymptomatic subjects relates to coronary risk factors and their interaction. J Am Coll Cardiol 1994;24:1468-74.

12. Joannides R, Haefeli WE, Linder L, Richard V, Bakkali EH, Thuillez C, Luscher TF. Nitric oxide is responsible for flow-dependent dilation of human peripheral conduit arteries in vivo. Circulation 1995;91:1314-19.

13. Anderson TJ, Uehata A, Gerhard MD, Meredith IT, Knab S, Delagrange D, Lieberman EH, Ganz P, Creager MA, Yeung AC. Close relation of endothelial function in the human coronary and peripheral circulations. J Am Coll Cardiol 1995;26:1235-41.

14. Lieberman EH, Gerhard MD, Uehata A, Selwyn AP, Ganz P, Yeung AC, Creager MA. Flow-induced vasodilation of the human brachial artery is impaired in patients 40 years of age with coronary artery disease. Am J Cardiol 1996;78:1210-14.

15. Corretti MC, Plotnick GD, Vogel RA. Correlation of cold pressor and flow-mediated brachial artery diameter responses with the presence of coronary artery disease. Am J Cardiol 1995;75:783-7.

16. Shoemaker JK, Halliwill JR, Hughson RL, Joyner MJ. Contributions of acetylcholine and nitric oxide to forearm blood flow at exercise onset and recovery. Am J Physiology. 1997;273:H2388-95.

17. Shoemaker JK, MacDonald MJ, Hughson RL. Time course of brachial artery diameter responses to rhythmic handgrip exercise in humans. Cardiovascular Research. 1997;35:125-31.

18. Faraci FM. Role of endothelium-derived relaxing factor in cerebral circulation: large arteries vs. microcirculation. Am J Physiology 1991;261(4 Pt 2):H1038-42.

19. Wafford JL, Kahl FR, Joward GR, McKinney WM, Toole JF, Crouse JR. Relation of extent of extracranial carotid artery atherosclerosis as measure by b-mode ultrasound to the extent of coronary atherosclerosis. Arthrioscler Thromb 1991;11:1786-94.

20. Salonen R, Salonen JT. Determinants of carotid intima-media thickness: a population-based ultrasonography study in eastern finnishment. J Intern Med 1991;229:225-31.

21. Folsom AR, Eckfeldt JH, Weitzman S, Ma J, Chambless LE, Barnes RW, Cram KB, Hutchinson RG. For the atherosclerosis risk in communities (aric) study investigators. Relation of carotid artery wall thickness to diabetes mellitus, fasting glucose and insulin, body size and physical activity. Stroke 1994;25:66-73.

22. Ghiadoni L. Taddei S. Virdis A. Sudano I. Di Legge V. Meola M. Di Venanzio L. Salvetti A. Endothelial function and common carotid artery wall thickening in patients with essential hypertension. Hypertension 1998;32:25-32.

23. Stadler RW. Karl WC. Lees RS. New methods for arterial diameter measurement from b-mode images. Ultrasound in Medicine & Biology 1996;22:25-34.

24. Uehata A, Lieberman EH, Gerhard MD, Anderson TJ, Ganz P, Polak JF, Creager MA, Yeung AC. noninvasive assessment of endothelium-dependent flow-mediated dilation of the brachial artery. Vascular Medicine 1997;2:87-92.

25. Rubenfire M, Rajagopalan S, Mosca L. Carotid artery vasoreactivity in response to sympathetic stress correlates with coronary disease risk and is independent of wall thickness. J Am Coll Cardiol 2000;36(7):2192-97.

26. Celemajer DS, Sorensen KE, Gooch VM, Spiegelhalter DJ, Miller OI, Sullivan ID, Lloyd JK, Deanfield JE. Noninvasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet 1992;340:1111-15.

27. Zeiher AM, Drexler H, Wollschlaeger H, Saurbier B, Just H. Coronary vasomotion in response to sympathetic stimulation in humans: importance of the functional integrity of endothelium. J Am Coll Cardiol 1989;14:1181-90

28. Dubois-Rande JL, Dupouy P, Aptecar E, Bhatia A, Teiger E, Hittinger L, Berdeaux A, Castaigne A, Geschwind H. Comparison of the effects of exercise and cold pressor test on the vasomotion responses of normal and atherosclerotic coronary arteries and their relation to the flow-mediated mechanism. Am J Cardiol 1995;76:467-73.

29. Gordon JB, Ganz P, Nabel EG, Fish RD, Zebede J, Mudge GH, Alexander RW, Selwyn AP. Atherosclerosis influences the vasomotor response of epicardial coronary arteries to exercise. J Clin Invest 1989;83:1946-52.

30. He J, Jiang ZL, Tanaka H, Ikehara T, Takahashi A, Yamaguchi H, Miyamoto H, Iritani T, Kinouchi Y. Changes in carotid blood flow and electrocardiogram in humans during and after walking on a treadmill. Eur J Appl Physiol & Occupational Physiol 1993;67: 486-91.

31. Hellstrom G, Fischer-Colbrie W, Wahlgren NG, Jogestrand T. Carotid artery blood flow and middle cerebral artery blood flow velocity during physical exercise. Jour of Appl Physio 1996;81:413-418.

32. Samnegård H, Carlens P. Effect of Physical Exercise on Internal Carotid Artery Blood Flow After Arterial Reconstruction. Acta Radiologica 1975 [Old Series],30:6,220 — 228

33. Liao J, Bettmann M, Sandor T, Tucker J, Coleman S, Creager M. Differential impairment of vasodilator responsiveness of peripheral resistance and conduit vessels in humans with atherosclerosis. Circ Res 1991;68:1027-34.

34. Lindqvist M, Davidson S, Hjemdahl P, Melcher A. Sustained forearm vasodilation in humans during mental stress is not neurogenically mediated. Acta Physiologica Scandinavica 1996;158:7-14.