

## EFFECT OF PROLONGED STRENUOUS EXERCISE ON ENDOTHELIAL FUNCTION IN NON-ELITE RUNNERS

R Ramírez-Velez R<sup>1</sup>. robin640@hotmail.com. Aguilar de Plata AC<sup>1</sup>.  
caplataa@yahoo.es. Ramirez JH<sup>2</sup>. jorgeramirez@yahoo.com

1. *Nutrición Group. University of Valle. Santiago de Cali.*

2. *University ICESI. Santiago de Cali. Colombia.*

### ABSTRACT

**Objectives.** To determine the impact of prolonged strenuous exercise on endothelial function in non-elite runners. **Methods.** Nine males participating as recreational runners (age:  $49.5 \pm 5.1$ y) at the Santiago of Cali Half-marathon (21.1 Km) were studied. Endothelium dependent femoral artery flow-mediated dilatation (FA-FMD) was evaluated one day before the race and at 1h, 24h, 48h, and 6 days after finishing the half-marathon. **Results.** A decrease on FA-FMD was observed at 1h after the Half-marathon, followed by a non-significant recovery trend starting at 24h up to 6 days after the race. Increase in the posthyperemic diameter of the femoral artery was observed at 1h after race ending, with a trend to baseline values in subsequent measures. **Conclusion.** Femoral artery diameter increased after prolonged running could explain the reduction of FA-FMD. More studies with larger sample size are needed to determine the effects of prolonged running on femoral artery endothelial function.

**Keywords:** Exercise. Endothelium. Running. Vasodilatation

### 1. INTRODUCTION

Epidemiological studies have shown that people who participate in programs of regular physical activity achieve a considerably improvement on cardiovascular health.[1] This is consistent with the observation that a decreased aerobic exercise capacity is a good predictor of all-cause mortality.[2] However, high-intensity resistant training reduces arterial compliance and increases arterial stiffness.[3]

Endothelium-dependent vasodilatation function can be examined non-invasively in humans by measuring brachial artery mediated dilatation.[4,5] It has been demonstrated that regular exercise improved brachial artery flow mediated dilatation (FMD). In fact, endothelial dysfunction plays a role in the pathogenesis of atherosclerosis,[6] and impaired endothelial function has been observed several years before traditional markers of cardiovascular disease appear. Green *et al.*[7] reported that short-term aerobic and resistance training improves endothelium-dependent nitric oxide (NO)-mediated vascular function in both conduit and resistance vessels. In addition, there are several studies of endothelial function in moderately endurance-trained men,[8] but there are none in highly endurance-trained men athletes. Furthermore, high-intensity endurance training at 70–80% of  $VO_{2max}$  has been linked to decreased antioxidant capacity and reduced endothelial function in moderately well-trained subjects.[9] However, it is unknown what happens with the endothelial function after prolonged strenuous exercise in recreational runners. This study evaluated the changes on endothelium dependent femoral artery flow-mediated dilatation

(FA-FMD) in male recreational runners participating in a half marathon (distance 21.1 Km). We hypothesized that a prolonged and intensive bout of exercise would be associated with impaired endothelium-dependent nitric oxide (NO)-mediated vascular function.

## 2. METHODS

**Study subjects.** Ten healthy, non-smoking males and recreational runners were invited to participate in the study. Exclusion criteria included a previous diagnosis of cardiovascular disease, presence of running injuries, family history of premature cardiovascular disease and diabetes. Written informed consent was obtained from participants and the investigation complied with the principles outlined in the Declaration of Helsinki, previously approved by the *Universidad del Valle Human Ethical Committee (UV114-09)*. Assessment of endothelium dependent femoral artery flow-mediated dilatation (FA-FMD), posthyperemic femoral artery diameter (FA-P) and baseline femoral artery diameter (FA-B) were performed by an experienced investigator using a high-resolution ultrasound device (Siemens SG-60, USA), equipped with a 7.5 MHz linear array transducer, and an integrated electrocardiography package. The technique was performed following the protocol described by Corretti *et al.*[10]

**Study protocol.** Baseline data for FA-B, FA-P and FA-FMD were collected in an initial assessment at 24 h (5 subjects) and 48 h (4 subjects) before the start of the race. After race completion the measurements were performed at 1 h, 24 h, 48 h and 6 days. On all testing days, the measurements were performed within a 2-h period to minimize the impact of circadian rhythm variation on vascular function. Race conditions were warm and humidity with temperatures reaching 29°C at midday.

**Statistical analyses.** Non-parametric tests (*Wilcoxon*) were used for the analysis of pre and post-race values of FA diameter, FA-FMD, weight, blood pressure and heart rate. One-way ANOVA with repeated measures was used for the analysis of FA-FMD and femoral artery diameters at baseline, 1 h, 24 h, 48 h and 6<sup>th</sup> day. GraphPad Prism 4.0b for MAC OSX was used for the statistical analysis and graph development. Data is presented as the mean  $\pm$  Standard Deviation (SD) and Standard Error of the Mean (SEM) when it was appropriate.  $P < 0.05$  was accepted as significant.

## 3. RESULTS

Nine male provided written informed consent to participate in the study. Subjects were  $49.5 \pm 5.1$  years, BMI  $24.0 \pm 1.8$  kg/m<sup>2</sup>, height  $166 \pm 6$  cm. Seven subjects had history of physical activity of at least 6 years and 2 subjects have been training for over one year. All nine runners finished the 21.1 Km of the Half-marathon, eight presented for post-race evaluation, and seven completed all appointments in the study protocol, mean race time was ( $109 \pm 7$ , Range 96-121 minutes). Anthropometric, cardiovascular, and sonographic parameters of the femoral artery, before and after the race, are shown in Table 1. FA-FMD was significantly reduced at 1h post-race, but not at 24h, 48h and 6 days, compared with baseline data (Figure 1). A non-statistically significant increase

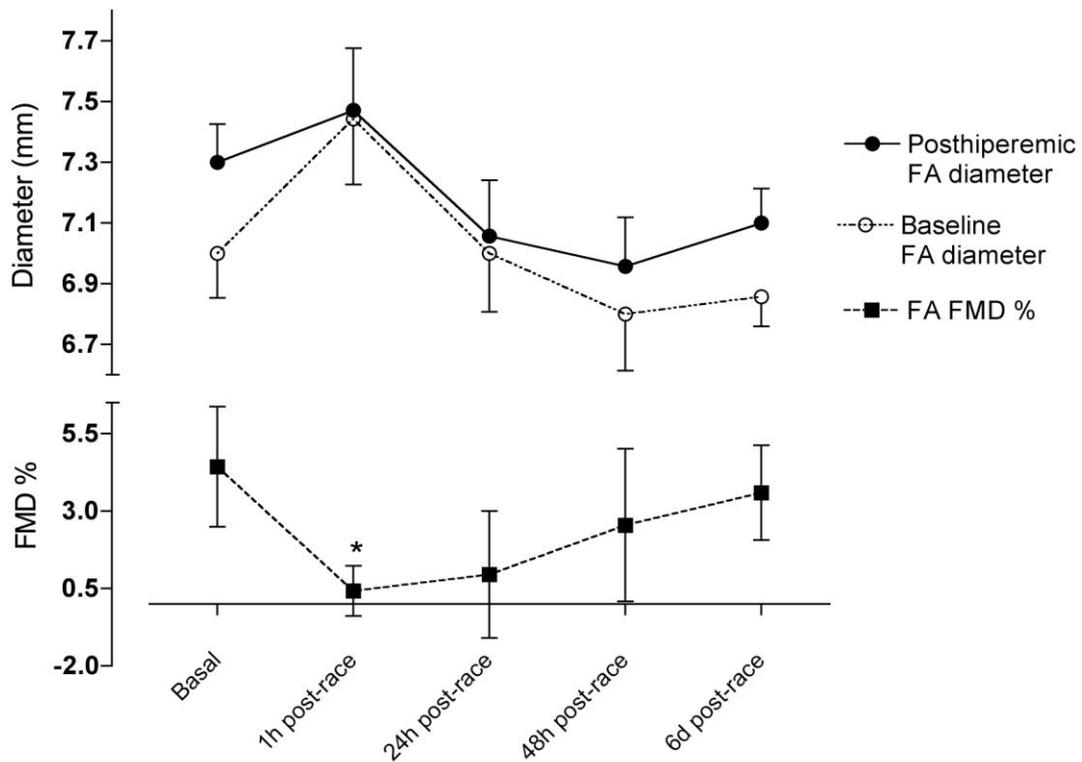
in FA-P was observed at 1 h, with a trend for recovery to baseline values in subsequent measures.

**Table 1. Cardiovascular and anthropometric parameters at baseline and 1h after the race.**  
Data is presented as mean ± SE.

Parameter	Baseline	Postrate (1h)	P Value
Weight, kg	56.6 ± 8.9	55.2 ± 8.3	0.018
Heart Rate, beats/min	55.5 ± 6.5	74.1 ± 26.7	0.109
Systolic Blood Pressure, mm Hg	134.8 ± 20.0	114.1 ± 10.9	0.012
Diastolic Blood Pressure, mm Hg	86.3 ± 13.3	66.8 ± 5.7	0.011
Artery diameter, mm	7.0 ± 0.4	7.4 ± 0.5	0.051
Peak flow artery, cm/seg <sup>3</sup>	25.3 ± 7.4	23.6 ± 5.9	0.591
FMD, %	4.2 ± 4.5	0.2 ± 2.1	0.042

FMD: Flow Mediated Dilatation

**Figure 1. Flow-mediated dilatation (FMD) at different moments in non-elite runners**



(\*p<0.05)

#### 4. DISCUSSION

To the best of our knowledge, this is the first study attempting to assess vascular function after a prolonged intense bout of exercise in male recreational runners participating in 21.1 Km. Increased production of NO in endothelium by shear stress during exercise has been proposed as the main mechanism underlying vasodilatation during exercise.[6] However, other vasoactive substances such as prostacyclin, or endothelium-derived hyperpolarizing factor (EDHF) have also a role in vascular function. FA-FMD was decreased at 1 h after the race, findings that are consistent with previous studies.[7-9] FA posthyperemic diameter was increased at 24 h, with a trend for recovery in subsequent measures; however these changes were not statistically significant probably due to the limited sample size used in this study. Other studies performed in marathon runners had proposed that shear rate and oxidative stress during intensive running could have detrimental effects on FA endothelial function.[7] An increase on the systemic levels of inflammatory cytokines (IL-6, IL-8, TNF- $\alpha$ ) and reduction on the circulatory levels of hematopoietic progenitor cells has also been proposed as possible mechanisms of endothelial dysfunction after acute exercise.[11,12] Furthermore, other studies performed in athletes had shown differential impacts on flow mediated dilation, reporting that exercise cause a deleterious effect in vascular beds from active muscular groups (i.e. femoral artery) without changes on arteries from extremities no involved in the exercise (i.e. brachial artery).[7,13] However, the results obtained in this study suggest that prolonged running generates a maximum peak in femoral vasodilatation, which decreases the vasodilator response caused by occlusion.

The hypothesis that prolonged running do not decrease endothelial function is partially supported by the study of Rognmo *et al.*[8] In this investigation, the authors reported that high-intensity interval running exercise, in trained and sedentary males, generates a rise in NO bioavailability, increases the antioxidant status, but however decreases endothelium dependent brachial artery flow mediated dilation. Other studies performed on rat aortic vascular rings has shown that a single acute exercise session increases calcium influx into endothelial cells with release of NO,[14] improved endothelium-dependent vasodilatation for 48 h,[15] and augments receptor mediated-vasodilatation responses.[16] Future studies focused to determine the clinical impact of strenuous running on femoral endothelial function are needed.

#### 5. ACKNOWLEDGEMENTS

We thank Ricardo Agredo, Carlos A. López, Jessica Consuegra and Alejandra Jerez for help of the vascular ultrasound and medical support. We also want to give special thanks to Roger Arce and Adolfo Contreras for their critical review of this manuscript. Robinson Ramírez-Velez doctoral research is financially supported by COLCIENCIAS.

**COMPETING INTEREST:** None to declare

## 6. REFERENCES

1. Thompson PD. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease. *Arterioscler Thromb Vasc Biol* 2003;23:1319-21.
2. Kemi JO, Haram PE, Loennechen JP, *et al.* Moderate vs. high exercise intensity: Differential effects on aerobic fitness, cardiomyocyte contractility, and endothelial function. *Cardiovasc Res* 2005;67:161-72.
3. Okamoto T, Masuhara M, Ikuta K. Combined aerobic and resistance training and vascular function: effect of aerobic exercise before and after resistance training. *J Appl Physiol* 2007;103:1655-61.
4. Celermajer DS, Sorensen KE, Gooch VM, *et al.* Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. *Lancet* 1992;340:1111-5.
5. Accini L, Sotomayor A, Trujillo F, *et al.* Colombian Study to Assess the Use of Noninvasive Determination of Endothelium-Mediated Vasodilatation (CANDEV). Normal Values and Factors Associated. *Endothelium* 2001;8:157-66.
6. Pyke KE, Tschakovsky ME. The relationship between shear stress and flow-mediated dilatation: implications for the assessment of endothelial function. *J Physiol* 2005;568:357-9.
7. Green D, Walsh JH, Maiorana A, *et al.* Comparison of resistance and conduit vessel nitric oxide-mediated vascular function *in vivo*: effects of exercise training. *J Appl Physiol* 2004;97:749-55.
8. Rognmo Ø, Bjørnstad TH, Kahrs C, *et al.* Endothelial function in highly endurance-trained men: effects of acute exercise. *J Strength Con Res* 2008;22:535-42.
9. Bergholm R, Makimattila S, Valkonen, *et al.* Intense physical training decrease circulating antioxidants and endothelium-dependent vasodilation *in vivo*. *Atherosclerosis* 1999;145:341-9.
10. Corretti MC, Anderson TJ, Benjamin EJ, *et al.* International brachial artery reactivity task force. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the international brachial artery reactivity task force. *J Am Coll Cardiol* 2002;39:257-65.
11. Siegel AJ, Stec JJ, Ridker PM, *et al.* Effect of marathon running on inflammatory and hemostatic markers. *Am J Cardiol* 2001;88:918-920.
12. Bonsignore MR, Morici G, Bonanno A, *et al.* Circulating hematopoietic progenitor cells in runners. *J Appl Physiol* 2002;93:1691-1697.

13. Green D, Cheetham C, Mavaddat L, *et al.* Effect of lower limb exercise on forearm vascular function: contribution of nitric oxide. *Am J Physiol Heart Circ Physiol* 2002;283:H899–H907.

14. Jen CJ, Chan HP, Chen HI. Acute exercise enhances vasorelaxation by modulating endothelial calcium signaling in rat aortas. *Am J Physiol Heart Circ Physiol* 2002;282:H977-82.

15. Haram PM, Adams V, Wisløff U, *et al.* Time-course of endothelial adaptation following acute and regular exercise. *Eur J Cardiovasc Prev Rehabil* 2006;13:585-91.

16. Cheng L, Yang C, Chen H, *et al.* Acute exercise enhances receptor-mediated endothelium-dependent vasodilation by receptor upregulation. *J Biomed Sci* 1999;6:22-7.

## **FICHA DE INFORMACIÓN ADICIONAL**

**TÍTULO DE LA COMUNICACIÓN.** Effect of prolonged strenuous exercise on endothelial function in non-elite runners

**AUTORES.** Robinson Ramírez-Velez, Ana Cecilia Aguilar de Plata, Jorge Hernán Ramírez

**CENTRO DE TRABAJO (INSTITUCIÓN, EMPRESA, UNIVERSIDAD, DEPARTAMENTO, ETC.).** Universidad del Valle. Sede San Fernando. Escuela de Ciencias Básicas Médicas. Departamento de Ciencias Fisiológicas. Sección Bioquímica.

**DIRECCIÓN POSTAL DEL CENTRO DE TRABAJO.** Calle 4B 36-00. Edificio 116. Oficina 5004. Santiago de Cali, Valle del Cauca. Colombia.

**E-MAIL Y TELÉFONO DE CONTACTO.** Teléfono/Fax N° (+577) - 558 5603.

**ÁREA TEMÁTICA DEL CONGRESO A LA QUE PERTENECE EL TRABAJO.** Entrenamiento.

**DESARROLLO DEL TRABAJO PRESENTADO.** Ciencias Biomédicas

**REFERENCIAS BIBLIOGRÁFICAS.** Incluido en el texto

**ANEXOS CON GRÁFICOS, TABLAS, IMÁGENES, ETC.** Incluido en el texto

### **CURRÍCULUM**



**ROBINSON RAMIREZ-VELEZ.** Physical Therapy. University Maria Cano, Colombia. Cardiac and Pulmonary Rehabilitation Exercise Specialist. School of Rehabilitation. University of Rosario, Colombia. *Fellow in* Exercise of Physiology. University of Sao Pablo, Brazil. Ph.D. Student. Biochemistry, School of Medicine, University of Valle, Colombia. Professor Full Time. Department of Physiological Sciences, Biochemistry School of Medicine, University of Valle

**MATERIAL DE APOYO REQUERIDO (RECURSOS AUDIOVISUALES, CONEXIÓN INTERNET, ETC.).** Video Beam