

# Maximum dilation of the brachial artery in smoking and nonsmoking pregnant and non-pregnant women\*

*Avaliação da dilatação máxima da artéria braquial em gestantes e não gestantes, fumantes e não fumantes*

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**Abstract** **OBJECTIVE:** To evaluate the time required to achieve maximum brachial artery dilation by means of flow-mediated dilation, as well as the differences in such dilation as four groups of smoking and nonsmoking pregnant and non-pregnant women are compared. **MATERIALS AND METHODS:** Cross-sectional study where the brachial artery diameter was measured considering four time spans following pressoric stimulus (30, 60, 90 and 120 seconds) in four groups of women in the age range between 20 and 30 years as follows: nonsmoking pregnant women ( $n = 47$ ) and smoking pregnant women ( $n = 33$ ) with gestational age between 24 and 28 weeks, nonsmoking ( $n = 34$ ) and smoking ( $n = 19$ ) non-pregnant women. **RESULTS:** The evaluation of dilation of the brachial artery at the different time spans following pressoric stimulus demonstrated maximum dilation for all the groups at "60 seconds" following the cuff deflation ( $p < 0.01$ ). Brachial artery flow-mediated dilation was greater among nonsmoking pregnant women as compared with smoking ones ( $p = 0.03$ ), as well as in the group of nonsmoking, non-pregnant women as compared with the smoking ones ( $p = 0.03$ ). **CONCLUSION:** The smoking habit does not interfere in the time span required to achieve maximum brachial artery dilation. **Keywords:** Ultrasonography; Endothelium; Endothelial function; Pregnant women; Smokers.

**Resumo** **OBJETIVO:** Avaliar, por meio da dilatação mediada por fluxo da artéria braquial, em que tempo ocorre a máxima dilatação da artéria braquial e se existe diferença nesta avaliação ao comparar mulheres gestantes e não gestantes, fumantes e não fumantes. **MATERIAIS E MÉTODOS:** Estudo transversal, no qual o diâmetro da artéria braquial foi avaliado em quatro tempos após estímulo pressórico (30, 60, 90 e 120 segundos) em quatro grupos de mulheres entre 20 e 30 anos de idade assim distribuídos: mulheres gestantes entre 24 e 28 semanas de idade gestacional não fumantes ( $n = 47$ ) e fumantes ( $n = 33$ ), e mulheres não gestantes não fumantes ( $n = 34$ ) e fumantes ( $n = 19$ ). **RESULTADOS:** A avaliação da dilatação da artéria braquial nos diferentes tempos após o estímulo pressórico foi máxima para todos os grupos no tempo "60 segundos" após a desinsuflação ( $p < 0,01$ ). A dilatação mediada por fluxo da artéria braquial foi maior entre as mulheres gestantes não fumantes em comparação às fumantes ( $p = 0,03$ ), assim como no grupo de mulheres não gestantes não fumantes em comparação às fumantes ( $p = 0,03$ ). **CONCLUSÃO:** O hábito de fumar não interferiu no tempo em que ocorre a máxima dilatação da artéria braquial. **Unitermos:** Ultrassonografia; Endotélio; Função endotelial; Gestantes; Fumantes.

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## INTRODUCTION

Smoking is considered the main cause for avoidable deaths in the world and is the second major cause of death, killing one out of ten persons. Currently it is estimated that there are approximately 1.3 billion smokers in the world, with 5 million deaths caused by smoking every year. According

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to the World Health Organization (WHO), if current trends remain unchanged, close to 10 million people will die every year from 2020 onward<sup>(1)</sup>.

In the same manner as smoking, cardiovascular disorder involves high socioeconomic costs and is the first primary cause of death in developed countries. It is known that its physiopathology is basically associated with an alteration of the endothelial function<sup>(2)</sup> and that the endothelial dysfunction is a systemic process observed in an atherosclerotic environment<sup>(3)</sup>.

A normal pregnancy leads to significant changes in the female vascular system and

hemodynamics as well as in the endothelium. Simultaneous and subsequent events cause a decrease in the peripheral vascular resistance, as well as a decrease in blood pressure and increase in the cardiac output, with a consequential increase in flow in systemic and pulmonary circulation<sup>(4)</sup>. In the contrary sense, nicotine acts on the maternal circulation by releasing catecholamines, causing an increase in blood pressure, tachycardia, peripheral vasoconstriction and a decrease in the placental flow, resulting in decreased oxygenation and compromising fetal nutrition<sup>(5)</sup>. Additionally, nicotine causes autonomic imbalance, irregularities in the coronary blood flow and endothelial dysfunction<sup>(6,7)</sup>.

The consequences of smoking on pregnancy and on the cardiovascular dynamics are the motivating factors for the study of the influence of tobacco on the endothelium. A noninvasive method for the evaluation of the endothelial function by means of ultrasonography, proposed by Celermajer et al.<sup>(6)</sup>, is recommended by the International Brachial Artery Reactivity Task Force and is expressed as a change in the brachial artery diameter as a percentage of its basal diameter<sup>(8)</sup>.

The international terminology used for the method is FMD<sup>(6,8,9)</sup>, an acronym for flow-mediated dilation. However, some disagreement is observed among Brazilian studies, with two terms being utilized: FMD<sup>(10,11)</sup>, as "flow-mediated dilation", and another term simply called DILA<sup>(12-15)</sup>. In the present study, the FMD acronym is adopted.

The objective of the present study is to evaluate the alterations in the endothelial function induced by cigarette smoking (maximum time of brachial artery dilation) in pregnant and non-pregnant women.

## MATERIALS AND METHODS

### Subjects

Pregnant women were invited to participate in the study, with gestational ages ranging between 24 and 28 weeks, and non-pregnant women, all of them with ages ranging between 20 and 30 years, who were voluntarily submitted obstetric and gynecologic ultrasonography in the period from July 2007 to February 2009.

A total sample of 133 women was selected and divided into four groups as follows: pregnant women ( $n = 80$ ) [nonsmokers ( $n = 47$ ) and smokers ( $n = 33$ )] and non-pregnant women ( $n = 53$ ) [nonsmokers ( $n = 34$ ) and smokers ( $n = 19$ )]. Smoking participants, both pregnant and non-pregnant women were questioned on the approximate number of smoked cigarettes per day. All the participants signed a term of free and informed consent, and the study was approved by the Committee for Ethic in Research of the Institution.

### Sonographic study

For the FMD evaluation, all the patients were asked to have their last pre-study meal no later than 10:00 PM on the previous day, as well as avoiding ingestion of alcohol and alcohol-containing products, or other products containing caffeine or chocolate. The smoking pregnant and non-pregnant women were asked to refrain from smoking after 10:00 PM of the previous day.

Before being positioned for the sonographic study, all the patients were measured and weighted for calculation of their body mass index, besides having the blood pressure measured.

Once they were positioned, the patients were monitored with the electrocardiograph coupled with the HD 11 ultrasonography apparatus (Philips Medical System; Bothel, WA, USA), remaining in rest for 10 minutes or more in a room at a temperature of  $22 \pm 2^\circ\text{C}$  and dimmed lighting, in order to provide good relaxation conditions. The next step was the placement of the linear transducer on the medial aspect of the arm,

at 5 to 10 cm above the antecubital fold, insonating the brachial artery posteriorly to the biceps and laterally to the brachial muscle (Figure 1). A standardized measurement limited by intima/lumen interfaces was adopted as parameter for the measurement of the brachial artery diameter. The measurement was made taking as a reference the end-diastolic phase represented by the R wave at the electrocardiogram. Before the cuff inflation, a 5-second film was acquired for later measurement of basal brachial artery diameter (Figure 2).

The pressure of the sphygmomanometer cuff inflation on the right forearm was standardized at 200 mmHg for all the patients, with the occlusion being maintained for five minutes. After cuff deflation, four 5-second films were acquired at 30, 60, 90 and 120 seconds, for later measurement of post-occlusion arterial diameter.

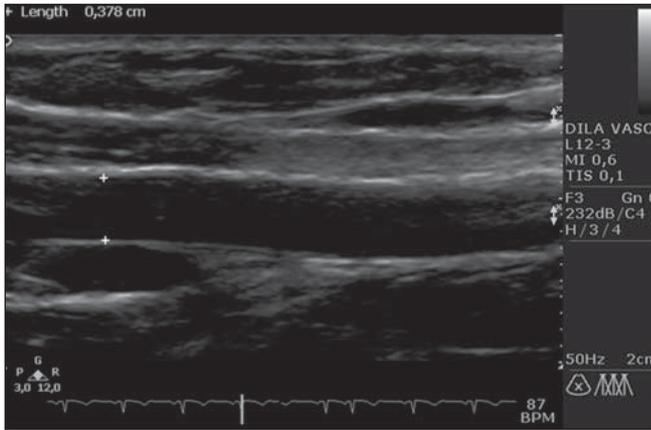
For all five acquired films, three measurements were performed on the R wave, with a sharper brachial artery image (Figure 3). All the sonographic images were recorded in the apparatus itself and later the data were transferred to a Microsoft Excel worksheet (Microsoft Corporation; Redmond, WA, USA).

The mean value for the three measurements of the arterial diameter was considered as the final value. For the FMD calculation, the following formula was utilized for each one of the time spans (30, 60, 90 and 120 seconds):

$$FMD (\%) = [(final \text{ diameter of the brachial artery}) - (initial \text{ diameter of the brachial artery})] / (initial \text{ diameter of the brachial artery} \times 100).$$



**Figure 1.** Photographic image showing the positioning of the upper limb (note that the limb is not lifted) and the transducer positioned on the medial aspect of the arm.



**Figure 2.** Echographic image of brachial artery in a smoking, pregnant woman. Longitudinal section where the measurement of the brachial artery (0.378 cm) is observed before cuff inflation. Observe the calipers positioned on the intimal layer of the vessel lumen, and the electrocardiogram with the marker on the R wave corresponding to the end-diastole phase.



**Figure 3.** Echographic image of brachial artery in a smoking, pregnant woman. Longitudinal section where the measurement of the brachial artery (0.398 cm) is observed after the cuff inflation. Observe the calipers positioned on the intimal layer of the vessel lumen, and the electrocardiogram with the marker on the R wave corresponding to the end-diastole phase.

**Statistics**

The non-paired *t*-test was utilized in the comparison among groups, as the variables presented a parametric distribution. For the evaluation of maximum brachial artery dilation at different time spans (30, 60, 90 and 120 seconds) the ANOVA repeated measures test was utilized. In all these tests, a significance level of 5% was adopted. The softwares SPSS 16.0 for Windows (SPSS Inc.; Chicago, IL, USA) and GraphPad 5.0 for Windows (GraphPad Software; San Diego, CA, USA) were utilized for data analysis.

**RESULTS**

As regards age, no statistically significant difference was observed in any of the comparisons (Table 1). As regards gestational age, the groups were similar, with no significant difference between nonsmoking ( $25.19 \pm 1.13$ ) and the smoking pregnant women ( $25.44 \pm 1.29$ ). Among the smokers, the pregnant women smoked more cigarettes per week ( $110.51 \pm 58.14$ ) as compared with the non-pregnant ones ( $78.52 \pm 45.17$ ), with a statistically significant difference ( $p = 0.04$ ).

As regards to systolic arterial pressure (SAP, in mmHg), no significant difference was observed between smoking and non-smoking pregnant women. The smoking non-pregnant women presented higher SAP than the nonsmoking non-pregnant ones ( $p = 0.01$ ). Also, a statistically signifi-

**Table 1** Comparison of anthropometric and clinical data among the four studied groups.

		Non-smokers	Smokers	<i>p</i>
Age (years)	Pregnant	25.33 ± 3.25	24.54 ± 3.13	0.28
	Non-pregnant	25.28 ± 2.77	26.03 ± 2.88	0.37
	<i>p</i>	0.94	0.10	
Systolic pressure (mmHg)	Pregnant	102.72 ± 12.38	105.45 ± 10.46	0.30
	Non-pregnant	97.06 ± 11.35	107.05 ± 13.91	0.01
	<i>p</i>	0.04	0.64	
Diastolic pressure (mmHg)	Pregnant	66.98 ± 8.85	67.94 ± 10.12	0.65
	Non-pregnant	65.82 ± 8.36	71.47 ± 14.50	0.13
	<i>p</i>	0.55	0.31	
Heart rate (bpm)	Pregnant	79.83 ± 12.29	81.09 ± 14.33	0.67
	Non-pregnant	71.97 ± 8.33	71.31 ± 12.74	0.82
	<i>p</i>	< 0.01	0.02	
Body mass index (kg/m <sup>2</sup> )	Pregnant	24.76 ± 3.83	24.51 ± 3.54	0.77
	Non-pregnant	24.32 ± 3.47	25.07 ± 7.01	0.66
	<i>p</i>	0.60	0.70	

Obs.: Data presented as mean ± standard deviation. *p* values calculated by the non-paired *t* test.

cant difference was observed when comparing nonsmoking pregnant and non-pregnant women: the pregnant ones presented higher SAP than the non-pregnant ones ( $p = 0.04$ ) (Table 1). The use of cigarettes had no significant effect on SAP among pregnant and non-pregnant women.

No significant difference was observed in relation to diastolic arterial pressure (DAP) and body mass index among pregnant and non-pregnant participants, smokers and non-smokers as described on Table 1. The heart rate was higher among the smoking and in nonsmoking pregnant women, but no significant difference was observed between these two groups (Table 1).

As regards the basal brachial artery diameter, no significant difference was observed in any of the comparisons (Table 2). In the evaluation of the time at which maximum brachial artery dilation was achieved, this was observed at 60 seconds after the cuff deflation when the whole sample was analyzed in all the groups (Figure 3 and Table 3).

After the maximum dilation was established, the FMD was compared among the groups, being greater among the nonsmoking pregnant women as compared with smoking pregnant participants. The result was similar for the non-pregnant group: the nonsmoking participants had greater FMD

**Table 2** Comparison of brachial artery diameter and FMD among the four studied groups.

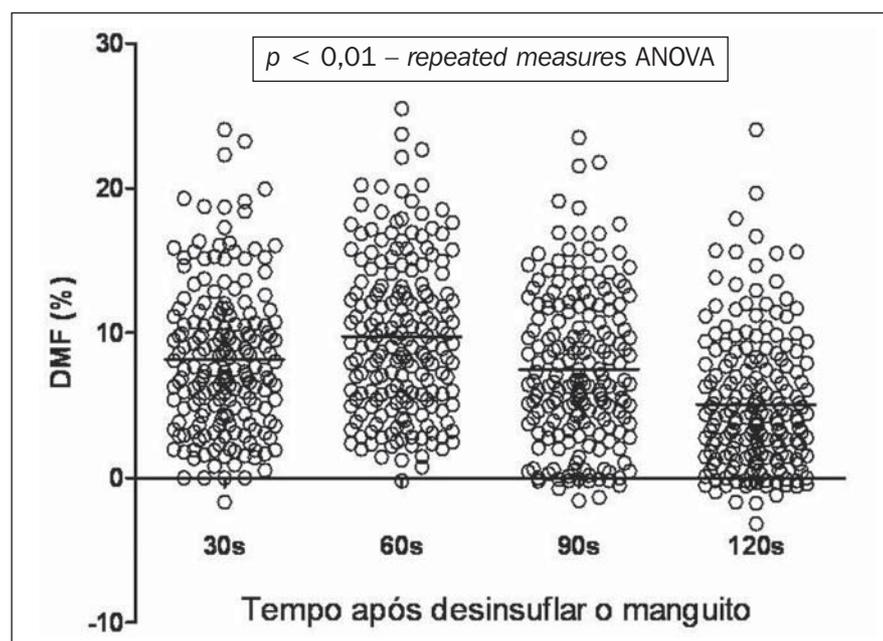
		Non-smokers	Smokers	$p$
Brachial artery diameter (mm)	Pregnant	3.06 ± 0.31	3.18 ± 0.39	0.13
	Non-pregnant	3.01 ± 0.38	3.02 ± 0.42	0.96
	$p$	0.57	0.18	
FMD (%)	Pregnant	11.50 ± 5.77	8.74 ± 4.83	0.03
	Non-pregnant	10.52 ± 4.76	7.21 ± 5.57	0.03
	$p$	0.42	0.30	

Obs.: Data presented as mean ± standard deviation.  $p$  values calculated by the non-paired  $t$  test. FMD, brachial artery flow-mediated dilation.

**Table 3** Comparison of brachial artery FMD among the different time spans (30, 60, 90 and 120 seconds) in the different groups.

	$n$	30 seconds	60 seconds	90 seconds	120 seconds	$p$
Overall	133	8.17 ± 4.87	9.95 ± 5.44	7.99 ± 4.85	5.40 ± 4.23	< 0.01
NSPW	47	9.15 ± 5.44	11.50 ± 5.77	9.46 ± 5.25	6.03 ± 4.73	< 0.01
SPW	33	7.21 ± 4.43	8.74 ± 4.83	7.35 ± 4.15	5.02 ± 4.31	< 0.01
NSNPW	34	8.69 ± 4.66	10.52 ± 4.76	8.06 ± 4.32	5.74 ± 3.89	< 0.01
SNPW	19	6.24 ± 3.90	7.21 ± 5.57	5.31 ± 4.81	3.89 ± 3.09	< 0.01

Obs.: Data presented as mean ± standard deviation.  $p$  value calculated by the ANOVA repeated measures test. NSPW, nonsmoking pregnant women; SPW, smoking pregnant women; NSNPW, nonsmoking non-pregnant women; SNPW, smoking non-pregnant women.

**Figure 4.** Comparison of FMD among the different time spans (30, 60, 90 and 120 seconds) considering the whole sample of the present study ( $n = 133$ ).

than the smoking participants ( $p = 0.03$ ) (Table 2).

## DISCUSSION

As the technique was applied with cuff inflation on the forearm, the whole sample demonstrated maximum and significant

dilation at 60 seconds. Studies have demonstrated that the maximum brachial artery dilation occurs around 60 seconds after cuff deflation<sup>(8,16-18)</sup>; other studies based on such evidences only use this time as a reference to obtain FMD<sup>(19-21)</sup>. These two factors motivated the evaluation of cigarette smoking influence on the maximum dila-

tion, and if such time should be the reference when one studies the FMD and the smoking habit.

For the nonsmoking group, it was expected that the maximum dilation occurred at 60 seconds or close to this time span, which would be in agreement with studies that demonstrate maximum dilation between 45 and 75 seconds<sup>(8,16)</sup>. Among non-smoking pregnant women, studies demonstrate that maximum dilation is also close to this time<sup>(22,23)</sup>.

As regards cigarette influence, a study on brachial artery dilation in 11-year-old children exposed to cigarette smoke, has demonstrated that maximum dilation is delayed in the group with highest exposure as compared with the less exposed one, in which the maximum dilation is observed at around 60 seconds<sup>(17)</sup>.

After the determination of maximum dilation, the FMD difference among groups was evaluated, observing that both smoking and nonsmoking pregnant women presented smaller FMD as compared with control groups. Studies have demonstrated that FMD decreases in active smokers<sup>(24,25)</sup>, as well as in passive smokers<sup>(26)</sup>. As regards smoking pregnant women, a study has also demonstrated a decrease in FMD in this group<sup>(9)</sup>.

Considering that the main objective of the present study was the evaluation of cigarette smoking on the endothelium, a well defined age group was selected (20 to 30 years) so that aging would not affect the FMD<sup>(27)</sup>. Likewise, all the pregnant women were submitted to evaluation between the 24th and 28th gestational weeks, to avoid the influence of gestational age on the FMD, considering that studies demonstrate differences in FMD at the different gestational ages<sup>(28,29)</sup>.

No difference was observed in SAP among smoking and nonsmoking pregnant women, which did not occur among the non-pregnant women. As the DAP is analyzed, no significant difference was found in any group. This can be explained by the fact that the patients went through an abstinence period, as it was expected that there would be a difference in arterial pressure between smoking and nonsmoking pregnant women<sup>(30,31)</sup>. The fact of having developed the study with normotensive

pregnant women was important to avoid interference in FMD, as hypertension may play an influence on it<sup>(32)</sup>.

The results of the present study demonstrated higher heart rate among the pregnant women, both in the smoking and non-smoking groups. It was actually expected that in the smoking group the heart rate would be higher<sup>(30,31)</sup>, however no significant difference was observed. This can be explained by the fact that the participants were oriented to refrain from smoking for a period, a fact that has been demonstrated by other authors<sup>(9,33)</sup>.

As the body mass index was analyzed, no interference on FMD was expected, as all the patients in the sample presented a body mass index < 30 kg/m<sup>2</sup><sup>(34)</sup>.

As regards the brachial artery diameter, no significant difference among groups was observed; therefore it was expected that there would be no interference on FMD, as studies had demonstrated that the higher is the basal brachial artery diameter, the lower is FMD<sup>(20,24)</sup>.

This is a technique that requires training, besides an accurate technical skill to be performed. The investigator must be skilled, and appropriate equipment coupled with electrocardiograph is required.

The assessment of brachial artery flow-mediated dilation is another useful tool to detect individuals with cardiovascular diseases, and with the standardization of the technique, FMD tends to become a widely accepted technique for evaluating the endothelial function.

## CONCLUSION

Maximum brachial artery dilation was achieved at 60 seconds, independently of being the women pregnant or not. However, the FMD was smaller among the smoking women, pregnant or not, demonstrating that smoking compromises the endothelial function.

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