Vascular Reactivity: Evaluation of an acute suprasystolic occlusion with impedance plethysmography

M C Herrera¹, M Bonaudo, A Conde² and L Palavecino²

¹ Departamento de Bioingeniería, Facultad de Ciencias Exactas y Tecnología, Universidad Nacional de Tucumán e INSIBIO, CONICET, Tucumán, Argentina
² Carrera de Ingeniería de Biomédica, Facultad de Ciencias Exactas y Tecnología, Universidad Nacional de Tucumán

Email: mherrera@herrera.unt.edu.ar

Abstract. — In the clinical set, the evaluation of endothelium-dependent vasodilator response of large vessels is carried out using ultrasound equipment for vascular flow determinations and during administration of vasoactive drugs. This work proposes to use a substantially cheaper technique and a sustained cuff arterial occlusion in order to cause vasodilation. Impedance plethysmography is used to detect the arterial pulse wave over radial artery while the forearm is occluded by above the recording site. From these plethysmographic waves, three indexes and their changes -between control and maximal response post-occlusion- were calculated. 33 complete records obtained from healthy low-risk volunteers were analyzed. Between control and post-occlusion maximal response, “average percentual change of pulse wave amplitude” were (35±13)%, “stiffness index” did not show significant differences (6,38±0,98 vs 6,38±0,94 and “reflection index” was significant lower (58±15 vs 35±16)%. These results indicate that: 1- cuff occlusion maneuver was effective to cause endothelium-dependent vasodilation, 2- changes of pulse wave amplitude and reflection index could be used as markers of athero-arteriosclerotic damage in the vascular bed, even in sub-clinical conditions.

1. Introduction

Disease and damage in blood vessels have been widely recognized as one of a major contributory factor of the cardiovascular risk. In general, cardiovascular risk profile is evaluated by a series of parameters that include arterial pressure analysis, deep evaluation of life habits (sedentarysm, smoking), blood lipidic profile, diabetes mellitus and previous familiar records of cardiovascular disease, among others [1]. Without rejecting traditional techniques, a new, non-invasive and simple plethysmographic method has been added; called contour analysis of arterial pulse (CAP) offers new possibilities in evaluation and early detection of the cardiovascular disease [2].

The arterial pulse wave is formed by a complex interaction between the left ventricle and the circulatory system [3]. It consists of a first systolic peak and a second diastolic peak with a point of inflexion that happens in a time (ΔT) after the first one (Fig. 1). The systolic peak is caused by the pressure transmitted directly by the left ventricle towards the aorta, whereas the diastolic peak is caused mainly by the reflected wave in the femoral aorta bifurcation (retrograde wave).
Preliminary studies suggest that CAP has a complex, but predictable, relation with the condition and behavior of peripheral arteries and it is possible to extrapolate its response to the large arteries and even, to the coronary arteries [4-6].

Moreover, CAP has been used to characterize vascular diseases and for monitoring vessel response to vasoactive drugs [7], also, for evaluating endothelium function, controlled by substances liberation like endothelin (vasoconstrictive) or nitric oxide (vasodilator) [8].

CAP includes:
1- the amplitude of direct and retrograde pulse waves analysis using the “Reflection Index” (RI) that depends of the vascular tone [9] and
2- of the temporary distance between systolic and diastolic waves analysis using the “Stiffness Index” (SI) that evaluates the arterial stiffness.

In a previous work, our group studied amplitude changes only in systolic wave between control (at rest) and post cuff occlusion maneuver incorporating the temporary arterial response [10].
In the present study, using a self-made impedance plethysmograph to obtain arterial pulse wave, the indexes - RI and SI- have been evaluated in response to an occlusion maneuver in the radial artery in healthy subjects.
This maneuver produces a temporary occlusion of the blood flow and allows, when the flow is reestablished, evaluate endothelium-dependent mediated response [10], known as “vascular reactivity” or “reactive hyperemia”.
Several studies have presented before mentioned indexes at rest and others, under the action of vasoactive substances, mainly nitroglycerine [11].
In the present study, the objective is to evaluate the effectiveness of a simple, non-invasive and repeatable cuff occlusive maneuvers to produce vasodilation endothelium-dependent response.

2. Materials
Arterial pulse wave was obtained using an impedancimetric device previously developed at the Departamento de Bioingeniería, Universidad Nacional de Tucumán [12]. For wave analysis, a commercial acquisition system (BIOPAC System Inc) and processing software (AcqKnowledge II for MP100WSW) with a sampling rate of 1000Hz per channel were used.

3. Methods

3.1. Indexes Calculations

![Diagram of pulse wave](image)

**Fig. 1.** Depict the typical arterial pulse waveform obtained by plethysmography and its characteristic parameters. ΔT, time between the systolic and the first diastolic peak; a, amplitude of the first peak; b, amplitude of the second peak.
The first index, called “Stiffness Index” (SI) [11], is defined as,

\[ \text{SI} = \frac{h}{\Delta T} \]  

where \( \Delta T \) is the temporal distance between the systolic and diastolic peaks (Fig. 1) and, \( h \) is the subject height [in meters]. Not being known the distance between the left ventricle and the descending aorta bifurcation, \( h \) subject height is used because there is a known relationship between them [11]. In addition, the pulse wave velocity is the most validated measure of “arterial stiffness”.

The second index to calculate, called “Reflection Index” (RI), is defined as the ratio between the amplitudes of the second peak (b) and the first peak (a), respectively, in % (Fig. 1),

\[ \text{RI} = \frac{b}{a}.100 \]  

Finally, we calculate the amplitude changes of systolic wave between control (at rest) (\( a_{\text{CONTROL}} \)) and the maximum amplitude obtained in post-occlusive period (\( a_{\text{MAX}} \)), in %.

\[ \Delta a = \left( \frac{a_{\text{MAX}} - a_{\text{CONTROL}}}{a_{\text{MAX}}} \right).100 \]  

This parameter, \( \Delta a \), is a measure of the vasodilator response of the radial arterial and, it is used to “evaluate” the vascular reactivity and the functionality of the involved endothelium.

3.2. Procedure

33 healthy subjects were studied before a questionnaire for cardiovascular risk stratification. Informed consent was requested and a paper-copy of it was given back to them.

After questionnaire, the procedure sequence was:

1. Rest for 5 min.
2. Weight and height measurement.
3. Arterial pressure determination at contra-lateral forearm.
4. Plethysmographic vascular evaluation.

The used impedance plethysmograph takes impedance variations that result proportional to the forearm blood volume changes (or radial artery pulsatile behavior).

The subjects were examined after 5 minutes rest in supine position. The studied forearm was placed at level of the left atrium and a couple of metallic electrodes (like those of the ECG) were positioned, preferably following the radial artery line, approximately 2 cm below the cubital fold, separated 5 cm to 10 cm between them.

A sphygmanometry cuff was placed in the upper arm over the record site and was inflated 50 mmHg above the systolic pressure for 3 minutes (suprasystolic occlusion). No wrist cuff was used to avoid hand circulation and only one suprasystolic occlusive test was performed by subject.

Continuous record and storage of data were performed from 30sec before cuff occlusion (basal or CONTROL) up to 3min after release the cuff (POST) including 3 minutes of occlusion (INTRA).
A complete maneuver is shown in Figure 2 with a simultaneously electrocardiographic record.

![Figure 2](image)

**Fig. 2.** Typical example of a time course of impedance plethysmographic record in each maneuver period. A- Complete maneuver with indications about the occlusive maneuver stages: control or basal conditions, suprasystolic occlusion and postischemic occlusion. The acute suprasystolic occlusion vanishes the pulses during occlusive period and, after desocclusion, the arterial pulse is augmented first dimishing up to normalization later. B: Changes of pulse amplitude in preischemic (Control) and the maximum amplitude during postischemic period. The difference between the two mentioned values rise up to 45%. No normalized ECG is simultaneously registered.

Evaluation of all plethysmographic was performed by two independent operators using a processing software (AcqKnowledge II for MP100WSW). For every record, were evaluated: 1- basal characteristics preocclusion (Control) and 2 - the maximum obtained response (MAX) on the post desocclusion period.

3.3. **Statistics:**

Population characteristics are presented as averages ± SD. The occlusive maneuver effect over the predefined indexes was studied by the association between $S_{I_{\text{CONTROL}}}$ vs $S_{I_{\text{MAX}}}$ and $R_{I_{\text{CONTROL}}}$ vs $R_{I_{\text{MAX}}}$, respectively, using regression analysis.

The effect of the maneuver on indexes was evaluated with ANOVA at $p < 0.005$.

4. **Results**

33 healthy subjects (17 men and 16 female; 11-48 years old; average IMC of 23 kg/cm²) were studied previous cardiovascular risk stratification by means of a questionnaire of risk factors and analysis of lipids and glycemia. Healthy subjects were selected of an universitary population that it was qualified like “low risk” according to the "Framingham Score" [1].

The population characteristics are shown in TABLE I.
TABLE I
CHARACTERISTICS OF THE POPULATION

| Characteristics   | Mean | SD  |
|-------------------|------|-----|
| Weight (Kg)       | 66   | 12  |
| Age (years)       | 33   | 11  |
| IMC (Kg/m²)       | 23   | 4   |
| PAS (mmHg)        | 98   | 16  |
| PAD (mmHg)        | 61   | 10  |
| SICONTROL (m/seg) | 6,38 | 0,98|
| RICONTROL (%)     | 58   | 15  |

TABLE II presents the means ± SD of the evaluated indexes at rest (CONTROL) and the maximum post-occlusion response (MAX), respectively.

TABLE II
INDEXES IN REST AND MAXIMUM RESPONSE

| INDEXES     | CONTROL ±SD | MAX ±SD |
|-------------|-------------|---------|
| SI (m/seg)  | 6,38 ± 0,98 | 6,38 ± 0,94 |
| RI (%)      | 58 ± 15     | 35 ± 16* |
| Δα (%)      | ------      | 35 ± 13  |

* Significant difference with p<0.005 compared with the control.

It is observed that the response mediated by endothelium has produced an increase of (35±13) % in the amplitude of the pulse.

Only significant differences were found in the Reflection Index RI between the situations CONTROL vs MAX maximum vasodilator response whereas the Stiffness Index SI did not show significant differences between both situations.

Figure 3 shows the linear regression between RI_CONTROL vs RI_MAX:

Fig. 3. RICONTROL vs RIMAX. Linear regression: see the parameters equation in the box. r, coefficient of correlation. p, probability. The solid and dashed lines show the regression of the points and the confidence interval (95 %), respectively.
It is observed that the maneuver produces changes in the amplitude diastolic peak respect of the amplitude systolic peak demonstrated in the slope of the regression (0.749). A slope minor than 1 (one) means a reduction of the relation b/a, or diastolic peak/systolic peak.

The Figure 4 shows the linear regression between SI\textsubscript{CONTROL} vs SI\textsubscript{MAX}.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig4.pdf}
\caption{SICONTROL vs SIMAX. Linear regression: see the equation in the box. r, coefficient of correlation. p, probability. The solid and dashed lines show the regression of the points and the confidence interval (95 \%), respectively.}
\end{figure}

When the stiffness index was evaluated, the regression line (in Fig 4) has a slope near 1 (0.903) with a good correlation coefficient (r=0.947). The dashed lines that indicate the confidence interval (95 \%) are to close, then, clearly the occlusive maneuver does not modify that index.

5. DISCUSSION

The arterosclerotic damage of the large arteries is a major contributory factor to the cardiovascular morbi-mortality patients with low risk [13]. Nowadays, the technologies tend to look for indexes to know the arteries conditions and increase the possibility to determine a "sub-clinical form" of the deterioration beginning [14]. In this context, is that there are looked technologies and procedures that allow a non-invasive, reproducible and low cost form of arteries evaluation tending to a massive "screening" for low risk populations [15-16].

In this work there has been used low cost self-made impedance plethysmograph and, an easily realizable occlusive maneuver that elicited a vasodilator response corroborated by the changes in $\Delta a$ (35±13)%.

The ultrasound technologies, extensively reported in the bibliography, have an advantage of being non-invasive but the imaging equipment required is not easily portable, is expensive and also relies heavily on the ability of the operator. Finally, in most case, need to use vasoactive drugs to obtain endhotelial response.
On the other hand, plethysmography is a low cost technique (its cost is 20 % of ultrasound based equipment) and does not need specializing personnel. Respect of the maneuver, it has been found that the sustained occlusion for at least 3 min with a simple cuff elicit an endothelial depend response, similar to obtained with drugs [11,15] but without invasive condition.

Moreover, the observed decrease in the reflexion index RI during occlusive period match with the results obtained by other authors using NTG [11] to provoke reactive hyperemia.

About arterial stiffness, and considering that it is a measure that depends on structural components of vessel, it is logical to think that an transitory occlusive maneuver cannot elicit changes in the corresponding index.

6. Conclusions

The results allow concluding that:

1- occlusive maneuver produces endothelial response according to the observed in healthy subjects,

2- change in arterial pulse amplitude (between control an maximal response) is a measure of the vascular reactivity,

3- reflection index shows the vessel response to occlusive process but, it still needs major analysis, whereas stiffness index does not show changes.

Finally, the technique and the occlusive procedure allow to evaluate endothelium mediated response in large vessels and they might be used for monitoring sub-clinical cardiovascular disease.

Acknowledgements

This work has been partially financed by the Program Nro 26/E349 of the Consejo de Investigaciones de la UNT, CIUNT and INSIBIO, CONICET

REFERENCES

A. W. Haider, M. G. Larson, S. S. Franklin, D. Levy. “Systolic Blood Pressure, Diastolic Blood Pressure and Pulse Pressure as Predictors of Risk for Congestive Heart Failure in the Framingham Heart Study”, Ann Intern Med. vol. 138, pp. 10-16, 2003.

F. M. Clara, M. L. Cayrol, A. G. Scandurra, G. J. Meschino, M. G. Garzillo, E. Moyano, A. R. Introzzi. “La técnica de análisis de onda de pulso en la determinación de riesgo cardiovascular”, Rev Fed Arg Cardiol, vol. 34, pp. 213-220, 2005.

M. F. O'Rourke, A. Pauca, Xiong-Jing Jiang, “Pulse wave analysis”, Blackwell Science Ltd Br J Clin Pharmacol, vol. 51, pp. 507-522, 2001.

D. K. Arnett, S. P. Glasser, G. McVeigh, R. Prineas, S. Finklestein, J. N. Cohn, A. Sinaiko. “Presión arterial y distensibilidad arterial en jóvenes: Estudio de la Presión Arterial de Jóvenes de Minnesota”, AJH (Ed. Exp.), vol. 3, pp. 272-278, 2001.

S. C. Millasseau, F. G. Guigui, R. P. Kelly, K. Prasad, J.R Cockcroft, J. M. Ritter and P. J. Chowienczyk, “Noninvasive Assessment of the digital Volumen Pulse: Comparison with peripheral pressure pulse”, Hypertension, vol. 36, pp. 952-956, 2000.

S. C. Millasseau, R. P. Kelly, J. M. Ritter, P. J. Chowienczyk, “Determination of age-related increases in large artery stiffness by digital pulse contour analysis”, Clinical Science, vol. 103, pp. 371-377, 2002.
J. N. Cohn, S. Finkelstein, G. McVeigh, D. Morgan, L. LeMay, J. Robinson, J. Mock, “Noninvasive Pulse Wave Analysis for the Early Detection of Vascular Disease”, *Hypertension*, vol. 26, pp. 503-508, 1995.

J. E Parra, F. Mora, G. Villegas, E. Romero-Vechione, J. Vasquez “Desarrollo de un plstemógrafo de impedancia para evaluar la hiperemia reactiva en el antebrazo”, *Acta científica Venezolana*, vol. 54, pp. 2-11, 2003.

J.M. Padilla, E.J. Berjano, J. Sáiz, L. Fácila, P. Díaz, S. Mercé, “Assessment of Relationships between Blood Pressure, Pulse Wave Velocity and Digital Volume Pulse”, *Computers in Cardiology*, vol. 33, pp. 893-896, 2006.

G. Feldman, M. C. Herrera, “Técnica impedancimétrica: variabilidad de la respuesta vascular ante apremio suprasistólico”, *Rev Fed Arg Cardiol*, vol. 32, pp. 254-258, 2003.

S. C. Millasseau, R. P. Kelly, J. M. Ritter, P. J. Chowienczyk, “The Vascular Impact of Aging and Vasoactive Drugs: Comparison of Two Digital Volume Pulse Measurements”, *AJH*, vol. 16, pp. 467–472, 2003.

G. Feldman, M.C. Herrera, “Dispositivo y procedimiento para valoración del comportamiento vascular”, patente en trámite INPI LP030103671, oct 2003.

K. Kobayashi, M. Akishita, W. Yu, M. Hashimoto, M. Ohni, K. Toba, “Interrelationship between non-invasive measurements of atherosclerosis: flow-mediated dilation of brachial artery, carotid intima-media thickness and pulse wave velocity”, *Atherosclerosis*, vol. 173, pp. 13-18, 2003.

J. P. Werba, L. A. Cuniberti, V. Martinez, R. Rey, “Atherosclerosis subclínica un índice objetivo de susceptibilidad y riesgo cardiovascular”, *Medicina (Buenos Aires)*, vol. 59, pp. 382-384, 1999.

I.S. Mackenzie, I.B. Wilkinson and J.R. Cockcroft, “Assessment of arterial stiffness in clinical practice.”, *QJM Med*, vol. 95, pp. 67-74, 2002.

J. Yoshio Matsui, K. Kario, J. Ishikawa, K. Eguchi, S. Hoshide, K. Shimada,”Reproducibility of Arterial Stiffness Indices (Pulse Wave Velocity and Augmentation Index) Simultaneously Assessed by Automated Pulse Wave Analysis and Their Associated Risk Factors in Essential Hypertensive Patients.”, *Hipertens Res*, vol. 27, pp. 851-857, 2004.