Carotid wall stress calculated with continuous intima-media thickness assessment using B-mode ultrasound

A F Pascaner[1,2], D Craiem[1,2], M E Casciaro[1,2], R Danielo[3], S Graf[1,2] and E Guevara[3]
[1]Facultad de Ingeniería y Ciencias Exactas y Naturales, Universidad Favaloro. Buenos Aires, Argentina. [2]CONICET. Buenos Aires, Argentina. [3]Hospital Universitario de la Fundación Favaloro, Unidad de Ecocardiografía y Doppler Vascular. Buenos Aires, Argentina.

E-mail: apascaner@favaloro.edu.ar

Abstract. Cardiovascular risk is normally assessed using clinical risk factors but it can be refined using non-invasive infra-clinical markers. Intima-Media Thickness (IMT) is recognized as an early indicator of cardiovascular disease. Carotid Wall Stress (CWS) can be calculated using arterial pressure and carotid size (diameter and IMT). Generally, IMT is measured during diastole when it reaches its maximum value. However, it changes during the cardiac cycle and a time-dependant waveform can be obtained using B-mode ultrasound images. In this work we calculated CWS considering three different approaches for IMT assessment: (i) constant IMT (standard diastolic value), (ii) estimated IMT from diameter waveform (assuming a constant cross-sectional wall area) and (iii) continuously measured IMT. Our results showed that maximum wall stress depends on the IMT estimation method. Systolic CWS progressively increased using the three approaches ($p<0.001$). We conclude that maximum CWS is highly dependent on wall thickness and accurate IMT measures during systole should be encouraged.

1. Introduction

Several studies have aimed at detecting cardiovascular diseases in an early stage and thus improve risk prediction [1-3]. Besides traditional risk factors (such as age, smoking and hypertension), different infra-clinical factors were studied in order to refine the risk assessment of a given patient. This is the case of Intima-Media Thickness (IMT), Pulse Wave Velocity (PWV) [4-6], arterial compliance [7], mechanical stress in the arterial wall [8], to name a few. In this work we propose a new approach to calculate the arterial wall stress at the level of the common carotid artery.

The carotid wall stress depends on the blood pressure and the arterial geometry. Normally, the artery is represented as a cylinder with a thick wall. Using B-mode ultrasound it is possible to estimate arterial diameter and IMT [9][10]. During diastole, diameter variations are slow and IMT tends to reach its maximum value, thus making it the preferred moment for IMT estimation during the cardiac cycle [11]. However, using modern equipment and digital image processing techniques, we have shown that it is possible to assess diameter and IMT waveforms during the entire cardiac cycle [10]. The continuous assessment of IMT and carotid diameter allows the calculation of the time-varying arterial wall stress.

The aim of this work was to compare different maximum stress values assuming that IMT: (i) was constant and its value was estimated during diastole, (ii) was calculated assuming constant Cross-Sectional Wall Area (CSWA) from diameter measures and (iii) was continuously estimated with the proposed algorithm [10]. For this purpose, a cohort of healthy volunteers and intermediate cardiovascular risk patients was evaluated using B-mode ultrasound sequences.

2. Materials and methods

2.1. Study population
The population under study was comprised of healthy volunteers and cardiovascular patients. Volunteers were prospectively recruited under the following inclusion criteria: being less than 30 years old, non-smokers, non-diabetics and not having been diagnosed with neither hypertension nor hypercholesterolemia. Intermediate cardiovascular risk patients were retrospectively selected by the Echocardiography and Vascular Doppler Unit of the Favaloro Foundation Hospital. Table 1 shows clinical data of volunteers and patients.

Table 1. Clinical data of the subjects. Values are expressed as mean ± standard deviation or n (%). We used a T-test to compare continuous variables and a χ^2 statistic for dichotomous variables.

Parameter	Volunteers	Patients	p
Number of subjects	45	19	-
Age, years old	21.8 ± 1.6	54.4 ± 7.8	<0.01
Male, n (%)	25 (56%)	14 (74%)	n.s.
Body mass index, kg/m^2	23 ± 3	28 ± 6	<0.01
Systolic pressure, mmHg	121 ± 14	130 ± 12	<0.01
Diastolic pressure, mmHg	77 ± 8	74 ± 9	n.s.
Pulse pressure, mmHg	44 ± 12	56 ± 9	<0.01
Smokers, n (%)	0 (0%)	12 (63%)	<0.01
Hypertensive, n (%)	0 (0%)	11 (58%)	<0.01
Hypercholesterolemia, n (%)	0 (0%)	13 (68%)	<0.01
Diabetes, n (%)	0 (0%)	2 (11%)	<0.05
Heart rate, bpm	74 ± 11	68 ± 11	<0.05
Carotid plaques, n (%)	0 (0%)	9 (47%)	<0.01
Femoral plaques, n (%)	0 (0%)	11 (58%)	<0.01

2.2. Continuous diameter and IMT measurement
Each subject underwent an ultrasound examination performed by a professional with a high resolution device (Philips HD11XE) and a 10 MHz linear transducer. Five-second sequences of B-mode ultrasound images of the common carotid artery were recorded. All sequences were acquired during a single breath-hold. For volunteers, both left and right carotid arteries were registered. For patients, only the available registers in one or two carotids were processed. We developed a software that imported the sequences and measured frame-by-frame diameter and IMT, thus obtaining continuous waveforms. A detailed explanation of the software can be found in [10]. Briefly, the user selected a Region Of Interest (ROI) in the first image of every sequence. Each column of pixels within the ROI was considered as a vector of grey level intensity. Three interfaces were detected in each column: (i) near wall intima-lumen, (ii) far wall lumen-intima and (iii) far wall media-adventitia. The algorithm searched for the maximum gradient of intensity to determine their locations. The definitive interfaces

were considered as the mean value of all columns in the ROI. Diameter was considered as the distance between (i) and (ii) and IMT as the distance between (ii) and (iii).

For every sequence, IMT values were smoothed with a 3-point moving-average filter. The waveforms were separated in heartbeats using extreme diameter values. For each beat, diastole and systole were considered as the points where minimum and maximum diameter occurred, respectively. Diastolic and systolic diameters and IMTs were averaged for all the heartbeats (a minimum of three) obtaining four values for each sequence: diastolic diameter (D_d), systolic diameter (D_s), diastolic IMT (IMT_d) and systolic IMT (IMT_s). Blood pressure was measured in the brachial artery with an automatic oscillometric device (Omron BP742).

2.3. Stress calculation

Normal stress in a body is defined as the extending force divided by the area of the cross-section:

$$\tau = \frac{F}{A} \tag{1}$$

where τ is normal stress, F is the force and A is the cross-sectional area. We considered the artery as a perfect cylinder with a thick wall in which only an internal pressure is acting (blood pressure). With this model, we can define medial radius R as follows:

$$R = \frac{r_e + r_i}{2} \tag{2}$$

where r_e and r_i are external and internal radius of the cylinder, respectively. Wall stress at R can be expressed in terms of external and internal radii [12]:

$$\tau = \frac{2P(r_e r_i)^2}{({r_e}^2 - {r_i}^2)R} \tag{3}$$

where P is blood pressure. We measured continuous diameter (D) and IMT in volunteers and patients using B-mode ultrasound sequences and calculated r_e and r_i as follows:

$$\begin{aligned} r_i &= \frac{D}{2} \\ r_e &= \frac{D}{2} + IMT \end{aligned} \tag{4}$$

Diastolic wall stress was calculated using diastolic pressure, diameter and IMT values. Systolic wall stress was calculated in three different ways, using the same systolic diameter and pressure but changing IMT estimation. IMT was considered as: (i) standard IMT measured in diastole (IMT_d), (ii) estimated systolic IMT assuming a constant CSWA (IMT_{s_est}) and (iii) systolic IMT measured with the proposed algorithm (IMT_s). In the case (i), IMT_d was considered constant and the diastolic standard value was used. In the case (ii), IMT_{s_est} was calculated considering that the arterial wall is incompressible [13], i.e., its CSWA remains constant within the cardiac cycle. CSWA can be calculated as follows:

$$CSWA = \pi\, IMT(D + IMT) \tag{5}$$

Assuming a constant CSWA value during the cardiac cycle, IMT_{s_est} can be calculated with diameter and IMT_d:

$$IMT_{s\_est} = \frac{-D_s + \sqrt{{D_s}^2 + 4IMT_d(D_d + IMT_d)}}{2} \tag{6}$$

No longitudinal stretch was considered. However, it has been shown that the carotid arterial length changes during systole and this change affects significantly the mechanical properties of the arterial wall [10]. For this reason, we also proposed the case (iii), and we measured IMT during systole to obtain its actual value.

3. Results

3.1. Diameter and IMT measurements

Table 2 shows mean diastolic and systolic diameter and IMT values for volunteers and patients. A Student's t-test was used to compare values.

Table 2. Obtained values of diastolic and systolic diameter and the three estimations of IMT. Values are expressed as mean ± standard deviation.

Parameter	Volunteers	Patients	p
Number of carotids	90	27	-
D_d (mm)	5.16 ± 0.48	5.73 ± 0.88	<0.01
D_s (mm)	6.00 ± 0.56	6.25 ± 0.93	n.s.
IMT_d (mm)	0.45 ± 0.09	0.58 ± 0.11	<0.01
$IMT_{s\ est}$ (mm)	0.40 ± 0.08	0.54 ± 0.10	<0.01
IMT_s (mm)	0.37 ± 0.09	0.53 ± 0.12	<0.01

Both in patients and in volunteers D_d was lower than D_s ($p<0.01$) and IMT_d was higher than IMT_s ($p<0.01$) and IMT_{s_est} ($p<0.01$). IMT_{s_est} was higher than IMT_s in volunteers and in patients ($p<0.01$ and $p<0.05$, respectively).

3.2. Wall stress results

Diastolic and systolic wall stresses for volunteers and patients are shown in figure 1. From left to right: diastolic wall stress, systolic wall stress using IMT_d, systolic wall stress using IMT_{s_est} and systolic wall stress using IMT_s.

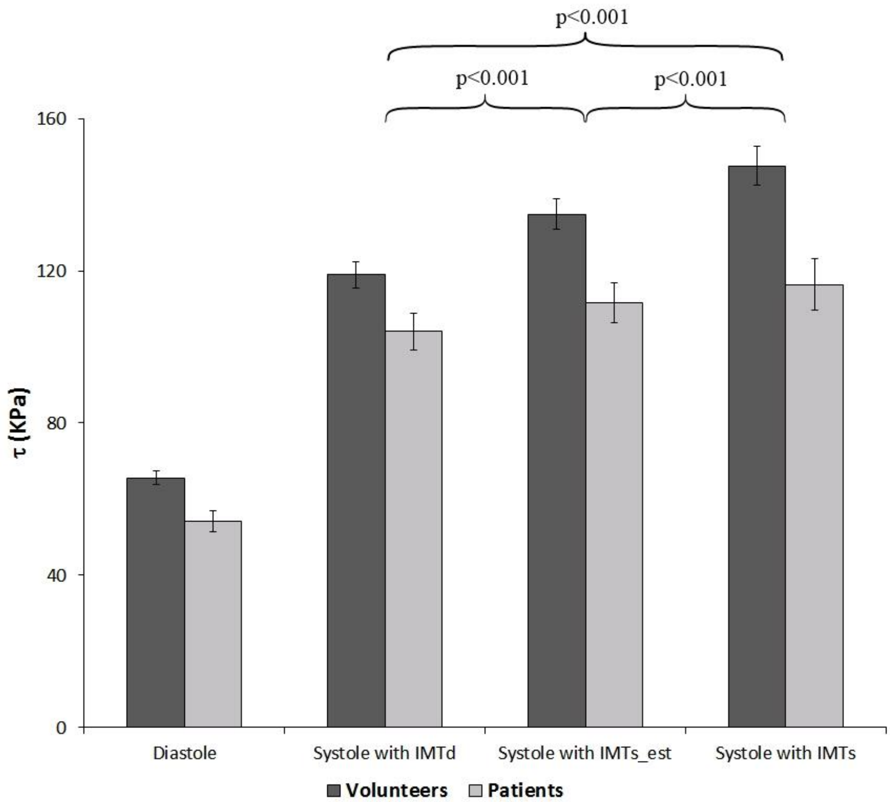

Figure 1. Minimal (diastolic) and maximal (systolic) wall stress in the carotid artery wall for volunteers and patients. Bars indicate standard error.

Wall stresses in systole for the three IMT estimations were higher than in diastole ($p<0.001$). It can be observed that as systolic IMT approaches the real, smaller, value (from left to right), wall stress increases ($p<0.001$). Finally, we observed that wall stresses were systematically higher in volunteers with respect to patients ($p<0.05$ for systolic wall stress with IMT_d and $p<0.01$ for the rest).

4. Discussion

We have found that there are significant differences in the estimation of the maximum stress exerted over the carotid artery, depending on the IMT estimation method. These differences were significant for both volunteers and patients. It can be observed in figure 2 that as IMT decreases, stress increases. Accordingly, if IMT is continuously assessed during the cardiac cycle, higher maximum stresses were found.

In figure 1, it is noteworthy that patients had a lower maximum wall stresses than volunteers, despite having a significantly higher systolic pressure. Probably, higher arterial pressure triggers an IMT increase as a protection mechanism to preserve arterial wall stress. This IMT increase reduces stress, according to equations (1) and (3). Whether this compensation mechanism was entirely responsible of the lower values of wall stresses found in patients with respect to volunteers, need to be further investigated.

This study had some limitations that need to be addressed. Firstly, it is arguable whether measuring IMT in systole is possible, since its value is near the ultrasound resolution. Nonetheless, it has been reported that technology advances allowed for accurate IMT estimation even in young subjects, where IMT values tend to be smaller [14]. The use of automated algorithms become indispensable [10]. Finally, we used the brachial pressure to calculate carotid wall stress, although central pressure should have been employed. Some studies have shown an amplification phenomenon, which makes systolic pressure in the periphery (e.g. in the brachial artery) higher than central pressure (e.g. in the carotid artery) [13]. In order to have more accurate results, central pressure could be estimated from brachial pressure and continuous Cross-Sectional Area (CSA) estimations [15]. Meinders et al proposed an exponential model and an iterative algorithm that converges into central pressure. We have tested this algorithm in a volunteer using brachial diastolic and systolic pressure and continuous carotid diameter estimations (from which continuous CSA was calculated). Figure 2 shows (on the left hand) the exponential fit between CSA and blood pressure and (on the right hand) A) estimated central pressure waveform, B) measured carotid diameter waveform, C) IMT estimations using (i) standard diastolic IMT (IMT_d), (ii) estimated IMT assuming constant CSWA (IMT_{s_est}) and (iii) continuously measured IMT (IMT_s) and D) calculated wall stress with the three different IMT assumptions. Note the incremental wall stress values for cases (i), (ii) and (iii) (also observed in figure 1). This preliminary test showed that central systolic pressure resulted 131 mmHg when brachial systolic pressure was 133 mmHg (1.5% error). As a future work, we can repeat this analysis for all subjects although pressure differences should remain negligible.

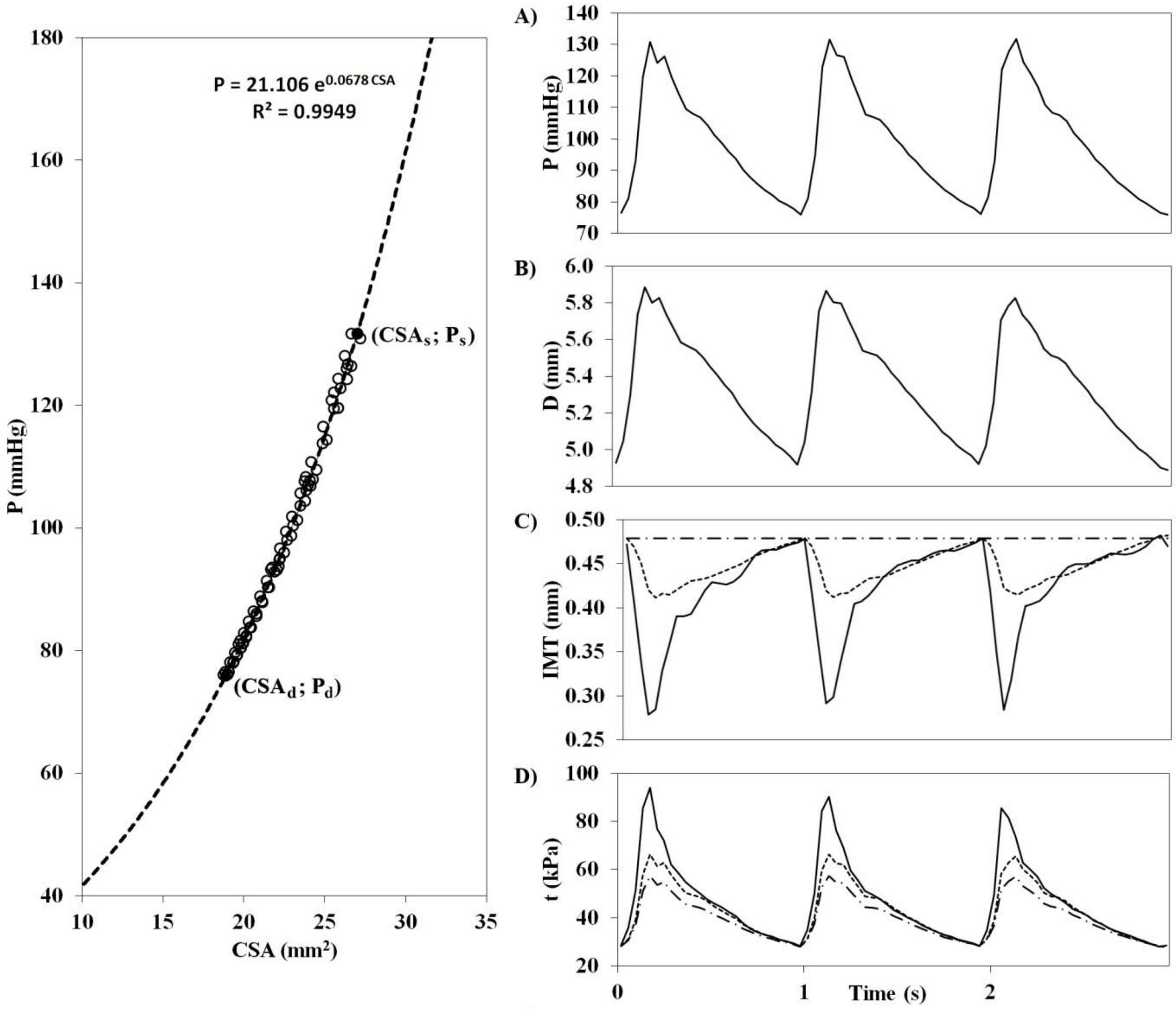

Figure 2. On the left: exponential estimation of central pressure using CSA. Dashed line is the estimated function and solid line represents the range of the representative volunteer. On the right: A) estimated pressure waveform, B) measured diameter waveform, C) IMT_d, IMT_{s_est} and IMT_s (dashed-dotted, dashed and solid lines, respectively) and D) calculated wall stress with the three approaches of IMT (same line types as in C)).

5. Conclusion

In this work we proposed a method to calculate the maximum carotid wall stress using continuous IMT measurements. We verified that IMT estimation methods can significantly modify carotid wall stress estimation. The estimation of true IMT values during systole was possible using an image processing algorithm that continuously measured simultaneous IMT and diameter values. The carotid wall stress is highly dependent on wall thickness and accurate IMT measures during systole should be encouraged.

6. Acknowledgement

This work was partly supported by the grant PICT 2012 Number 0406 of the “Ministerio de Ciencia y Tecnología” (Argentine).

7. References

[1] Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson I and Struijker-Boudier H 2006 Expert consensus document on arterial stiffness: methodological issues and clinical applications *Eur Heart J* **27** 2588-605

[2] Xanthakis V, Enserro D M, Murabito J M, Polak J F, Wollert K C, Januzzi J L, Wang T J, Tofler G and Vasan R S 2014 Ideal cardiovascular health: associations with biomarkers and subclinical disease and impact on incidence of cardiovascular disease in the Framingham Offspring Study *Circulation* **130** 1676-83

[3] Xanthakis V, Sullivan L M, Vasan R S, Benjamin E J, Massaro J M, D'Agostino R B, Sr. and Pencina M J 2014 Assessing the incremental predictive performance of novel biomarkers over standard predictors *Stat Med* **33** 2577-84

[4] Koivistoinen T, Virtanen M, Hutri-Kahonen N, Lehtimaki T, Jula A, Juonala M, Moilanen L, Aatola H, Hyttinen J, Viikari J S, Raitakari O T and Kahonen M 2012 Arterial pulse wave velocity in relation to carotid intima-media thickness, brachial flow-mediated dilation and carotid artery distensibility: the Cardiovascular Risk in Young Finns Study and the Health 2000 Survey *Atherosclerosis* **220** 387-93

[5] Mutlu B, Tigen K, Gurel E, Ozben B, Karaahmet T and Basaran Y 2011 The predictive value of flow-mediated dilation and carotid artery intima-media thickness for occult coronary artery disease *Echocardiography* **28** 1141-7

[6] Nagai K, Shibata S, Akishita M, Sudoh N, Obara T, Toba K and Kozaki K 2013 Efficacy of combined use of three non-invasive atherosclerosis tests to predict vascular events in the elderly; carotid intima-media thickness, flow-mediated dilation of brachial artery and pulse wave velocity *Atherosclerosis* **231** 365-70

[7] Reneman R S, van Merode T, Hick P, Muytjens A M and Hoeks A P 1986 Age-related changes in carotid artery wall properties in men *Ultrasound Med Biol* **12** 465-71

[8] Makris G C, Nicolaides A N, Xu X Y and Geroulakos G 2010 Introduction to the biomechanics of carotid plaque pathogenesis and rupture: review of the clinical evidence *Br J Radiol* **83** 729-35

[9] Graf S, Gariepy J, Massonneau M, Armentano R L, Mansour S, Barra J G, Simon A and Levenson J 1999 Experimental and clinical validation of arterial diameter waveform and intimal media thickness obtained from B-mode ultrasound image processing *Ultrasound Med Biol* **25** 1353-63

[10] Pascaner A F, Craiem D, Casciaro M E, Danielo R, Graf S and Guevara E 2015 Continuous assessment of carotid intima-media thickness applied to estimate a volumetric compliance using B-mode ultrasound sequences *Physiol Meas* **36** 397-407

[11] Haller C, Schulz J, Schmidt-Trucksass A, Burkardt H, Schmitz D, Dickhuth H H and Sandrock M 2007 Sequential based analysis of Intima-Media Thickness (IMT) in common carotid artery studies *Atherosclerosis* **195** e203-9

[12] Armentano R L and Cabrera Fischer E I 1994 Biomecánica arterial. Fundamentos para su abordaje en la clínica médica

[13] Nichols W W and O'Rourke M F 1998 McDonald's Blood flow in arteries. Theoretical, experimental and clinical principles

[14] Jourdan C, Wuhl E, Litwin M, Fahr K, Trelewicz J, Jobs K, Schenk J P, Grenda R, Mehls O, Troger J and Schaefer F 2005 Normative values for intima-media thickness and distensibility of large arteries in healthy adolescents *J Hypertens* **23** 1707-15

[15] Meinders J M and Hoeks A P 2004 Simultaneous assessment of diameter and pressure waveforms in the carotid artery *Ultrasound Med Biol* **30** 147-54