



*Dossier de presse*

*Press book*

## **French Core Laboratory IMT Commercializes Cardio Ultrasound Software**

**March 04, 2009**

by **Kathy Mahdoubi**, Editorial Coordinator

As a result of extensive involvement in clinical trials, Paris-based Intelligence in Medical Technologies, or IMT, has developed cardio ultrasound software that measures intima-media thickness and other risk factors for cardiovascular disease.

For more than 10 years, IMT has taken part in large, prospective and cross-sectional drug studies, many focused on the epidemiology and treatment of atherosclerosis in superficial blood vessels. These studies present compiled data from at least 25,000 participants and 600 medical centers in 50 different countries.

Founder Dr. Pierre-Jean Touboul applied the computing techniques developed during clinical trials to IMT's flagship cardio ultrasound software product, M'Ath, which stands for measurement of atherosclerosis. Touboul is well published in the medical community and has more than 25 years of experience with cardiovascular disease and imaging, says Aurelia Puech-Bournonville, study project manager at IMT.

"There are two faces to the company," Puech-Bournonville tells DOTmed News. "One is for the software and its development and the other is for central reading and clinical studies."

Touboul started working on a prototype for the software about sixteen years ago and the business side of IMT was created in 2002. M'Ath now has 1,200 users on five continents, and because the technology is just emerging, there is tremendous room for expansion across Europe, South America, the Middle East and Asia, she says.

The technology is a non-invasive means of examining the first two layers of the carotid arteries. More than 50,000 carotid arteries have been measured in clinical trials using the M'Ath software.

"This software offers the capability to measure intima media thickness, plaque thickness, and density stenosis degree and distensibility using automated detection algorithms," Puech-Bournonville explains. "Flow-mediated vasodilation of the brachial artery can also be measured in real time."

### **A Growing Sense of Urgency**

Puech-Bournonville has watched the cardiovascular community shift from low interest in the measurement of intima-media thickness to a growing sense of urgency from facilities wanting to implement the technology.

"The measurement of IMT is really a new way of seeing things," says Puech-Bournonville. "The mentality has changed dramatically within the past three or four years. Now everybody wants our software."

M'Ath can run on any PC and plugs directly into the video output of any ultrasound device, including 3-D technologies, and it supports a variety of image formats and languages, says Puech-Bournonville. The software is independent and upgradeable, thereby preventing early obsolescence. IMT also sells the license in a turnkey workstation that comes with a high-performance laptop.

M'Ath is FDA approved and has received ISO 9001 certification and uses the CE mark. IMT organizes training for their software at their facilities in Paris, on site, or online. In addition, IMT has a development team currently working on IMT Live, which is designed for ultrasound image acquisition.

IMT is not the only producer of software that measures intima-media thickness in the field of ultrasonography.

"Other manufacturers have started to create similar technologies but they don't have the years of experience that we do," Puech-Bournonville says.

It appears to be a growing market for IMT. Slowing economies have not had too detrimental an effect on their bottom line. Puech-Bournonville attributes this to the affordability of the M'Ath software. Imaging centers spend several thousands of dollars for ultrasound equipment, whereas the software comes in packages for as low as 1,500 euros, she says.

Representatives of IMT are scheduled to attend the 2009 European Congress of Radiology (ECR) Conference in Vienna March 6 - 10.

# Mannheim Carotid Intima-Media Thickness Consensus (2004–2006)

**An Update on Behalf of the Advisory Board of the 3rd and 4th Watching the Risk Symposium 13th and 15th European Stroke Conferences, Mannheim, Germany, 2004, and Brussels, Belgium, 2006**

P.-J. Touboul M.G. Hennerici S. Meairs H. Adams P. Amarenco N. Bornstein L. Csiba  
M. Desvarieux S. Ebrahim M. Fatar R. Hernandez Hernandez M. Jaff S. Kownator  
P. Prati T. Rundek M. Sitzer U. Schminke J.-C. Tardif A. Taylor E. Vicaut K.S. Woo  
F. Zannad M. Zureik

## Key Words

Intima-media thickness · Consensus · Vascular ultrasound · Randomized clinical trials · Carotid diseases

## Abstract

Intima-media thickness (IMT) is increasingly used as a surrogate end point of vascular outcomes in clinical trials aimed at determining the success of interventions that lower risk factors for atherosclerosis and associated diseases (stroke, myocardial infarction and peripheral artery diseases). The necessity to promote further criteria to distinguish early atherosclerotic plaque formation from thickening of IMT and to standardize IMT measurements is expressed through this updated consensus. Plaque is defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value or demonstrates a thickness >1.5 mm as measured from the media-adventitia interface to the intima-lumen interface. Standard use of IMT measurements is based on physics, technical and disease-related principles as well as agreements on how to perform, interpret and document study results. Harmonization of carotid image acquisition and analysis is needed for the comparison of the IMT results obtained from epidemiological and interventional studies around the world. The consensus con-

cludes that there is no need to 'treat IMT values' nor to monitor IMT values in individual patients apart from exceptions named, which emphasize that inside randomized clinical trials should be performed. Although IMT has been suggested to represent an important risk marker, according to the current evidence it does not fulfill the characteristics of an accepted risk factor. Standardized methods recommended in this consensus statement will foster homogenous data collection and analysis. This will help to improve the power of randomized clinical trials incorporating IMT measurements and to facilitate the merging of large databases for meta-analyses.

Copyright © 2007 S. Karger AG, Basel

## Introduction

Decades of silent arterial wall alterations precede vascular clinical events, which then reflect advanced atherosclerotic disease. The first morphological abnormalities of arterial walls can be visualized by B-mode ultrasonography. This high-resolution, noninvasive technique is one of the best methods for the detection of early stages of atherosclerotic disease, because it is rapidly applicable, readily available and demonstrates the wall structure

# Design, Baseline Characteristics and Carotid Intima-Media Thickness Reproducibility in the PARC Study

P.J. Touboul<sup>a</sup> E. Vicaut<sup>b</sup> J. Labreuche<sup>a</sup> J.P. Belliard<sup>c</sup> S. Cohen<sup>d</sup>  
S. Kownator<sup>e</sup> I. Pithois-Merli<sup>f</sup> on behalf of the Paroi Artérielle et Risque  
Cardiovasculaire Study Investigators

<sup>a</sup>Department of Neurology and Stroke Center, Bichat Claude Bernard University Hospital and Medical School, Denis Diderot University Paris-VII, and <sup>b</sup>Clinical Research Unit, Fernand Widal Hospital, Paris, <sup>c</sup>Paris, <sup>d</sup>Marseille, <sup>e</sup>Thionville and <sup>f</sup>Pfizer, Paris, France

## Key Words

Intima-media thickness · Cardiovascular risk ·  
Ultrasound, artery wall

## Abstract

**Background:** Intima-media thickness (IMT) is associated with an increased risk of cardiovascular and cerebral ischemic events, but its correlation with the absolute cardiovascular risk is not known in large populations. The Paroi Artérielle et Risque Cardiovasculaire (PARC) Study is an epidemiological study designed to correlate conventional assessment of cardiovascular risk with the mean IMT of the common carotid. **Methods:** In the PARC study, 6,416 subjects were enrolled, including 80.7% subjects with cardiovascular risk factors and 19.3% without. A specific methodology was designed to harmonize the acquisition and processing of data at the 283 centers. Interreader agreement on image quality and IMT measurement of the common carotid artery (CCA-IMT) was assessed from a random sample of 10% of the PARC study population. **Results:** The intraclass correlation coefficient was 0.98 (95% CI 0.966–0.985), and the accuracy was high (standard deviation of the error measurement: 0.0185 mm). **Conclusions:** The reproducibility of

the measurements assessed by means of the intraclass correlation coefficient and the accuracy of the CCA-IMT measurement obtained in the PARC Study demonstrate the feasibility of large multicenter studies of IMT measurement.

Copyright © 2005 S. Karger AG, Basel

## Background

Ultrasound measurement of the thickness of the two inner layers (i.e. the intima and media) of the arterial wall was first correlated with anatomy [1] 20 years ago, thus bringing a new dimension to cardiovascular risk evaluation. The association between intima and media thickness (IMT) and cardiovascular risk factors was then demonstrated by several epidemiological studies [2–7]. One of the major advances to result from its introduction is based on its ability to detect early arterial disease in asymptomatic individuals. However, many studies conducted in different countries have shown that IMT values differ from one country to another, which could partly account for the limitations of conventional cardiovascular risk evaluation [8].

## KARGER

Fax +41 61 306 12 34  
E-Mail [karger@karger.ch](mailto:karger@karger.ch)  
[www.karger.com](http://www.karger.com)

© 2005 S. Karger AG, Basel  
1015-9770/05/0191-0057\$22.00/0

Accessible online at:  
[www.karger.com/ced](http://www.karger.com/ced)

Pierre-Jean Touboul  
Hôpital Bichat, Service du Prof. Amarenco  
46, rue Raymond-Huchard  
FR-75018 Paris (France)  
Tel. +33 6 87 84 78 49, Fax +33 1 40 61 01 62, E-Mail [pjt@noos.fr](mailto:pjt@noos.fr)

## Carotid artery intima media thickness, plaque and framingham cardiovascular score in Asia, Africa/Middle East and Latin America: the PARC-AALA Study

Pierre-Jean Touboul · Rafael Hernández-Hernández · Serdar Küçüköglü · Kam-Sang Woo · Eric Vicaut · Julien Labreuche · Chris Migom · Honorio Silva · Raul Vinueza · for the PARC-AALA Investigators

Received: 31 August 2006 / Accepted: 14 November 2006  
© Springer Science+Business Media B.V. 2006

### Abstract

**Objective** The PARC-AALA (Paroi artérielle et Risque Cardiovasculaire in Asia Africa/ Middle East and Latin America) study was designed to evaluate the correlation between intima-media thickness of the common carotid artery (CCA-IMT), carotid plaque and absolute cardiovascular risk in a multi-ethnic population.

**Methods** An international, cross-sectional, study including 79 centres from 21 countries in Asia, Africa, the Middle East and Latin America. Two thousand three hundred and twenty-eight subjects, meeting all inclusion criteria, were stratified by risk factors groups (no modifiable factor or at least both uncontrolled hypertension and hypercholesterolemia). CCA-IMT, presence of plaque and cardiovascular risk factors were assessed for each individual.

**Results** Some intergeographical characteristics in demographics, and risk factors were found accompanying early atherosclerosis marker differences. In Asia where the subjects were at lower risk, the mean CCA-IMT was 4% lower than in Africa/ Middle East and Latin America. On multiple linear regression analysis CCA-IMT and carotid plaque were independently associated with increased Framingham cardiovascular score (FCS) without heterogeneity across geographic regions. CCA-IMT and carotid plaque explained roughly 20% of the FCS in both genders.

**Conclusion** The PARC-AALA study confirms the correlation between CCA-IMT and FCS in three different populations. Intima-media thickness (IMT) and plaque evaluation may represent a complementary predictive tool for detection of cardiovascular disease in individuals.

This work was supported by Pfizer Inc., New York, USA.

P.-J. Touboul (✉) · J. Labreuche  
Department of Neurology and Stroke Centre, Denis Diderot University-Paris VII., 48 Rue R Huchard, Paris 75018, France  
e-mail: pjtw@noos.fr

R. Hernández-Hernández  
Clinical Pharmacology Unit, School of Medicine, Universidad Centroccidental, Barquisimeto, Venezuela

S. Küçüköglü  
Istanbul University Institute of Cardiology, Istanbul, Turkey

K.-S. Woo  
Prince of Wales Hospital, Hong Kong, P.R. China

E. Vicaut  
Lariboisière Hospital, Paris, France

C. Migom · H. Silva · R. Vinueza  
Pfizer Inc., New York, USA

**Keywords** Carotid plaque · Framingham score · Hypercholesterolemia · Hypertension · Intima media thickness · Ultrasound

# Plasma Homocysteine Levels and Parkinson Disease: Disease Progression, Carotid Intima-media Thickness and Neuropsychiatric Complications

Sharon Hassin-Baer, MD,\*† Oren Cohen, MD,\*† Eli Vakil, PhD,||  
Ben-Ami Sela, PhD,‡ Zeev Nitsan, MD,\* Roseline Schwartz, MSc,\*  
Joab Chapman, MD, PhD,\* and David Tanne, MD,\*§

## Abstract

### Objective:

To determine whether plasma homocysteine (Hcy) levels are associated with clinical characteristics, neuropsychological and psychiatric manifestations and cardiovascular comorbidity in patients with Parkinson disease (PD).

### Background:

Elevated Hcy levels are linked to atherosclerosis, vascular disease, depression, and dementia. Patients with PD treated with L-dopa have been shown to have elevated Hcy levels.

### Design/Methods:

Idiopathic PD patients were evaluated using the Unified Parkinson's Disease Rating Scale, Hoehn and Yahr stage, Parkinson Psychosis Rating Scale, Beck Depression Inventory, Frontal Assessment Battery, Mini-Mental Status Examination, and several tests for frontal type cognitive functions. Fasting blood samples were collected for the measurement of Hcy, and carotid B-mode ultrasound was performed to measure intima-media thickness of the common carotid arteries.

### Results:

Seventy-two consecutive PD patients (46 men; average age,  $68.7 \pm 11.6$  years; average disease duration,  $7.0 \pm 4.7$  years) were recruited. All but 10 patients were treated with L-dopa. The average level of Hcy was  $16.4 \pm 7.8$   $\mu\text{mol/L}$ , and 38.9% of the patients had Hcy level above the reference range ( $>15.0$   $\mu\text{mol/L}$ ). The Hcy levels were associated with PD duration as they were with L-dopa treatment duration but were not associated with the parameters of disease severity or with L-dopa dose. The Hcy levels were associated neither with the common carotid intima-media thickness nor with cardiovascular morbidity. No association was found between Hcy and the neuropsychiatric features of PD such as depression, cognitive performance, or psychosis.

### Conclusions:

Hyperhomocystinemia is common in L-dopa-treated PD patients but was not associated with neuropsychological complications (depression, dementia, and cognitive decline associated with frontal lobe functioning or psychosis), enhanced disease severity, or vascular comorbidity.

**Key Words:** Parkinson disease, neuropsychiatric complications, homocysteine

(*Clin Neuropharmacol* 2006;29:305–311)

Nonmotor complications in Parkinson disease (PD) become increasingly important as disease progresses. Among them are cognitive decline, dementia, depression, and psychosis.<sup>1,2</sup> Their pathogenesis in PD is multifactorial. Elevated levels of homocysteine (Hcy), a sulfur-containing amino acid that occupies a central location in the metabolic pathways of thiol compounds, were shown in epidemiological and experimental studies to be linked with several conditions associated with vascular pathology including coronary artery disease, vascular dementia, and ischemic stroke.<sup>3–5</sup> Neurodegenerative processes have also been linked to elevated Hcy, including cognitive decline and Alzheimer disease.<sup>6–9</sup> Moreover, genetic and clinical data suggest roles for folate deficiency and Hcy in the pathogenesis of some psychiatric disorders such as depression and schizophrenia.<sup>10,11</sup>

Plasma Hcy levels are elevated in patients with PD treated with L-dopa,<sup>12–16</sup>

\*Department of Neurology and †Parkinson's Disease and Movement Disorders Clinic, Sagol Neuroscience Center, ‡Department of Chemical Pathology and §Stroke Center, Chaim Sheba Medical Center, Tel Hashomer, Affiliated to Sackler School of Medicine, Tel Aviv University, Israel and ||Department of Psychology, Bar Ilan University, Ramat-Gan, Israel.

Address correspondence and reprint requests to Sharon Hassin-Baer, MD, Department of Neurology and Parkinson's Disease and Movement Disorders Clinic, Chaim Sheba Medical Center, Tel Hashomer, 52621, Israel; E-mail: shassin@post.tau.ac.il

Copyright © 2006 by Lippincott Williams & Wilkins

DOI: 10.1097/01.WNF.0000236763.16032.60

# Carotid intima-media thickness by B-mode ultrasound as surrogate of coronary atherosclerosis: correlation with quantitative coronary angiography and coronary intravascular ultrasound findings

Mauro Amato<sup>1</sup>, Piero Montorsi<sup>1,2</sup>, Alessio Ravani<sup>1</sup>, Elisa Oldani<sup>1</sup>, Stefano Galli<sup>1,2</sup>, Paolo M. Ravagnani<sup>1,2</sup>, Elena Tremoli<sup>1,3</sup>, and Damiano Baldassarre<sup>1,3\*</sup>

<sup>1</sup>Centro Cardiologico Monzino, IRCCS, Via Parea 4, 20138 Milan, Italy; <sup>2</sup>Institute of Cardiology, School of Medicine, University of Milan, Milan, Italy; and <sup>3</sup>Department of Pharmacological Sciences, University of Milan, Via Balzaretti 9, 20133 Milan, Italy

Received 6 February 2007; revised 4 May 2007; accepted 22 May 2007; online publish-ahead-of-print 27 June 2007

See page 2049 for the editorial comment on this article (doi:10.1093/eurheartj/ehm320)

## KEYWORDS

Angiography;  
IVUS;  
Ultrasound;  
Carotid;  
Coronary

**Aims** Although well supported by postmortem studies, the reliability of carotid atherosclerosis as surrogate marker of coronary atherosclerosis has been put in doubt by *in vivo* studies showing a poor correlation between carotid intima-media thickness (IMT) detected by external carotid ultrasound (ECU) and coronary stenosis assessed by quantitative coronary angiography (QCA). In the present study, we have investigated whether a stronger *in vivo* correlation between the two arteries can be obtained by using homogeneous variables such as carotid and coronary IMT, detected by ECU and intravascular ultrasound (IVUS), respectively.

**Methods and results** ECU, QCA, and IVUS measurements were made in 48 patients. Carotid IMT was correlated with both angiographic and IVUS findings. A significant but weak correlation was observed between ECU and QCA variables ( $r \approx 0.35$ ,  $P < 0.05$ ); the correlation between ECU and IVUS measurements of IMT was higher, with correlation coefficients ranging from 0.49 to 0.55. In patients with a QCA diagnosis of normal/intermediate coronary atherosclerosis, the presence of a carotid- $IMT_{mean} > 1$  mm was associated with an 18-fold increase in risk of having a positive IVUS test (OR = 17.99, 95% CI 1.83–177.14,  $P = 0.013$ ) and with a seven-fold increased risk of having a significant IVUS coronary stenosis (OR = 7.4, 95% CI 1.27–44.0,  $P = 0.028$ ).

**Conclusion** Carotid atherosclerosis correlates better with coronary atherosclerosis when both circulations are investigated by the same technique (ultrasound) using the same parameter (IMT). This supports the concept that carotid IMT is a good surrogate marker of coronary atherosclerosis.

## Introduction

High resolution B-mode ultrasound is a non-invasive technique widely used to assess atherosclerosis in superficial arteries. It allows the accurate measurement of the distance between blood-intima and media-adventitia interfaces of the carotid wall, which is defined as carotid intima-media thickness (IMT).<sup>1</sup> Several authors have suggested that carotid IMT is a marker of atherosclerosis in other vascular beds.<sup>2–4</sup> Indeed, an increased carotid IMT has been associated with a number of atherosclerosis risk factors,<sup>5–7</sup> with the prevalence and extent of coronary artery disease (CAD)<sup>8,9</sup> and with the incidence of new coronary and cerebral events.<sup>4,10</sup> In view of these relationships, carotid IMT has been proposed as a surrogate endpoint to be

used in clinical trials as an alternative to coronary atherosclerosis.<sup>11</sup>

In spite of the widespread use of carotid IMT as a surrogate for CAD, validation studies evaluating the correlation between carotid IMT measured by external carotid ultrasound (ECU) and CAD measured by quantitative coronary angiography (QCA) showed a relatively poor correlation ( $r < 0.36$  on average).<sup>12–20</sup> This finding has cast doubt on the reliability of carotid atherosclerosis as a surrogate marker of coronary atherosclerosis. Postmortem studies, however, have shown a far greater degree of correlation between the two arterial districts,<sup>21–24</sup> which suggests that the poor correlation observed in ECU vs. QCA studies may be due more to technical issues than to differential effects of the traditional vascular risk factors on the carotid and coronary tissues.

Intravascular ultrasound (IVUS) is a unique imaging modality for the direct examination of vessel dimensions

\* Corresponding author. Tel: +39 02 58002253; fax: +39 02 58002623.  
E-mail address: damiano.baldassarre@unimi.it

# Intima-Media Thickness

## A Marker of Accelerated Atherosclerosis in Women with Systemic Lupus Erythematosus

BARBARA MARIA COLOMBO,<sup>a</sup> GIUSEPPE MURDACA,<sup>a</sup>  
MATTEO CAITI,<sup>a</sup> GUIDO RODRIGUEZ,<sup>b</sup> LIDIA GRASSIA,<sup>c</sup>  
EDORADO ROSSI,<sup>c</sup> FRANCESCO INDIVERI,<sup>a</sup> AND FRANCESCO PUPPO<sup>a</sup>

<sup>a</sup>Department of Internal Medicine, University of Genova, Genova, Italy

<sup>b</sup>Department of Clinical Neurophysiology, University of Genova, Genova, Italy

<sup>c</sup>Department of Haematology, San Martino Hospital, Genova, Italy

**ABSTRACT:** Accelerated atherosclerosis is an emerging problem in patients with systemic lupus erythematosus (SLE). We planned an observational study to determine whether in patients with SLE carotid intima-media thickness (IMT) represents an early sign of accelerated atherosclerosis and to confirm that SLE adds to the traditional cardiovascular Framingham risk factors. Thirty females with SLE (age 18–65 years) underwent anamnestic, clinical, and laboratory evaluation and B-mode ultrasonography of carotid arteries, which provides a direct and noninvasive assessment of subclinical atherosclerosis. IMT measurements were performed on the right and left common carotid arteries 1.0 cm proximal to the carotid bulb and the mean IMT value was calculated with a dedicated software. The Framingham Point Score was also calculated for each subject. SLE patients showed a mean IMT value of  $0.73 \pm 0.12$  (SD) mm. This value is significantly ( $P < 0.05$ ) higher than that reported for an age-matched healthy female control population ( $0.66 \pm 0.11$  SD mm). A preliminary evaluation of the Framingham Point Score, estimating the 10-year risk for women to develop cardiovascular events, indicated an increased risk of early cardiovascular events in SLE patients. In our study we have shown that patients with SLE have an increased mean IMT value compared with a healthy females control. Moreover, the evaluation of the Framingham Point Score suggests that SLE is an additional risk factor for cardiovascular disease.

**KEYWORDS:** systemic lupus erythematosus; SLE; accelerated atherosclerosis; intima-media thickness; IMT; Framingham Point Score

Address for correspondence: Barbara Maria Colombo, Dipartimento di Medicina Interna (Di.M.I.), Viale Benedetto XV, 6, 16132 Genova, Italy. Voice: +390103538691; fax: +390103537573. [bmcolombo@libero.it](mailto:bmcolombo@libero.it)

Ann. N.Y. Acad. Sci. 1108: 121–126 (2007). © 2007 New York Academy of Sciences.  
doi: 10.1196/annals.1422.014



# Variation in non-invasive measurements of vascular function in healthy volunteers during daytime

Ewoud TER AVEST\*, Suzanne HOLEWIJN†, Anton F. H. STALENHOEF\* and Jacqueline DE GRAAF\*

\*Department of Medicine, Division of General Internal Medicine, University Medical Center, Nijmegen, The Netherlands, and †Vascular Laboratory, University Medical Center, Nijmegen, The Netherlands

## A B S T R A C T

Although it is often recommended to standardize the time of day when performing non-invasive measurements of vascular function, the exact influence of the time of day on the outcome of IMT (intima-media thickness), PWV (pulse wave velocity), AIX (augmentation index) and FMD (flow-mediated dilatation) measurements has not been reported before. Nineteen healthy volunteers visited our department on two different occasions: the first visit was at 09:00 hours after an overnight fast, and the second visit was at 14:00 hours after a standardized breakfast. Non-invasive measurements of atherosclerosis were performed twice at 09:00 hours and once on the second visit at 14:00 hours. Measurement of IMT, PWV, AIX and FMD was reproducible according to the method of Bland and Altman. The absolute difference between repeated measurements at 09:00 hours showed no significant difference compared with the absolute difference between 09:00 and 14:00 hours for IMT ( $0.029 \pm 0.014$  compared with  $0.021 \pm 0.014$  mm;  $P = 0.27$ ), PWV ( $0.63 \pm 0.50$  compared with  $0.75 \pm 0.74$  m/s;  $P = 0.52$ ), AIX ( $4.0 \pm 4.0$  compared with  $5.5 \pm 5.2\%$ ;  $P = 0.35$ ) and FMD ( $3.8 \pm 3.7$  compared with  $4.2 \pm 2.9\%$ ;  $P = 0.70$ ). In conclusion, our results show that, in healthy volunteers during the daytime, IMT, PWV, AIX and FMD outcomes are not confounded by variation in the exact time of the examination as long as other (exogenous) conditions, including food intake, smoking and intake of alcohol, are carefully controlled for.

## INTRODUCTION

Atherosclerosis is known to be a gradual process which can be measured with a variety of non-invasive techniques, each of which quantifies a different stage in the atherosclerotic process. Early functional changes can be quantified by FMD (flow-mediated dilatation), AIX (augmentation index) and PWV (pulse wave velocity), whereas IMT (intima-media thickness) and ABI (ankle-brachial blood pressure index) measurements can be used to quantify later and more structural changes in the arterial wall. As NIMA (non-invasive measurements of

atherosclerosis) become more and more important in clinical practice to evaluate the risk of CHD (coronary heart disease) and the effect of treatment, reliable and reproducible tests should be available, preferably during the course of the whole day for practical reasons.

It is recommended by International Task forces [1,2] to standardize patient conditions when performing NIMA, since there is abundant evidence that various exogenous variables, including smoking [3,4], vitamin intake [5,6], alcohol intake [7,8], use of oral contraceptives [9] and food intake [10–12], affect the outcome of PWV, AIX and FMD measurements. It is also often recommended

**Key words:** augmentation index, diurnal variation, flow-mediated dilatation, intima-media thickness, pulse wave velocity.

**Abbreviations:** ABI, ankle-brachial blood pressure index; AIX, augmentation index; CHD, coronary heart disease; FMD, flow-mediated dilatation; IMT, intima-media thickness; NIMA, non-invasive measurements of atherosclerosis; PWV, pulse wave velocity.

**Correspondence:** Dr Ewoud ter Avest (email E.teravest@aig.umcn.nl).

# Individual Measurement and Significance of Carotid Intima, Media, and Intima–Media Thickness by B-Mode Ultrasonographic Image Processing

Jang-Ho Bae, Wuon-Shik Kim, Charanjit S. Rihal, Amir Lerman

**Objective**—We assessed the clinical significance of intima (IT), media (MT), and intima–media (IMT) thickness of the common carotid artery using B-mode ultrasonographic image processing.

**Methods and Results**—One hundred seventy consecutive patients underwent common carotid artery scanning using high-resolution ultrasonography. A total of 150 patients could be analyzed off-line using ultrasonographic image processing, devised for individual measurement of IT, MT, and IMT. By univariate analysis, IT (range, 0.27 to 0.41 mm) was associated with age, whereas MT (range, 0.27 to 0.74 mm) and IMT (range, 0.49 to 1.12 mm) were associated with age, fibrinogen, and creatinine. Among atherosclerosis risk factors, hypertension was associated with thickness of all 3 layers, whereas smoking was associated with IT only. By multivariate analysis, IT was associated with age, hypertension, and smoking, whereas MT and IMT were associated with age, hypertension, and blood urea nitrogen level.

**Conclusions**—Carotid IT is associated with smoking, whereas age and hypertension are associated with thickness of all 3 arterial layers. Our results suggest a differential response of the vasculature to systemic risk factors. (*Arterioscler Thromb Vasc Biol.* 2006;26:2380-2385.)

**Key Words:** carotid arteries ■ atherosclerosis ■ risk factors ■ arterial intima ■ arterial media

Carotid artery intima–media thickness (IMT), which is the sum of the intima (IT) and media (MT) thickness, is independently associated with atherosclerotic risk factors and adverse cardiovascular events.<sup>1–4</sup> Therefore, it has been used as an important atherosclerosis surrogate in clinical practice and in many clinical studies since Pignoli et al introduced the direct measurement of carotid IMT with ultrasound.<sup>5</sup>

Abnormal neointima formation is the main pathophysiological consequence of obliterative vascular disease, although atherosclerotic changes may also include smooth muscle proliferation and inflammatory processes in the media and adventitia.<sup>6,7</sup> Therefore, we hypothesized that the intima and media have different clinical responses and roles to cardiovascular risk factor exposure and the development and pathophysiology of atherosclerosis.

We aimed to evaluate the response of the intimal and medial layers of the common carotid artery (CCA) to atherosclerosis risk factors, in terms of thickness of the layers, as assessed by high-resolution ultrasonography with an automated image-processing algorithm.

## Methods

### Study Population

One hundred seventy consecutive patients referred for ischemic heart disease screening were studied. Patients were included in this study if they provided informed consent and did not meet any of the following exclusion criteria: history of neck irradiation, carotid arterial surgery, previous dissection of the aorta or carotid artery, or cervical trauma. Twenty of the 170 patients (11.8%) enrolled were excluded from analysis because of poor delineation of the borders between the intima and media layers. This study was approved by the ethics committee of Konyang University Hospital and conducted in accordance with the Declaration of Helsinki. Patient laboratory data collected within 2 weeks of enrollment included a lipid profile and measurement of blood glucose, homocysteine, and fibrinogen levels.

### Carotid Artery Scanning

The CCA was studied with high-resolution ultrasonography (Hewlett-Packard Sonos 5500) with a broadband (11 to 3 L) linear array transducer (Figure 1). Carotid arterial scanning was performed by a certified, blinded sonographer in a dark, air-conditioned room. The far wall of the right CCA was scanned longitudinally while the patient was in the supine position with head extended. To optimize the image quality, the depth control was fixed at 4 cm. The transducer frequency was set to 11 MHz during the entire analysis.

Original received April 26, 2006; final version accepted July 25, 2006.

From the Division of Cardiology (J.-H.B.), Konyang University Hospital, Daejeon, South Korea; Bio-signal Research Laboratory (W.-S.K.), Korea Research Institute of Standards and Science, Daejeon, South Korea; and the Division of Cardiovascular Diseases (C.S.R., A.L.), Mayo Clinic, Rochester, Minn.

J.-H.B. and W.-S.K. contributed equally to this work.

Correspondence to Jang-Ho Bae, MD, Division of Cardiology, Konyang University Hospital, 685 Gasowon-dong, Seo-gu, Daejeon, South Korea. E-mail janghobae@yahoo.co.kr.

© 2006 American Heart Association, Inc.

*Arterioscler Thromb Vasc Biol.* is available at <http://www.atvbaha.org>

DOI: 10.1161/01.ATV.0000240420.36229.f9

## A study Influence of atherosclerosis risk factors on carotid artery wall thickness

W.-S. Kim<sup>1</sup>, J.-H. Bae<sup>2</sup>, H.-T. Jeong<sup>3</sup>, G.-Y. Noh<sup>1</sup>, H.-M. Choi<sup>1</sup>, Y. K. Park<sup>1</sup>, J. H. Hwang<sup>4</sup>

<sup>1</sup>Bio-signal Research Lab., Korea Research Institute of Standards and Science, Daejeon, Korea

<sup>2</sup>Division of Cardiology, Konyang University Hospital, Daejeon, Korea

<sup>3</sup>Department of Biomedical Engineering, Chungnam National University, Daejeon, Korea

<sup>4</sup>Department of Electronic Engineering, Hanbat National University, Daejeon, Korea

**Abstract**— The severity of carotid intima-media thickness (IMT), which is the sum of intima thickness (IT) and media thickness (MT), is an independent predictor of transient cerebral ischemia, stroke, and coronary events such as myocardial infarction. Evaluation of carotid IMT using ultrasonography is a validated quantitative method for assessing atherosclerosis, which is closely correlated with pathological findings observed in the carotid artery. However, the individual clinical significance of each layer of carotid artery has not been well studied. We intended to measure the IT, MT, and the IMT of carotid artery separately and tried to analyze the clinical significance. Two hundred and fifty consecutive patients (125 males, 125 females) underwent carotid artery scanning using high-resolution ultrasound. The images were off-line analyzed using B-mode ultrasound image processing, devised in our research. We measured the IT, MT, and IMT semi-automatically at the far wall of designated 1cm length of the right common carotid and calculated the average values over the 200 points. The IT ( $p < 0.05$ ), MT ( $p < 0.05$ ) as well as IMT ( $p < 0.01$ ) of patients with atherosclerotic disease were significantly thicker than that of the patients without atherosclerotic disease. Patients with hypertension showed significantly thicker IT ( $p < 0.05$ ), MT ( $p < 0.01$ ), and IMT ( $p < 0.01$ ) than that of the patients without hypertension. However, only IT was thicker in patients with smoking ( $p < 0.05$ ) than that of the patients without smoking. Smoking was associated only with intima while hypertension was associated with the all three layer's thickness. This result suggests the atherosclerotic process can be different by cardiovascular risk factors. Therefore, clinical study with specific risk factors such as hypertension or smoking as in our study needs to focus on specific layer of vessel wall. **Key words:** Carotid artery, Intima thickness (IT), Media thickness (MT), Intima-media thickness (IMT), Ultrasound

**Keywords**— Carotid artery, Intima thickness (IT), Media thickness (MT), Intima-media thickness (IMT), Ultrasound

### I. INTRODUCTION

Evaluation of carotid intima media wall thickness (IMT) using ultrasonography is a validated quantitative method for assessing atherosclerosis [1], that is closely correlated with pathological findings observed in the carotid artery [2]. Moreover, the appearance of atherosclerosis in the carotid

artery has been highly associated with atherosclerosis in the aorta and the incidence of coronary heart disease [3]. Therefore, the severity of carotid IMT is an independent predictor of transient cerebral ischemia, stroke, and coronary events such as myocardial infarction [4]. Carotid IMT consists of intima thickness (IT) and media thickness (MT). Arterial intima layer is the innermost coat of blood vessels, consisting of a thin lining of endothelial cells oriented longitudinally and arterial media layer is the middle coat of blood vessel walls, composed principally of thin cylindrical smooth muscle cells and elastic tissue, accounting for the bulk of the wall of most arteries. Abnormal neointima formation is the main pathophysiology of obliterative vascular disease, although atherosclerotic changes of vessel wall also includes smooth muscle proliferation and inflammatory process in media and adventitia. We hypothesized that IT and MT have a different clinical significance with regards to development and pathophysiology of atherosclerosis.

However, most studies used carotid IMT as a surrogate marker rather than separate measurement of IT and MT due to probably technical problems. It defines carotid IMT as the distance between the luminal border of the intima and the outer border of the media using high-resolution ultrasound. The border of intima layer can be identified as the first echogenic line from the lumen and the outer border of media layer as the second echolucent line in the high-resolution ultrasound. The measurement of carotid IMT is getting more precise by semiautomatic measurement rather than manual measurement [5]. And these semiautomatic measurements of carotid IMT give us more reliability in understanding many clinical studies as well as more important clinical significance about that. The neointima is developed by a migration, proliferation, and accumulation of vascular smooth muscle cells in the intima [6]. Medial thickness relates statistically to necrosis indirectly through associations with foam cells and fibroplasia.

We performed this study to evaluate the individual clinical significance of the intima layer and the media layer of the common carotid artery (CCA) by individual measurement using high-resolution ultrasound and newly devised image processing algorithm.

# Lack of difference in the intimal medial thickness between the left and right carotid arteries in the young

Arbel Y, Maharshak N, Gal-Oz A, Shapira I, Berliner S, Bornstein NM. Lack of difference in the intimal medial thickness between the left and right carotid arteries in the young.

Acta Neurol Scand 2007; 115: 409–412.

© 2007 The Authors Journal compilation © 2007 Blackwell Munksgaard.

**Background** – Carotid intimal medial thickening (c-IMT) is an established surrogate marker for atherosclerosis. There have been sporadic reports about an increase of c-IMT on the left carotid artery among populations with a mean age of  $\pm 50$  years. **Objective** – The purpose of this study was to evaluate whether there is a difference in c-IMT between the two carotid arteries in a group of young healthy adults. **Methods** – Ninety-eight healthy adults with a mean age of 28 years underwent blood tests to evaluate various cardiovascular risk factors as well as automated ultrasonic measurements of their c-IMT on both carotid arteries. **Results** – No significant difference was noted between c-IMT on both sides. In fact, the c-IMT on left carotid artery in men ( $n = 52$ ) was  $0.625 \pm 0.078$  mm while on the right carotid it was  $0.626 \pm 0.075$  mm ( $P = 0.884$ ). The values for women ( $n = 46$ ) were  $0.615 \pm 0.059$  mm and for men  $0.622 \pm 0.0618$  mm ( $P = 0.582$ ), respectively. **Conclusion** – As opposed to a noted increase of c-IMT on the left carotid artery in older individuals, we did not find this difference in a group of young and relatively healthy adults. It is possible that if mechanical stress forces contribute to an enhanced left c-IMT, it takes a relatively long time to become evident.

**Y. Arbel<sup>1\*</sup>, N. Maharshak<sup>1\*</sup>,  
A. Gal-Oz<sup>1</sup>, I. Shapira<sup>1</sup>,  
S. Berliner<sup>1</sup>, N. M. Bornstein<sup>2</sup>**

Departments of <sup>1</sup>Medicine D and <sup>2</sup>Neurology, Tel Aviv Sourasky Medical Center, Sackler Faculty of Medicine Tel Aviv University, Tel Aviv, Israel

Key words: carotid intimal media thickness; atherosclerosis; young; ultrasound

Itzhak Shapira, Tel-Aviv Sourasky Medical Center, 6 Weizman Street, Tel Aviv 64239, Israel.  
Tel.: + 972 3 6974254  
Fax: + 972 3 6973635  
e-mail: shapiraiz@tasmc.health.gov.il

\*These authors contributed equally to this work.

Accepted for publication 22 January 2007

## Introduction

It has been repeatedly shown that the measurement of the carotid intimal medial thickness (c-IMT) is a surrogate marker for an atherosclerotic disease (1–4). It is measured in both common carotid arteries (CCA) and expressed as the mean value obtained from these measurements (5). Yet it is not entirely clear whether the c-IMT is equal in both carotid arteries as several studies have shown a predilection for an increase of c-IMT in the left CCA. A putative explanation has been raised, namely that increased shear stress forces in the left carotid artery contribute to this inequality.

Acceptance of a different shear stress between the carotid arteries as a contributing factor would suggest that this difference be apparent from the beginning of the atherosclerotic process. However,

most studies in the past were performed in individuals at the age of 50 years or more, thus excluding the possibility to reveal the differences at an earlier stage of the disease.

We have presently embarked on a study that measured the c-IMT in a group of young adults. The findings are relevant for the understanding of potential mechanisms that underlie the development of increase of c-IMT at a relatively early stage of the disease.

## Patients and methods

We have presently recruited apparently healthy volunteers, members of the medical staff of the Tel Aviv Sourasky Medical Center in Tel Aviv Israel. A written informed consent was obtained according to the instructions of the local ethics commit-

tee. An inclusion criterion was a healthy adult with no known illnesses and between 20 and 40 years of age. We excluded individuals who presented with any infectious/inflammatory condition during the two weeks before enrollment. In addition, pregnant women and women during menstruation were excluded. One patient was excluded because he had evident plaques on both carotids.

In order to evaluate how healthy our cohort was, we compared them to individuals who were evaluated at the Tel Aviv Medical Center Inflammation Survey (TAMCIS) (6, 7). TAMCIS is a survey of apparently healthy individuals that is currently taking place at our medical center and includes a relatively large cohort of individuals attending the Tel Aviv Sourasky Medical Center for a routine health examination. We included all eligible patients from the TAMCIS cohort between the ages of 20 and 40. We excluded patients by the same criteria used on the study cohort.

Carotid artery atherosclerosis was determined by ultrasonographic measurement of the c-IMT of the CCA 1.5–3 cm proximal to the carotid artery bifurcation of the left and right sides. c-IMT was measured at the far wall of the carotid artery, on a 10-mm segment and was defined as the distance from the leading edge of the lumen–intima interface to the leading edge of the media–adventitia interface of the far wall (8). A computer software (M'ATH software) was used to calculate IMT by averaging 80–100 different samples of the examined carotid segment. The IMT value of each side represents an average of all the samples measured by the computer program.

Ultrasonographic scanning was performed by a single experienced sonography technician, blinded to the clinical data, who scanned the left and right CCAs using carotid duplex equipment (128XP/10, Acuson; Siemens, Erlangen, Germany) with a 7 MHz linear array transducer.

Venous blood was drawn from all the volunteers following a fasting period of 12 h and was analyzed for total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, and glucose by using routine methods of the medical center biochemistry laboratory. The erythrocyte sedimentation rate (ESR) was measured by the method of Westergren (9), quantitative fibrinogen by the method of Clauss (10) and a Sysmex 6000 (Sysmex Corporation, Hyaga, Japan) autoanalyzer, while the high-sensitivity C-reactive protein (hs-CRP) was performed by using a Boering BN II Nephelometer (DADE Boering, Marburg, Germany) (11).

#### Statistical analysis

All data were summarized and displayed as the mean  $\pm$  SD for the continuous variables [age, body mass index (BMI), inflammation markers, etc.], and as the number of patients in each group for categorical variables (smokers). The hs-CRP has a non-normal distribution, and thus we used a logarithmic transformation that converts it to a normal distribution for all statistical procedures such as *t*-tests; all the results expressed as hs-CRP are a back-transformed geometrical mean and standard deviation. The one-sample Kolmogorov–Smirnov test was used to verify that the logarithmic transformation is normally distributed. For all continuous variables the paired sample *t*-test was used to evaluate the difference between the groups, while for all categorical variables the chi-square test was used for assessing the significant difference between the groups.

A *P* value  $< 0.05$  was considered significant. The SPSS statistical package was used to perform all statistical evaluation (SSPS Inc., Chicago, IL, USA).

#### Results

We have evaluated 98 volunteers at a mean  $\pm$  SD age of  $28.5 \pm 4.4$  years (52 men and 46 women), a BMI of  $22.3 \pm 3.2$  kg/m<sup>2</sup> and with no known illnesses. Twelve (12.2%) of them were smokers. The mean  $\pm$  SD systolic blood pressure was  $114.9 \pm 14$  and the diastolic was  $73.5 \pm 8$  mmHg. Metabolic and inflammatory variables of male and female volunteers are presented in Tables 1 and 2. Each table also presents data regarding volunteers from the TAMCIS database. The lack of difference in mean and maximal c-IMT in both genders of the study population is represented in Table 3.

#### Discussion

The c-IMT has been extensively studied as a surrogate marker of the atherosclerotic disease (1–4). Increased c-IMT has been shown to be associated with increased incidence of myocardial infarction and stroke (12, 13). Thus, the accurate measurement of c-IMT could allow to single out individuals at risk for clinical events in advance.

However, c-IMT is usually presented as a mean of the two carotid arteries (5). If c-IMT is similar in both arteries, sampling one artery would be both time and cost-effective. In addition, risk factor models do not address any differences between the

**Table 1** Demographic and laboratory variables of the male study population

	Study population (n = 52)	TAMCIS (n = 727)	P value
Age (years)	28.6 ± 3.2	28.8 ± 3.6	0.822
Number of smokers	7 (13.5%)	138 (19%)	0.148
BMI (kg/m <sup>2</sup> )	23.8 ± 3.04	25.10 ± 3.2	0.004
Systolic blood pressure (mmHg)	121.4 ± 13.15	117.1 ± 9.8	0.042
Diastolic blood pressure (mmHg)	74.4 ± 7.4	73.15 ± 6.07	0.286
Glucose (mg/dl)	85.8 ± 8.6	87.8 ± 7.6	0.124
Total cholesterol (mg/dl)	169.1 ± 28.5	175.51 ± 30.2	0.131
LDL (mg/dl)	99.62 ± 25.19	106.70 ± 25.8	0.061
HDL (mg/dl)	50.1 ± 8.8	49.05 ± 9.7	0.410
Triglycerides (mg/dl)	101.24 ± 72.5	98.98 ± 52.6	0.830
Hemoglobin (g/dl)	14.9 ± 0.9	14.9 ± 0.9	0.781
WBCC (cells × 10 <sup>3</sup> /cm <sup>3</sup> )	6.5 ± 1.4	6.6 ± 1.5	0.605
ESR (mm/h)	5.6 ± 3.7	7.6 ± 6.3	0.001
Fibrinogen (mg/dl)	233.9 ± 41.6	238.3 ± 48.5	0.482
hs-CRP (mg/l)	1.4 ± 1.4	1.9 ± 3.4	0.316

TAMCIS, Tel Aviv Medical Center Inflammation Survey; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; WBCC, white blood cell count; ESR, erythrocyte sedimentation rate; hs-CRP, high-sensitivity C-reactive protein.

**Table 2** Demographic and laboratory variables of the female population

	Study population (n = 46)	TAMCIS (n = 366)	P value
Age (years)	27.8 ± 4.9	28.2 ± 3.9	0.665
Number of smokers	5 (10.8%)	85 (23.2%)	0.07
BMI (kg/m <sup>2</sup> )	20.8 ± 2.7	22.6 ± 3.6	0.000
Systolic blood pressure (mmHg)	108.7 ± 12.1	106.8 ± 9.5	0.364
Diastolic blood pressure (mmHg)	72.5 ± 8.9	68.9 ± 5.8	0.023
Glucose (mg/dl)	81.8 ± 6.2	83.6 ± 6.9	0.086
Total cholesterol (mg/dl)	181.2 ± 34.5	187.6 ± 28.7	0.240
LDL (mg/dl)	96.0 ± 26.8	102.0 ± 24.1	0.129
HDL (mg/dl)	70.4 ± 18.3	66.5 ± 14.40	0.178
Triglycerides (mg/dl)	79.9 ± 60.6	92.7 ± 43.6	0.180
Hemoglobin (g/dl)	12.8 ± 0.9	12.9 ± 1.0	0.291
WBCC (cells × 10 <sup>3</sup> /cm <sup>3</sup> )	6.4 ± 1.3	7.0 ± 1.8	0.006
ESR (mm/h)	13.9 ± 9.3	14.9 ± 8.6	0.529
Fibrinogen (mg/dl)	270.8 ± 43.8	278.9 ± 54.3	0.270
hs-CRP (mg/l)	1.9 ± 1.7	3.4 ± 4.9	0.163

TAMCIS, Tel Aviv Medical Center Inflammation Survey; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; WBCC, white blood cell count; ESR, erythrocyte sedimentation rate; hs-CRP, high-sensitivity C-reactive protein.

**Table 3** Comparison of intimal medial thickness (IMT) between the left and right carotid arteries in males (n = 52) and females (n = 46)

	Left carotid artery	Right carotid artery	P value
Males			
Mean IMT	0.625 ± 0.078	0.626 ± 0.075	0.884
Max IMT	0.756 ± 0.108	0.756 ± 0.118	0.998
Females			
Mean IMT	0.615 ± 0.059	0.622 ± 0.0618	0.582
Max IMT	0.742 ± 0.090	0.748 ± 0.098	0.726

carotid arteries. However, several studies (14–16) have noted an increased c-IMT in the left carotid artery. In addition, endarterectomies have a higher prevalence on the left side (17). It has been suggested that increased shear forces in the left carotid artery contribute to this phenomenon. These studies were conducted on patients with a mean age of 50.1 (14–16). Furthermore, many of the patients had plaques evident on their c-IMT examinations. One study noted that 36.9% of the patients had atherosclerotic plaques on their examinations. Examining c-IMT in young patients could help prevent unwanted clinical sequelae and therefore, help in the management of patients at risk for cardiovascular events.

To our knowledge, only one study examined c-IMT in young individuals. In 1998, Frost and Beischer (18) did not find a difference between carotid sides in healthy and diabetic patients in a group of 40 patients. However, they measured maximal IMT and not mean c-IMT. In addition, their measurement was done manually and consisted of only two samples in contrast to our study in which we included 80–100 computer-derived samples per patient.

We aimed to evaluate the differences in c-IMT between the carotid arteries in individuals without clinically evident atherosclerotic disease. All patients did not have plaques evident by c-IMT examination. Furthermore, they were much younger than individuals in other reported studies (mean age of 28 vs 50).

We failed to find any differences between both carotid sides. This could indicate that the differences seen in older people occur due to a combined effect of various atherosclerotic risk factors as well as the potential differences between the shear forces between the two carotid arteries.

Our population was compared with a larger cohort of apparently health individuals in order to make sure that our cohort is relatively healthy. In fact, they had a lower BMI, lower (although not significant) percent of smokers, and lower concentration of several inflammatory biomarkers.

There have been reports that IMT progression accelerates in the elderly and therefore could account for the difference in IMT seen at older ages that are non-existent in younger patients (19). Thus, we raise the possibility that if mechanical shear stress forces do contribute to an accelerated development of the atherosclerotic process in the left carotid artery, they probably need a relatively prolonged period of time to become evident. Further studies are needed to elucidate this point of interest.

References

1. MAGYAR MT, SZIKSZAI Z, BALLA J et al. Early-onset carotid atherosclerosis is associated with increased intima-media thickness and elevated serum levels of inflammatory markers. *Stroke* 2003;**34**:58–63.
2. SITZER M, MARKUS HS, MENDALL MA, LIEHR R, KNORR U, STEINMETZ H. C-reactive protein and carotid intimal medial thickness in a community population. *J Cardiovasc Risk* 2002;**9**:97–103.
3. SITZER M, PUAC D, BUEHLER A et al. Internal carotid artery angle of origin: a novel risk factor for early carotid atherosclerosis. *Stroke* 2003;**34**:950–5.
4. TOUBOUL PJ, LABREUCHE J, VICAUT E, AMARENCO P. Carotid intima-media thickness, plaques, and Framingham risk score as independent determinants of stroke risk. *Stroke* 2005;**36**:1741–5.
5. SIMON A, GARIEPY J, CHIRONI G, MEGNIEN JL, LEVENSON J. Intima-media thickness: a new tool for diagnosis and treatment of cardiovascular risk. *J Hypertens* 2002;**20**:159–69.
6. BERLINER S, SHAPIRA I, TOKER S, MELAMED S, SHIROM A, ROGOWSKI O. Benign hereditary leukopenia–neutropenia does not result from lack of low grade inflammation. A new look in the era of microinflammation. *Blood Cells Mol Dis* 2005;**34**:135–40.
7. ROGOWSKI O, TOKER S, SHAPIRA I et al. Values of high sensitivity C-reactive protein in each month of the year in apparently healthy individuals. *Am J Cardiol* 2005;**95**:152–5.
8. HENNERICI M, MEAIRS S. Imaging arterial wall disease. *Cerebrovasc Dis* 2000;**10**(Suppl. 5):9–20.
9. ANONYMOUS. Recommendation of measurement of erythrocyte sedimentation rate of human blood. *Am J Clin Pathol* 1977;**68**:505–7.
10. CLAUSS A. Gerinnungsphysiologische Schnellmethode zur Bestimmung des Fibrinogens. *Acta Haematol Basel* 1957;**17**:237–46.
11. RIFAI N, TRACY RP, RIDKER PM. Clinical efficacy of an automated high-sensitivity C-reactive protein assay. *Clin Chem* 1999;**45**:2136–41.
12. O'LEARY DH, POLAK JF, KRONMAL RA, MANOLIO TA, BURKE GL, WOLFSON SK, JR. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. *Cardiovascular Health Study Collaborative Research Group. N Engl J Med* 1999;**340**:14–22.
13. BALDASSARRE D, AMATO M, BONDIOLI A, SIRTORI CR, TREMOLI E. Carotid artery intima-media thickness measured by ultrasonography in normal clinical practice correlates well with atherosclerosis risk factors. *Stroke* 2000;**31**:2426–30.
14. RODRIGUEZ HERNANDEZ SA, KROON AA, VAN BOXTEL MP et al. Is there a side predilection for cerebrovascular disease? *Hypertension* 2003;**42**:56–60.
15. ONBAS O, KANTARCI M, OKUR A, BAYRAKTUTAN U, EDIS A, CEVIZ N. Carotid intima-media thickness: is it correlated with stroke side? *Acta Neurol Scand* 2005;**111**:169–71.
16. SUN Y, LIN CH, LU CJ, YIP PK, CHEN RC. Carotid atherosclerosis, intima media thickness and risk factors—an analysis of 1781 asymptomatic subjects in Taiwan. *Atherosclerosis* 2002;**164**:89–94.
17. MAXWELL BG, MAXWELL JG, BRINKER CC. Left-side preference in carotid endarterectomies. *Am Surg* 2000;**66**:793–6.
18. FROST D, BEISCHER W. Determinants of carotid artery wall thickening in young patients with Type 1 diabetes mellitus. *Diabet Med* 1998;**15**:851–7.
19. ALLAN PL, MOWBRAY PI, LEE AJ, FOWKES FG. Relationship between carotid intima-media thickness and symptomatic and asymptomatic peripheral arterial disease. The Edinburgh Artery Study. *Stroke* 1997;**28**:348–53.

# Comparison of Carotid Intima-Media Thickness in Patients With Stable Angina Pectoris Versus Patients With Acute Coronary Syndrome

Şenol Demircan, MD\*, Abdullah Tekin, MD, Gökür Tekin, MD, Semra Topçu, MD, Fatma Yiğit, MD, Tansel Erol, MD, Tuna Katırcıbaşı, MD, Alpay Turan Sezgin, MD, Mehmet Baltalı, MD, Bülent Özin, MD, and Haldun Müderrisoğlu, MD

In this study, we found that carotid intima-media thickness (IMT) was significantly increased and carotid artery atherosclerotic plaques were detected more frequently in patients who had early-onset coronary artery disease compared with control subjects ( $0.73 \pm 0.10$  vs  $0.60 \pm 0.10$  mm,  $p < 0.001$ , and 40% vs 11%,  $p < 0.001$ , respectively). Further, patients who had coronary artery disease and presented with an acute coronary syndrome were found to have significantly increased carotid IMT compared with patients who had stable angina pectoris ( $0.76 \pm 0.10$  vs  $0.70 \pm 0.10$  mm,  $p < 0.05$ ). The IMT was greater in the patients who had acute coronary syndrome than in those who had stable angina pectoris. © 2005 Elsevier Inc. All rights reserved. (Am J Cardiol 2005;96:643–644)

High-resolution B-mode ultrasound can measure the intima-media thickness (IMT) of the walls of the carotid arteries and the IMT correlates rather well to the presence of atherosclerotic narrowing of coronary arteries.<sup>1</sup> This report describes carotid IMT in patients who presented with acute coronary syndrome (ACS) and in those who presented with stable angina pectoris (SAP).

•••

We studied 146 patients who were <45 years old and categorized them into 3 groups. The first group consisted of 41 patients who had ACS and whose initial presentation was ST- or non-ST-segment elevation myocardial infarction or Braunwald's class IIIB unstable angina pectoris. The second group consisted of 32 patients who had chronic SAP. The remaining 73 subjects were included in the control group. Patients who had a history of myocardial infarction, unstable angina, percutaneous coronary intervention, carotid surgery, coronary bypass, chronic kidney disease, chronic inflammatory disease, or statin use were excluded from the study. Control subjects were chosen among those who had atypical chest pain, no history of coronary heart disease, and a negative result from stress testing.

A high-resolution ultrasound system equipped with a 13-MHz transducer (Vivid 7, General Electric Vingmed Ultrasound, Horten, Norway) was used for longitudinal scans of the far wall of the distal 2.0 cm of the 2 common carotid arteries, immediately proximal to the origin of the bifurcation, for assessing IMT. Three measurements of IMT were performed in the right and left carotid arteries and

were averaged to determine the mean IMT for each side and for the 2 sides combined. IMT was measured offline with computer software (M'ATH, Argenteuil, France), which can automatically define the IMT to within 0.001 mm. Carotid plaques were defined as a focal widening of the vessel wall relative to the adjacent wall that protruded into the lumen. For analysis, plaques were defined as simple or complex depending on their extension, echogenic composition, and surface characteristics as proposed by Lombardo et al.<sup>2</sup> The distance from the interface between the lumina and intima of the near wall to that of the far wall was defined as the lumen diameter. These procedures were performed within the first week of initial presentation to the hospital.

All patients who presented with ACS or SAP underwent coronary angiography. Significant coronary stenosis was defined by visual assessment as  $\geq 70\%$  luminal narrowing in

Table 1  
Baseline characteristics of study population

	ACS (n = 41)	SAP (n = 32)	Controls (n = 73)
Age (yrs)	41.2 $\pm$ 3.7	41.7 $\pm$ 2.8	41.8 $\pm$ 3.7
Men	36 (88%)	30 (93%)	66 (90%)
Hypertension	11 (27%)*	3 (9%)	22 (30%)
Diabetes mellitus	14 (34%)*†	3 (9%)	3 (4%)
Smoker	24 (58%)	10 (31%)	18 (25%)
Dyslipidemia‡	15 (37%)	7 (22%)	26 (36%)
No. of coronary arteries narrowed			
1	21 (54%)	25 (78%)	—
2	9 (23%)*	3 (9%)	—
3	9 (23%)*	4 (12%)	—
Body mass index (kg/m <sup>2</sup> )	27 $\pm$ 3	28 $\pm$ 4	28 $\pm$ 4
C-reactive protein (mg/L)	9 $\pm$ 7*†	4 $\pm$ 2	3 $\pm$ 1

\*  $p < 0.05$  compared with patients who had SAP.

†  $p < 0.05$  compared with control group.

‡ Plasma total cholesterol level  $> 200$  mg/dl or triglyceride level  $> 200$  mg/dl.

The Faculty of Medicine, Department of Cardiology, Başkent University, Adana, Turkey. Manuscript received February 3, 2005; revised manuscript received and accepted April 20, 2005.

\* Corresponding author: Tel.: 322-327-2727; fax: 322-327-1283.

E-mail address: senoldemircan@superonline.com (Ş. Demircan).



Table 2  
Ultrasonic properties of carotid arteries of the study population

	ACS (n = 41)	SAP (n = 32)	Controls (n = 73)	p Value <sup>‡</sup>
Mean carotid IMT (mm)	0.76 ± 0.10* <sup>†</sup>	0.70 ± 0.10 <sup>†</sup>	0.60 ± 0.09	<0.001
Left carotid IMT (mm)	0.80 ± 0.13* <sup>†</sup>	0.70 ± 0.10 <sup>†</sup>	0.62 ± 0.10	<0.001
Right carotid IMT (mm)	0.72 ± 0.12 <sup>†</sup>	0.71 ± 0.14 <sup>†</sup>	0.58 ± 0.09	<0.001
Left lumen diameter (mm)	5.99 ± 0.80 <sup>†</sup>	5.89 ± 0.78 <sup>†</sup>	5.56 ± 0.86	<0.001
Right lumen diameter (mm)	6.11 ± 0.89 <sup>†</sup>	5.70 ± 0.72 <sup>†</sup>	5.54 ± 0.88	<0.001
Left carotid flow velocity (cm/s)	107 ± 23	102 ± 24	112 ± 14	NS
Right carotid flow velocity (cm/s)	105 ± 22	101 ± 30	107 ± 16	NS
Carotid plaque occurrence	23 (57%)* <sup>†</sup>	6 (19%)* <sup>†</sup>	8 (11%)	
Simple plaques	8 (20%)* <sup>†</sup>	5 (16%)	7 (10%)	
Complex plaques	15 (37%)* <sup>†</sup>	1 (3%)	1 (1%)	

\* p <0.05 compared with patients who had SAP.

<sup>†</sup> p <0.05 compared with control group.

<sup>‡</sup> Analysis of variance.

any of the 3 major coronary branches or ≥50% luminal narrowing of the left main coronary artery.

Statistical analysis was performed with SPSS 9.0 for Windows (SPSS, Inc., Chicago, Illinois). Continuous variables are presented as mean ± SD, and categorical variables as percentage. Chi-square or Fischer's exact test was used for categorical variables. One-way analysis of variance with Dunnett's test or unpaired *t* test for pairwise comparisons was used for analysis of continuous variables. A multivariate logistic regression model in which age, gender, hypertension, diabetes, current smoking, dyslipidemia, and ischemic family history represented the independent variables was used to determine the increased carotid IMT. The IMT values within highest quartile were accepted as increased IMT. All p values <0.05 were accepted as statistically significant.

Baseline characteristics of the study population are presented in Table 1. There were 27 patients who had ST-segment elevation myocardial infarction, 7 who had non-ST-segment elevation myocardial infarction, and 7 patients who had unstable angina pectoris. Patients who had ACS were more likely to have positive family history for coronary artery disease, diabetes mellitus, and multivessel disease than were patients who had SAP or controls. Ultrasonic properties of carotid arteries of the study population are presented in Table 2. Prevalence of complex carotid artery atherosclerotic plaques was higher in patients who had ACS than in those who had SAP. Carotid IMT was significantly increased in patients who had ACS and SAP compared with controls. The IMTs of patients who had ACS were significantly increased compared with those of patients who had SAP. Logistic regression analysis showed that diabetes mellitus is the independent predictor of increased carotid IMT

(odds ratio 6.04, 95% confidence interval 1.24 to 29.29, p = 0.025).

...

This is the first study to show that patients who had an ACS were much more likely to have complex carotid plaques and greater IMT than were patients who had chronic SAP.

In the Atherosclerosis Risk In Communities (ARIC)<sup>3</sup> study, mean carotid IMT was consistently greater in those who had prevalent clinical cardiovascular disease than in those who did not have disease. A previous observational study demonstrated a significantly increased carotid IMT in patients who were 30 to 50 years of age and had survived a myocardial infarction compared with control subjects.<sup>4</sup> Our study extended this finding and demonstrated increased carotid IMT in patients who had ACS and those who had SAP. Our findings also showed significantly increased carotid IMT in patients who had ACS compared with those who had SAP.

1. Kablak-Ziembicka A, Tracz W, Przewlocki T, Pieniazek P, Sokolowski A, Konieczynska M. Association of increased carotid intima-media thickness with the extent of coronary artery disease. *Heart* 2004;90: 1286–1290.
2. Lombardo A, Biasucci LM, Lanza GA, Coli S, Silvestri P, Cianflone D, Liuzzi G, Burzotta F, Crea F, Maseri A. Inflammation as a possible link between coronary and carotid plaque instability. *Circulation* 2004;109: 3158–3163.
3. Burke GL, Evans GW, Riley WA, Sharrett AR, Howard G, Barnes RW, Rosamond W, Crow RS, Rautaharju PM, Heiss G. Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study. *Stroke* 1995;26:386–391.
4. Vrtovec B, Keber I, Gadzije V, Bardorfer I, Keber D. Carotid intima-media thickness of young coronary patients. *Coron Artery Dis* 1999; 10:407–411.

## Arterioesclerosis subclínica, factores de riesgo cardiovascular clásicos y emergentes en niños obesos chilenos

PILAR ARNAÍZ G.<sup>1</sup>, MÓNICA ACEVEDO B.<sup>2</sup>, SALESA BARJA Y.<sup>3</sup>, XIMENA BERRÍOS C.<sup>4</sup>, BEATRIZ GUZMÁN A.<sup>5</sup>, CLAUDIA BAMBS S.<sup>6</sup>, MYRIAM FERREIRO C.<sup>7</sup>, JACQUELINE CARVAJAL T.<sup>8</sup>, BERTA CASSIS A.<sup>8</sup>, CARLOS NAVARRETE R.<sup>9</sup>

1. Médico cardiólogo pediatra, Profesor Auxiliar de Pediatría, Pontificia Universidad Católica de Chile.
2. Médico cardiólogo de adultos, Profesor Auxiliar de Cardiología, Pontificia Universidad Católica de Chile.
3. Médico pediatra, Magister en Nutrición, Pontificia Universidad Católica de Chile.
4. Médico internista, Magister en Salud Pública, Profesor Titular de Salud Pública, Pontificia Universidad Católica de Chile.
5. Enfermera universitaria, Licenciada en Salud Pública, Pontificia Universidad Católica de Chile.
6. Médico internista, Pontificia Universidad Católica de Chile.
7. Médico becado en Cardiología Pediátrica, Pontificia Universidad Católica de Chile.
8. Enfermera universitaria, Pontificia Universidad Católica de Chile.
9. Magister en Estadística, Pontificia Universidad Católica de Chile.

### ABSTRACT

Arteriosclerosis can start in childhood and develops chronically depending on the load of cardiovascular risk factors (RF). **Objective:** To study classic RF, an emergent RF (high-sensitivity C-reactive protein: hsCRP) and two noninvasive early markers of atherosclerosis: brachial ultrasound endothelium-dependent dilation (EDD) and carotid intima-media thickness (IMT), in obese compared with normal children. **Method:** 26 obese children (BMI > Pc95) and 57 normal children (BMI: Pc 10 - 85) were evaluated with anthropometry, arterial pressure (AP), EDD, IMT, and determined plasmatic hsCRP, lipid profile and fast glucose. **Results:** 50% were girls and 41% prepubertal. Age:  $9.9 \pm 1.6$  vs  $9.8 \pm 1.8$  years (ns), zBMI:  $2.0 \pm 0.2$  vs  $0.17 \pm 0.6$ , waist circumference (%Media):  $133.5 \pm 16$  vs  $100.5 \pm 10\%$  in obese and normal respectively. The obese ones had higher Total Cholesterol, LDL-C, Triglyceride, hsCRP and lower HDL-C ( $p < 0.005$ ). There was no difference in DMF:  $9.03 \pm 5.2\%$  vs  $9.3 \pm 4.2\%$  and IMT:  $0.49 \pm 0.03$  vs  $0.50 \pm 0.03$  mm, fast glucose or AP. **Conclusion:** This group of obese chilean children present a higher load of classic RF, and hsCRP level that normal ones. Nevertheless, there was not difference in sub clinical arteriosclerosis subrogate markers. **(Key words:** Obesity, children, atherosclerosis, cardiovascular risk-factors).  
Rev Chil Pediatr 2007; 78 (2): 137-144

Trabajo recibido el 6 de diciembre de 2006, devuelto para corregir el 23 de enero de 2007, segunda versión el 23 de marzo de 2007, aceptado para publicación el 9 de abril de 2007.

Financiamiento: Financiado por el Centro de Investigaciones Médicas PUC (Concurso de Investigación para Becados año 2006) y por el Departamento de Pediatría (Concurso de Investigación para Académicos 2006).

Correspondencia a:  
Dra. Pilar Arnaiz G.  
parnaiz@med.puc.cl

## Original Article

# Cardiac troponin I and beta 2 microglobulin as risk factors for early-onset atherosclerosis in patients on haemodialysis

AYSEGUL ZUMRUTDAL,<sup>1</sup> SIREN SEZER,<sup>1</sup> SENOL DEMIRCAN,<sup>2</sup> GULSAH SEYDAOGLU,<sup>3</sup>  
F NURHAN OZDEMIR<sup>1</sup> and MEHMET HABERAL<sup>4</sup>

Departments of <sup>1</sup>Nephrology, <sup>2</sup>Cardiology and <sup>4</sup>General Surgery, Faculty of Medicine, Baskent University, Ankara and <sup>3</sup>Department of Biostatistics, Faculty of Medicine, Cukurova University, Adana, Turkey

**SUMMARY:**

**Aim:** To investigate the associations of different risk factors with carotid artery intima-media thickness (C-IMT) in non-diabetic haemodialysis (HD) patients who had no clinical evidence of atherosclerosis.

**Methods:** Seventy-two HD patients (43 men, 29 women; mean age:  $34.5 \pm 10.6$  years; mean time on HD:  $47.9 \pm 40.0$  months) and 40 age- and sex-matched healthy controls (26 men, 14 women; mean age:  $35.5 \pm 7.1$  years) participated in the study. The relationship between C-IMT and haematocrit-corrected erythrocyte sedimentation rate (Hct-corrected ESR), beta 2 microglobulin (beta2M) and serum cardiac troponin I (cTnI) levels beyond C-reactive protein (CRP), lipid profile and lipoprotein(a), fibrinogen, homocysteine and left ventricular hypertrophy (LVH) were examined.

**Results:** Mean C-IMT of the HD patients was significantly greater than that of the control subjects ( $0.59 \pm 0.06$  vs  $0.53 \pm 0.07$  mm,  $P = 0.002$ ). C-IMT of patients was positively correlated with age ( $r = 0.33$ ), body mass index ( $r = 0.40$ ), Hct-corrected ESR ( $r = 0.37$ ), CRP ( $r = 0.34$ ), beta2M ( $r = 0.34$ ), cTnI ( $r = 0.26$ ), triglyceride ( $r = 0.26$ ) and fibrinogen ( $r = 0.28$ ) levels ( $P < 0.05$  for all). The mean C-IMT was significantly greater in patients with LVH than it was in those without LVH ( $P = 0.004$ ). In multivariate regression analysis, age ( $P = 0.02$ ), beta2M ( $P = 0.001$ ), log-transformed CRP ( $P = 0.03$ ) and LVH ( $P = 0.01$ ) were independently related with C-IMT.

**Conclusion:** Besides well-known cardiovascular (CV) risk factors, cTnI and beta2M were related with C-IMT in that they may have important roles in early-onset atherosclerosis in this high-risk population.

**KEY WORDS:** beta 2 microglobulin, cardiac troponin I, carotid intima-media thickness, early-onset atherosclerosis, haematocrit-corrected erythrocyte sedimentation rate, inflammation.

Atherosclerotic vascular disease is the most frequent complication in patients undergoing chronic haemodialysis (HD) treatment. Carotid intima-media thickness (C-IMT) measuring has been the only non-invasive imaging test recommended by the American Heart Association for evaluation of cardiovascular (CV) risk.<sup>1</sup> It is considered a valid surrogate end point that can be used in intervention studies that are aimed at modifying CV risk factors.<sup>2</sup> Several studies have reported the association of different CV risk factors (age, diabetes mellitus, systolic hypertension, left ventricular concentric hypertrophy, smoking, intact parathormone, lipid abnormalities, homocysteine and also inflammation (C-reactive protein)) with increased C-IMT in HD patients.<sup>3–8</sup> Furthermore, prognostic value of ultrasonographic measurement of C-IMT in dialysis patients was

shown in a few studies. Nishizawa *et al.* found that increased C-IMT was an independent predictor of CV mortality in the HD population. Kato *et al.* showed that measurement of C-IMT was useful for predicting long-term mortality in patients on maintenance HD.<sup>4,9</sup> In the current study, beyond well-known CV risk factors, we wanted to investigate the association of different parameters with C-IMT such as haematocrit-corrected erythrocyte sedimentation rate (Hct-corrected ESR), beta 2 microglobulin (beta2M) and serum cardiac troponin I (cTnI) in a selected group of HD patients without any clinical evidence of atherosclerosis. To avoid the masking effects of age and vasculopathic diseases, we evaluated correlates of C-IMT in patients less than 55 years old, and without diabetes mellitus.

Although ESR is widely used in the general population as an inflammation marker, it was judged to be of no clinical utility in chronic HD patients in the mid-1980s. However, it has recently been proposed that after correction of ESR values according to Hct levels in HD patients, Hct-corrected ESR could serve to select the inflammation-afflicted HD patients from those without this comorbid state.<sup>10</sup> Patients

Correspondence: Dr Aysegul Zumrutdal, Baskent University Faculty of Medicine, Adana Teaching and Research Center, 39/601250 Yuregir, Adana, Turkey. Email: azumrutdal@yahoo.com

Accepted for publication 6 June 2005.

Original Article

**Microalbuminuria, but not cystatin C, is associated with carotid atherosclerosis in middle-aged adults**

Nicolas Rodondi<sup>1,2</sup>, Patrick Yerly<sup>3</sup>, Anne Gabriel<sup>4</sup>, Walter F. Riesen<sup>5</sup>, Michel Burnier<sup>6</sup>, Fred Paccaud<sup>2</sup> and Pascal Bovet<sup>2,4</sup>

<sup>1</sup>Department of Community Medicine and Public Health, Cardiovascular Prevention Clinic, University Outpatient Clinic, <sup>2</sup>Department of Community Medicine and Public Health, University Institute of Social and Preventive Medicine, <sup>3</sup>Department of Medicine, Division of Cardiology, University of Lausanne, Switzerland, <sup>4</sup>Unit for Prevention and Control of CVD (UPCCD), Ministry of Health, Republic of Seychelles, <sup>5</sup>Institute of Clinical Chemistry and Haematology, Kantonsspital, St-Gallen and <sup>6</sup>Department of Medicine, Division of Nephrology, University of Lausanne, Switzerland.

**Abstract**

**Background.** Cystatin C, a marker of renal function, has been shown to be an independent predictor of cardiovascular disease (CVD) in older adults, but few data are available in middle-aged adults. Moreover, no study has compared cystatin C and microalbuminuria as risk factors for CVD outcomes in middle-aged adults, and it is not known whether cystatin C is related to an early stage of atherosclerosis.

**Methods.** We evaluated the relationships between serum creatinine, estimated glomerular filtration rate (GFR), serum cystatin C (all divided into tertiles), microalbuminuria and carotid atherosclerosis in a population-based random sample of 523 adults aged 35–64 years from the Seychelles (Indian Ocean). GFR was estimated using the modification of diet in renal disease (MDRD) equation. Intima-media thickness (IMT) was assessed by B-mode ultrasound.

**Results.** The mean age of the study sample was 52 years, and 55% were women. Carotid IMT was higher in participants with microalbuminuria (802 vs 732 µm,  $P < 0.001$ ) and was inversely associated with GFR tertiles (from 728 to 809 µm,  $P$  for trend = 0.002). IMT was not associated with cystatin C or creatinine ( $P$  for trend = 0.10 and 0.16, respectively). In multivariate analyses adjusted for cardiovascular risk factors, the association between microalbuminuria and IMT remained ( $P = 0.047$ ), while the association between GFR and IMT disappeared ( $P$  for trend = 0.33).

**Conclusions.** Microalbuminuria, but not cystatin C, is associated with carotid atherosclerosis beyond traditional cardiovascular risk factors among

middle-aged adults. Cystatin C does not have a stronger relationship with carotid atherosclerosis in middle-aged adults than creatinine.

**Keywords:** Africa; albuminuria; atherosclerosis; cystatin; Seychelles

**Introduction**

Cardiovascular diseases (CVD) are the leading causes of mortality and morbidity in western and developing countries [1,2]. Screening and treatment is one strategy for the primary prevention of CVD, but the highest-risk patients should be identified to maximize the benefit/cost ratio of treatments [3]. In recent years, several tests, ranging from serum to urinary markers, have been proposed as new cardiovascular risk factors or markers that may improve risk prediction and help to identify the highest-risk patients [4,5]. Among markers of renal function that have been associated with increased cardiovascular risk, cystatin C has recently been shown to be an independent predictor of cardiovascular events in a prospective cohort of adults aged  $\geq 65$  years [6]. Microalbuminuria has also been suggested as an independent predictor of cardiovascular events, including in subjects without diabetes [7]. The presence of chronic kidney disease, either manifested by albuminuria or reduced estimated glomerular filtration rate (GFR), appears to be an independent risk factor for CVD in prospective studies, particularly in high-risk populations [7].

It remains to be determined whether a mild decrease in GFR or other early markers of renal dysfunction are associated with increased cardiovascular risk in low-risk populations [7]. The association of microalbuminuria with cardiovascular events has, indeed, been less consistent in low-risk populations [7,8].

Correspondence and offprint requests to: Nicolas Rodondi, MD, MAS, Cardiovascular Prevention Clinic, University Outpatient Clinic and University Institute of Social and Preventive Medicine, Department of Community Medicine and Public Health, University of Lausanne, Bugnon 44, 1011 Lausanne, Switzerland.  
Email: Nicolas.Rodondi@hospvd.ch

# Carotid intima-media thickness and carotid and/or iliofemoral plaques: comparison of two markers of cardiovascular risk in hypertensive patients

Jean-Michel Tartière, Olivier F. Henry, Hélène Safar, Jeanne-Marie Bureau, Xavier Girerd, Michel E. Safar and Jacques Blacher

**Objective** In order to optimize cardiovascular risk assessment, we compared the association of common carotid artery intima-media thickness (CCA-IMT) with carotid and/or iliofemoral (C/IF) plaques according to the presence or absence of cardiovascular disease (CVD) and belonging to a high cardiovascular risk group.

**Design** The study was conducted in 323 subjects presenting one or several cardiovascular risk factors in an internal medicine hospital department; 96 patients had one or more manifestations of cardiovascular disease.

**Results** Compared with patients with no C/IF plaques, patients with plaques at 1–4 sites presented an adjusted odds ratio (OR) [95% confidence interval] of presenting CVD of respectively [1: OR = 1.79 (0.64–5.04); 2: OR = 3.35 (1.27–8.85); 3: OR = 3.40 (1.09–10.62); 4: OR = 14.41 (3.75–55.40)]. On the other hand, the OR of CVD for 1 SD increment of CCA-IMT was: 0.95 (0.69–1.31). In the group of 199 patients, for which Framingham-based calculations of CV risks were methodologically accessible, both CCA-IMT and C/IF plaques were associated with all cardiovascular risks. Comparison of areas under receiver operating characteristic curves among association of C/IF

plaques and CCA-IMT with the presence of CVD showed a statistically significant difference ( $0.78 \pm 0.09$  versus  $0.64 \pm 0.09$ ,  $P < 0.001$ ).

**Conclusion** Arterial plaques may constitute a better marker of the presence of CVD than CCA-IMT. Comparisons according to 10-year Framingham equations did not show statistical significance, but both measures seemed to be highly predictive and possibly complementary. Prospective studies are needed to confirm these findings. *J Hypertens* 21:739–746 © 2003 Lippincott Williams & Wilkins.

*Journal of Hypertension* 2003, 21:739–746

**Keywords:** atherosclerosis, carotid, intima-media thickness, hypertension, essential, plaque, cardiovascular risk

Department of Internal Medicine, Broussais Hospital, AP-HP, Paris, France.

Correspondence and requests for reprints to Professor M.E. Safar, Service de Médecine Interne, 96 rue Didot, Hôpital Broussais, 75674 Paris, Cedex 14, France.  
Tel: +33 (0)1 43 95 91 22; fax: +33 (0)1 45 43 38 94;  
e-mail: michel.safar@brs.ap-hop-paris.fr

Received 14 March 2002 Revised 29 December 2002  
Accepted 7 January 2003

## Introduction

Numerous studies have shown that carotid intima-media thickness (IMT) and presence of plaques are associated with cardiovascular risk factors [1–6]. Most recent prospective studies have shown an association between carotid IMT or aortic abdominal calcifications and occurrence of clinical manifestations of cardiovascular disease (CVD) [7–10]. Only two longitudinal studies have shown an association between carotid plaques and acute myocardial infarction or major cardiovascular events [10,11]. Most of these studies usually investigated carotid IMT and carotid plaques separately, and little information is available comparing the transverse association between these two determinants and the presence of CVD; even less information is available for other plaque locations such as iliofemoral arteries.

In the present study we examined the crude and adjusted associations between carotid IMT or carotid and/or iliofemoral (C/IF) plaques and the presence or absence of CVD or the level of cardiovascular risk group calculated from equations derived from the Framingham Heart Study and from the Framingham Offspring Study [12]. Finally, we compared the strengths of the associations of carotid IMT and, respectively, of carotid and/or iliofemoral plaques with the presence of CVD and with the 10-year Framingham cardiovascular risk.

## Methods

### Study cohort

From December 2000 to June 2001, around 400 patients entered the Department of Internal Medicine of Broussais Hospital for a cardiovascular check-up or-

