The Importance of Arterial Stiffness Measurement

TENSIOMed™ ARTERIOGRAPH

breakthrough in early diagnosis of arteriosclerosis

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The importance of arterial stiffness measurement

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Arterial stiffness measurement in medical practice

Arterial stiffness has become an important subject in the assessment of cardiovascular risk and the evaluation of therapeutic effectiveness on arterial function. The reason for this is that several non-invasive methods have recently come into consideration to measure important parameters for the aortic stiffness, the elasticity of the arteries and the endothelial status. A number of longitudinal studies have shown that these parameters, such as pulse wave velocity (PWV) and augmentation index (Aix), are independent risk factors of fatal cardiovascular events, above and beyond traditional risk factors (1). In the last ESH Guidelines (2007) for the management of Arterial Hypertension PWV occurs as a major diagnostic element and it is also involved in risk stratification (2).

The role of central blood pressure is also mentioned in the Guidelines. Recently published studies (ASCOT and CAFE) have shown that classical blood pressure measurements which measure blood pressure only on the brachial artery are not satisfactory, because for instance BP lowering effect of diverse antihypertensive drugs may vary in effectiveness in different parts of the aortic pathway, while blood pressure measured on the upper arm may remain equal. This means that systolic aortic blood pressure should also be considered in BP lowering therapy. Already, devices exist that can estimate aortic blood pressure (SBPao) in a non-invasive way (3).

One of the available devices to measure the aforementioned parameters is the TensioClinic Arteriograph. The basic research and development was sponsored by the Hungarian government at an estimated cost of 2 Million USD (4). This measurement method is patented all over the world. It is a simple and fast method using analysis of aortic pressure waves. The signal is received by oscillometry through a special cuff pumped over the systolic blood pressure so the measurement is performed in “stop flow” condition (5).

The Arteriograph is validated against the devices Sphygmocor and Complior, widely used devices for measurement of PWV and Aix. There is an extended clinical research study at the University of Pécs/Hungary that aims at the invasive validation of the Arteriograph’s measured parameters (6).

There are more than 250 Arteriographs used in Hungary and more than 50 units used in other European countries. TensioMed Arterial Stiffness Competence Centre collects measured data from many users, and a large population database of arterial stiffness parameters can be found there. This situation allows extended research work for clinicians. Research groups from every quarter of the world are welcome to join in this research project.

The recently established Hungarian Arterial Stiffness Society is open for those who are interested in collaboration. The annual International Symposium on Arterial Stiffness in Budapest is a valuable event for specialists who use arterial stiffness evaluation in everyday practice (7). This includes specialists in hypertonology, cardiology, nephrology, neurology, gynaecology, diabetology and other fields which have an interest in arterial stiffness.

contents

(1) the significance of arterial stiffness as a risk factor

May subclinical arterial disease help to better detect and treat high-risk asymptomatic individuals?

Alain Simon and Jaime Levenson

The diagnosis of high risk of cardiovascular disease (CVD) in subjects without clinically overt CVD has been somewhat improved by integrating multiple traditional risk factors via appropriate risk score programs. Nevertheless, novel measures of CVD risk are being proposed and debated to further improve high-risk detection by their addition to, or their use in place of, traditional risk factors. Among such measures, non-invasive detection of subclinical arterial disease is a subject of growing interest. It may improve CVD risk evaluation and enable more intensive risk-reduction therapy in subjects judged to be at intermediate risk after preliminary risk factor assessment. However, the clinical utility and cost-effectiveness of high-risk diagnostic and therapeutic strategy guided by subclinical arterial disease remain untested. This uncertainty precludes systematic detection of subclinical arterial disease in routine clinical management for primary prevention, but such detection may be used at the discretion of the physician as a part of CVD risk assessment. **(*J Hypertens, 2005; 23:1939-1945.*)**

"Nevertheless traditional risk factors are far from accounting for all high-risk CVD conditions."

Performance of subclinical arterial disease detection as a screening test for coronary heart disease

Simon A, Chironi G, Levenson J.

Traditional risk factors are poor screening tests for coronary heart disease, whereas clinical arterial disease represents its strongest predictor. This raises the question whether subclinical arterial disease may also predict coronary disease. Using published data of prospective studies of subclinical arterial disease, we calculated the incidence of coronary event associated with the absence or presence of atherosclerosis as defined by dichotomous characterization of the following markers: low or high intima-media thickness or the absence or presence of plaque, assessed by carotid ultrasound; zero or high total coronary artery calcium score assessed by computed tomography; normal or decreased ankle-arm index pressure assessed by Doppler stethoscope; and low or high aortic pulse wave velocity assessed by mecanography. A dose-response relationship was found between the absence and presence of atherosclerosis and coronary event incidence. Yearly incidence was <1% in the absence of atherosclerosis regardless of the marker used. Coronary event incidence was >1% in the presence of atherosclerosis and increased in a gradual way, depending on the marker tested, to reach 3% maximum with massive coronary calcifications. The relation between clinically overt arterial disease, such as angina, transient ischemic attack, stroke, or myocardial infarct, and yearly incidence of subsequent events reported in the literature prolonged the dose-response curve of subclinical disease. Therefore, detection of arterial disease, not only clinically overt but also subclinical asymptomatic, is a worthwhile screening test for future coronary event. **(*Hypertension*, 2006 Sep;48(3):392-6.)**

Pulse wave analysis and pulse wave velocity: a critical rewiev of their strengths and weaknesses

Justine Ina Davies and Allan D. Struthers

The study of the pulse using the technique of applanation tonometry is undergoing a resurgence with the development of new computerized equipment. We aim here a present a critical review of the uses, potential uses, stregths and weaknesses of the technique of applanation tonometry of the assesment of augmentation index and pulse wave velocity. We will review the technique of applanation tonometry, the physiological factors

affecting pulse wave velocity and pulse wave analysis, the changes in pulse wave velocity and pulse wave analysis with pharmacological interventions, and the use of the technique of applanation tonometry as a prognosic tool. We conclude that, although the technique of applanation tonometry initially seems promising, several pertinent issues need to be addressed before it can be used reliably as a clinical research tool. Importantly the use of the technique of applanation tonometry to derive the central wave from non-invasively acquired peripheral data needs to be validated prospectively. **(*J Hypertens*, 2003; 21:463-472.)**

„... vascular stiffness precedes atherosclerosis and is a risk factor for atherosclerosis."

„... studies clearly demonstrate that PWV and the augmentation index are associated with the structural changes of atherosclerosis."

Noninvasive Assessment of Atherosclerosis: from Structure to Function

Endothelial Dysfunction - A Marker of Atherosclerotic Risk

Piero O. Bonetti, Lilach O. Lerman, Amir Lerman

Abstract - Endothelial dysfunction is a systemic disorder and a key variable in the pathogenesis of atherosclerosis and its complications. Current evidence suggests that endothelial status is not determined solely by the individual risk factor burden but rather, may be regarded as an integrated index of all atherogenic and atheroprotective factors present in an individual, including known as well as yet-unknown variables and genetic predisposition. Endothelial dysfunction reflects a vascular phenotype prone to atherogenesis and may therefore serve as a marker of the inherent atherosclerotic risk in an individual. In line with this hypothesis, dysfunction of either the coronary or peripheral vascular endothelium was shown to constitute an independent predictor of cardiovascular events, providing valuable prognostic information additional to that derived from conventional risk factor assessment. Interventions like risk factor modification and treatment with various drugs, including statins and angiotensin-converting enzyme inhibitors, may improve endothelial function and thereby, potentially prognosis. Hence, given its reversibility and granted the availability of a diagnostic tool to identify patients at risk and to control the efficacy of therapy in clinical practice, endothelial dysfunction may be an attractive primary target in the effort to otpimize individualized therapeutic strategies to reduce cardiovascular morbidity and mortality. **(*Arterioscler Thromb Vasc Biol,* 2003; 23:168-175.)**

Arterial Stiffness and the Development of Hypertension

The ARIC Study

Duanping Liao, Donna K. Arnett, Herman A. Tyroler, Ward A. Riley, Lloyd E. Chambless, Moyses Szklo, Gerardo Heiss

Abstract - Decreased elasticity in large and medium-sized arteries has been postulated to be associated with cardiovascular diseases. We prospectively examined the relation between arterial elasticity and the development of hypertension over 6 years of follow-up in a cohort of 6992 normotensive men and women aged 45 to 64 years at baseline from the biracial, population-based Atherosclerosis Risk in Communities (ARIC) Study. Arterial elasticity was measured from high-resolution B-mode ultrasound examination of the left common carotid artery as adjusted arterial diameter change (in micrometers, simultaneously adjusted for diastolic blood pressure, pulse pressure, pulse pressure squared, diastolic arterial diameter, and height), Peterson's elastic modulus (in kilopascals), Young's elastic modulus (in kilopascals), and "beta" stiffness index. Incident hypertension (n=5551) was defined as systolic blood pressure > or = 160 mmHg, diastolic blood pressure > or = 95 mmHg, or the use of antihypertensive medication at a follow-up examination conducted every 3 years. The age-, ethnicity-, center-, gender-, education-, smoking-, heart rate-, and obesity-adjusted means (SE) of baseline adjusted arterial diameter change, Peterson's elastic modulus, Young's elastic modulus, and "beta" stiffness index were 397 (5), 148 (2.0), 787 (12.7), and 11.43 (0.16), respectively, in persons who developed hypertension during follow-up, in contrast to 407 (1), 124 (0.6), 681 (3.7), and 10.34 (0.05), respectively, for persons who did not. The similarly adjusted cumulative incident rates of hypertension from the highest to the lowest quartiles of

arterial elasticity were 6.7%, 8.0%, 7.3%, and 9.6%, respectively, when measured by adjusted arterial diameter change (P<0.01). One standard deviation decrease in arterial elasticity was associated with 15% greater risk of hypertension, independent of established risk factors for hypertension and the level of baseline blood pressure. These results suggest that lower arterial elasticity is related to the development of hypertension. **(*Hypertension,* 1999; 34:201-206.)**

Prognostic Value of Aortic Pulse Wave Velocity as Index of Arterial Stiffness in the General Population

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Background - Few population studies addressed the prognostic significance of aortic pulse wave velocity (APWV) above and beyond other cardiovascular risk factors.
Methods and Results - We studied a sex- and age-stratified random sample of 1678 Danes aged 40 to 70 years. We used Cox regression to investigate the prognostic value of APWV, office pulse pressure (PP), and 24-hour ambulatory PP while adjusting for mean arterial pressure (MAP) and other covariates. Over a median follow-up of 9.4 years, the incidence of fatal and nonfatal cardiovascular end points, cardiovascular mortality, and fatal and nonfatal coronary heart disease amounted to 154, 62, and 101 cases, respectively. We adjusted for sex, age, body mass index, MAP measured in the office (conventional PP and APWV) or by ambulatory monitoring (24-hour PP), smoking, and alcohol intake. With these adjustments, APWV maintained its prognostic significance in relation to each end point (P<0.05), whereas office and 24-hour PP lost their predictive value (P>0.19), except for office PP in relation to coronary heart disease (P=0.02). For each 1-SD increment in APWV (3.4 m/s), the risk of an event increased by 16% to 20%. In sensitivity analyses, APWV still predicted all cardiovascular events after standardization to a heart rate of 60 beats per minute, after adjustment for 24-hour MAP instead of office MAP, and/or after additional adjustment for the ratio of total to HDL serum cholesterol and diabetes mellitus at baseline.
Conclusions - In a general Danish population, APWV predicted a composite of cardiovascular outcomes above and beyond traditional cardiovascular risk factors, including 24-hour MAP. **(*Circulation,* 2006;113:664-670.)**

Aortic Pulse Wave Velocity Is Associated With the Presence and Quantity of Coronary Artery Calcium

A Community-Based Study

Iftikhar J. Kullo, Lawrence F. Bielak, Stephen T. Turner, Patrick F. Sheedy II, Patricia A. Peyser

Abstract - We investigated the relationship of aortic pulse wave velocity (aPWV), a measure of central arterial stiffness, with the presence and quantity of coronary artery calcium (CAC) in a community-based sample of adults without prior history of heart attack or stroke (n=401, mean age 59.8 years, 53% men). ECG-gated waveforms of the right carotid and right femoral artery were obtained by applanation tonometry, and aPWV was calculated using established methods. CAC was measured noninvasively by electron beam computed tomography, and CAC score was calculated. aPWV was significantly correlated with log(CAC+1; r=0.41; P<0.0001) and pulse pressure (r=0.47; P<0.0001). Multivariable logistic and linear regression models were used to identify independent predictors of the presence and quantity of CAC, respectively. In multivariable logistic regression analyses, aPWV was associated with the presence of CAC (P=0.011) after adjustment for age, male sex, total cholesterol, high-density lipoprotein cholesterol, diabetes, history of smoking, systolic blood pressure, body mass index, and use of hypertension and statin medications. In multivariable linearregression analyses, aPWV was significantly associated with log(CAC+1) after adjustment for the covariates enumerated above (P<0.0001). aPWV remained significantly associated with both the presence and quantity of CAC even after the additional adjustment for diastolic blood pressure. We conclude that a PWV is related to subclinical coronary atherosclerosis independent of conventional risk factors (including indices of blood pressure) and may be a biomarker of cardiovascular risk in asymptomatic individuals. **(*Hypertension,* 2006;47:174-179.)**

Aortic Pulse Wave Velocity, an Independent Marker of Cardiovascular Risk

H. Safar, J.-J. Mourad, M. Safar and J. Blacher

Summary - Aortic pulse wave velocity (PWV), a classical index of aortic stiffness, may be easily measured in humans using non invasive ultrasound methods of high reproducibility. Recent epidemiological studies have shown that, independently of confounding factors as age, blood pressure and cardiac mass, aortic PWV is a predictor of cardiovascular (CV) mortality in populations of hypertensive subjects, whether they have or not end-stage renal disease. Since aortic PWV is dominantly influenced by age, this finding may be of major importance for the evaluation of CV risk in geriatric populations. **(*Arch Mal Coeur,* 2002; 95:1215-8.)**

Stiffness of Capacitive and Conduit Arteries

Prognostic Significance for End-Stage Renal Disease Patients

Bruno Pannier, Alain P. Guérin, Sylvain J. Marchais, Michel E. Safar, Gérard M. London

Abstract - The aorta is the principal capacitive element of the arterial tree and its increased stiffness, determined by measurement of aortic pulse wave velocity (PWV), is a strong independent predictor of cardiovascular mortality in the general population and end-stage renal disease (ESRD) patients. Whether stiffness of ESRD patients' peripheral arteries has the same prognostic value has never been investigated. A cohort of 305 ESRD patients was followed for 70+/-49 months (mean+/-SD). Ninety-six deaths of cardiovascular origin occurred. At entry into the study, together with standard clinical and biochemical analyses, patients' aortic, brachial artery, and femorotibial PWV were determined. Based on KaplanMeier survival curve analyses and Cox proportional hazards analyses, adjusted for age, pulse pressure, and clinical data, aortic PWV was a significant and independent predictor of outcome. Neither brachial artery nor femotibial artery stiffness was able to predict cardiovascular outcome. Receiver operating characteristic curve analysis of aortic PWV indicated the cutoff value of 10.75 m/s, with 84% sensitivity, 73% specificity, 87% negative predictive value, and 72% positive predictive value. These results provide evidence that, in ESRD, increased stiffness of capacitive arteries, like the aorta, is an independent strong predictor of cardiovascular mortality, whereas stiffness of peripheral conduit arteries had no prognostic value. **(*Hypertension,* 2005; 45:592-596.)**

Reflection in the Arterial System and the Risk of Coronary Heart Disease

Tomoshige Hayashi, Yasunori Nakayama, Kei Tsumura, Kiyomichi Yoshimaru, and Hiroyasu Ueda

Background - Although it was reported that the augmentation index and inflection time are closely related to reflection in the arterial system and large artery function, it is not known whether these indices of the ascending aortic pressure waveform increase the risk of coronary heart disease (CHD). The purpose of this study was to evaluate whether the aortic reflection of the ascending aortic pressure waveform is related to an increased risk of CHD.

Methods - We enrolled 190 men and women who had chest pain, normal contractions, no local asynergy, and no history of myocardial infarction. We measured the ascending aortic pressure using a fluid-filled system. The inflection time was defined as the time interval from initiation of a systolic pressure waveform to the inflection point. We investigated the association between the inflection time and augmentation index of the ascending aorta and the risk of CHD.

Results - Both the inflection time and augmentation index were associated with an increased risk of CHD. The crude prevalence rates of CHD were 66.0% for the shortest quartile and 10.6% for the longest quartile of the inflection time, and 17.0% for the lowest quartile and 40.4% for the highest quartile of the augmentation index. The multipleadjusted odds ratio of CHD was 30.8 (95% confidence interval [CI] 7.43-128.05) for the

shortest quartile of the inflection time compared with the longest quartile and was 3.82 (95% CI 1.26-11.59) for the highest quartile of the augmentation index compared with the lowest quartile.
Conclusions - The augmentation index and inflection time were associated with an increased risk of CHD. **(*Am J Hypertens,* 2002;15:405-409.)**

Arterial Stiffness, Wave Reflections, and the Risk of Coronary Artery Disease

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Background - Increased arterial stiffness, determined invasively, has been shown to predict a higher risk of coronary atherosclerosis. However, invasive techniques are of limited value for screening and risk stratification in larger patient groups.
Methods and Results - We prospectively enrolled 465 consecutive, symptomatic men undergoing coronary angiography for the assessment of suspected coronary artery disease. Arterial stiffness and wave reflections were quantified noninvasively using applanation tonometry of the radial artery with a validated transfer function to generate the corresponding ascending aortic pressure waveform. Augmented pressure (AP) was defined as the difference between the second and the first systolic peak, and augmentation index (AIx) was AP expressed as a percentage of the pulse pressure. In univariate analysis, a higher AIx was associated with an increased risk for coronary artery disease (OR, 4.06 for the difference between the first and the fourth quartile [1.72 to 9.57; P<0.01]). In multivariate analysis, after controlling for age, height, presence of hypertension, HDL cholesterol, and medications, the association with coronary artery disease risk remained significant (OR, 6.91; P<0.05). The results were exclusively driven by an increase in risk with premature vessel stiffening in the younger patient group (up to 60 years of age), with an unadjusted OR between Aix quartiles I and IV of 8.25 (P<0.01) and a multiple-adjusted OR between these quartiles of 16.81 (P<0.05).
Conclusions - AIx and AP, noninvasively determined manifestations of arterial stiffening and increased wave reflections, are strong, independent risk markers for premature coronary artery disease. **(*Circulation,* 2004;109:184-189.)**

Augmentation index is associated with cardiovascular risk

Jens Nürnberger, Ayten Keflioglu-Scheiber, Anabelle M. Opazo Saez, Rene R. Wenzel, Thomas Philipp and Rafael F. Schäfers

Objectives - Augmentation index is a parameter measured by pulse wave analysis (PWA) and is used as a surrogate measure of arterial stiffness. The aim of this study was to assess whether augmentation index is associated with cardiovascular risk, as well as to evaluate whether the determinants of augmentation index are different in patients with cardiovascular disease compared to healthy subjects.
Design and methods - We related augmentation index to risk scores in 216 subjects with or without a cardiovascular disease. Subjects without cardiovascular disease were classified according to the 'coronary risk chart' of the European Society of Cardiology (ESC), and those with cardiovascular disease were classified using the SMART (Second Manifestations of ARTerial disease) score and the EPOZ (Epidemiological Prevention study Of Zoetermeer) function. Augmentation index was derived by PWA using carotid applanation tonometry. Augmentation index was also correlated to age, blood pressure, heart rate, smoking history, cholesterol, height, body mass index and gender in subjects categorized as healthy or with cardiovascular disease.
Results - Augmentation index significantly increased with increasing risk scores (P < 0.0001) and was significantly correlated to cardiovascular risk (ESC: P < 0.0001; SMART: P < 0.0001; EPOZ: P < 0.0001). In subjects with and without cardiovascular disease, augmentation index was correlated with diastolic blood pressure, heart rate, height and gender. Age was found to be significantly correlated with augmentation index only in healthy subjects but not in those with atherosclerotic disease.
Conclusions - Our findings suggest that augmentation index may be a useful marker of cardiovascular risk. Further studies are required to investigate the relationship between age and augmentation index in subjects with atherosclerotic disease. **(*J Hypertens,* 2002; 20:2407-2414.)**

Aortic Pressure Augmentation Predicts Adverse Cardiovascular Events in Patients With Established Coronary Artery Disease

Julio A. Chirinos, Juan P. Zambrano, Simon Chakko, Anila Veerani, Alan Schob, Howard J. Willens, Guido Perez, Armando J. Mendez

Abstract - Pulse pressure (PP), a marker of arterial stiffness, predicts cardiovascular risk. We aimed to determine whether augmentation pressure (AP) derived from the aortic pressure waveform predicts major adverse cardiovascular events (MACE) and death independently of PP in patients with established coronary artery disease (CAD). We prospectively followed-up 297 males undergoing coronary angiography for 1186±424 days. Ascending aortic pressure tracings obtained during catheterization were used to calculate AP (difference between the second and the first systolic peak).
Augmentation index (AIx) was defined as AP as a percentage of PP. We evaluated whether AP and AIx can predict the risk of MACE (unstable angina, acute myocardial infarction, coronary revascularization, stroke, or death) and death using Cox regression. All models evaluating AP included PP to assess whether AP adds to the information already provided by PP. Both AP and AIx significantly predicted MACE. The hazard ratio (HR) per 10 mm Hg increase in AP was 1.20 (95% confidence interval [CI], 1.08 to 1.34; *P*<0.001); the HR for each 10% increase in AIx was 1.28 (95% CI, 1.11 to 1.48; *P*=0.004). After adjusting for other univariate predictors of MACE, age, and other potential confounders, AP remained a significant predictor of MACE (HR per 10 mm Hg increase=1.19; 95% CI, 1.06 to 1.34; *P*=0.002), as did AIx (adjusted HR, 1.28; 95% CI, 1.09 to 1.50; *P*=0.003). AP was a significant predictor of death (HR per 10 mm Hg increase=1.18; 95% CI, 1.02 to 1.39; P=0.03). Higher AIx was associated with a trend toward increased mortality (HR_1.22; 95% CI, 0.98 to 1.52; *P*=0.056). Aortic AP predicts adverse outcomes in patients with CAD independently of PP and other risk markers. **(*Hypertension*, 2005;45:980-985.)**

Echogenic Carotid Plaques Are Associated With Aortic Arterial Stiffness in Subjects With Subclinical Carotid Atherosclerosis

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Abstract - A better understanding of the interrelationships between the structure and function of the large arteries would lead to optimize cardiovascular disease prevention strategies. In this study, we investigated the relationships of aortic arterial stiffness assessed by carotid-femoral pulse-wave velocity (PWV), with carotid plaque chogenicity assessed by B-mode ultrasound. We analyzed 561 subjects (without coronary heart disease or stroke) who were volunteers for free health examinations (age, 58.3+/-10.8 years; 32.6% women). Extracranial carotid plaque echogenicity was graded from 1 from1 (plaque appearing black or almost black) to 4 (plaque appearing white or almost white) according to the Gray-Weale classification. Plaques of grades 1 and 2 were defined as echolucent plaques, and plaques of grades 3 and 4 were defined as echogenic plaques. Fifty-one subjects (9.1%) had echolucent carotid plaques, 109 (19.4%) had echogenic plaques, and 401 (71.5%) had no plaques. Subjects with echogenic plaques had higher PWV mean (12.9+/-2.8 m/s) compared with those without plaques (11.1+/-2.3 m/s, P<0.001) and compared with those with echolucent plaques (11.3+/-2.3 m/s, P<0.01). The PWV means in subjects without plaques and those with echolucent plaques were similar and not statistically different (P=0.55). When multivariate adjustment for major known cardiovascular risk factors was performed, these results were not markedly modified. Similar patterns of results were also observed in many subgroups according to age, gender, and hypertensive status. This study provides the first evidence that echogenic but not echolucent carotid plaques are associated with aortic arterial stiffness. This association applies to individuals with normal blood pressure and those with elevated blood pressure. Assessment of the joint and interaction effects of plaque morphology and arterial stiffness on the occurrence of cardiovascular events would permit a better identification of high-risk subjects. **(*Hypertension,* 2003;41:519-527.)**

Aortic Augmentation Index Is Inversely Associated With Cardiorespiratory Fitness in Men Without Known Coronary Heart Disease

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Ray W. Squires, Takamu Kunihiro, Donald D. Hensrud, and Iftikhar J. Kullo

Background - We investigated whether the aortic augmentation index (AIx), a measure of arterial wave reflection and stiffness, is associated with cardiorespiratory fitness in men without known coronary heart disease (CHD).
Methods - Asymptomatic men (*n*= 201, mean age 51± 9.2 years) referred for a screening exercise electrocardiogram (ECG) underwent applanation tonometry to obtain radial artery pulse waveforms, and an ascending aortic pressure waveform was derived by a transfer function. The AIx is the difference between the first and second systolic peak of the ascending aortic pressure waveform, expressed as a percentage of the pulse pressure. Cardiorespiratory fitness was assessed by maximal oxygen consumption ($VO_{2\ max}$ mL/min/kg) during a symptom-limited graded exercise test. Multivariable regression analyses were used to identify significant independent determinants of AIx and of $VO_{2\ max}$.
Results - Diabetes was present in 2.5% of subjects, 34.8% had history of smoking, and 29% were hypertensive. Mean (± SD) AIx was 19.9% ± 9.0% and mean $VO_{2\ max}$ was 33.9 ± 6.4 mL/min/kg. In a multivariable linear regression model, AIx was positively associated with age, hypertension, and history of smoking and inversely with heart rate, height, and body mass index (BMI). The $VO_{2\ max}$ was significantly inversely related to AIx after adjustment for age, heart rate, height, and BMI (*r*= -0.22, *P*= .002), after further adjustment for CHD risk factors (total cholesterol, HDL-cholesterol, history of smoking, diabetes, hypertension) (*P*= .006), and after additional adjustment for behavioral factors (physical activity score, alcohol intake, and percent body fat) (*P* = .022).
Conclusions - These findings indicate that AIx, a measure of arterial wave reflection and stiffness, is inversely associated with cardiorespiratory fitness in men without CHD. **(*Am J Hypertens,* 2006;19:1019–1024.)**

Effect of antihypertensive treatment on small arteries of patients with previously untreated essential hypertension

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In a double-blind randomized trial, the effects of treatment with an angiotensin-converting enzyme (ACE) inhibitor (perindopril) and a beta-blocker (atenolol) on small artery structure were compared in previously untreated essential hypertensive patients. Subjects (diastolic blood pressure > or = 100 and < or = 120 mm Hg) were randomly assigned to treatment for 12 months with either perindopril (n = 13, 4 to 8 mg/d) or atenolol (n = 12, 50 to 100 mg/d); the dosage was adjusted upward and in some cases combined (n = 5, perindopril; n=2, atenolol) with thiazide diuretic to achieve target blood pressure (diastolic blood pressure below 90 mm Hg). Before and at the end of treatment, gluteal biopsies were taken under local anesthetic; from these biopsies, two small arteries were dissected and mounted on a myograph for morphometry. The reduction in blood pressure with atenolol (drop in mean blood pressure 28.4 +/- 1.8 mm Hg) was greater than with perindopril (20.6 +/- 1.8 mm Hg, P < 0.05). Perindopril treatment caused an increase in small artery diameter (231 +/- 14 to 274 +/- 13 microns, P < 0.05) and a reduction in the ratio of media thickness to lumen diameter (7.94 +/- 0.65% to 5.96 +/- 0.42%, P < 0.05), whereas atenolol had no effect (246 +/- 14 to 231 +/- 13 microns and 7.14 +/- 0.47% to 6.79 +/- 0.45%, respectively). The change in small artery morphology caused by perindopril was not accompanied by any change in media cross-sectional area, suggesting that the change was due to „remodeling."
(*Hypertension,* 1995 Apr;25(4 Pt 1):474-81.)

Effect of Different Antihypertensive Drug Classes on Central Aortic Pressure

Trefor Morgan, Jann Lauri, Denise Bertram, and Adrianne Anderson

Background - Central aortic systolic blood pressure (BP) is an important determinant of cardiac workload and cardiac hypertrophy. The relationship of central aortic systolic BP and brachial BP varies depending on the stiffness of blood vessels. It is not certain whether the different drug classes affect the brachial and aortic systolic BP in a similar manner.
Methods - In a double-blind crossover study, we measured the effects of the four major drug classes compared with placebo on central aortic pressure. Central aortic pressure and various indices were determined using the Sphygmo Cor apparatus. The study was undertaken in patients aged 65 to 85 years with systolic BP>150 mm Hg at study entry. Results are reported for 32 patients who had satisfactory applanation tonometry in all five periods.
Results - Calcium channel blockers and diuretics caused a greater fall in brachial artery systolic BP than angiotensin-converting enzyme (ACE) inhibitors or β-blocking drugs. On placebo, central aorta augmentation pressure and index were 23 mm Hg and 33.3%; on ACE inhibitors the values were 18 mm Hg and 30%; on β-blockers, 26 mm Hg and 38.5%; on calcium channel blockers, 16 mm Hg and 28%; and on diuretics, 17 mm Hg and 28.8%. The augmentation pressure on β-blocking drugs was greater than on the other three drug classes ($P< .05$), and augmentation pressures on ACE inhibitors, calcium channel blockers, and diuretics were less than on placebo ($P <.05$). The lowest central aortic pressures were achieved with calcium blocking drugs and diuretics.
Conclusions - Therapy based on brachial artery recordings may thus overestimate the effect of β-blocking drugs on central aortic systolic BP and underestimate the effectiveness of ACE inhibitors and calcium blocking drugs. The clinical importance of this discrepancy needs to be evaluated. **(*Am J Hypertens,* 2004;17:118–123.)**

Effect of very high-intensity statin therapy on regression of coronary atherosclerosis: the ASTEROID trial

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Context - Prior intravascular ultrasound (IVUS) trials have demonstrated slowing or halting of atherosclerosis progression with statin therapy but have not shown convincing evidence of regression using percent atheroma volume (PAV), the most rigorous IVUS measure of disease progression and regression.
Objective - To assess whether very intensive statin therapy could regress coronary atherosclerosis as determined by IVUS imaging.
Design and setting - Prospective, open-label blinded end-points trial (A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden [ASTEROID]) was performed at 53 community and tertiary care centers in the United States, Canada, Europe, and Australia. A motorized IVUS pullback was used to assess coronary atheroma burden at baseline and after 24 months of treatment. Each pair of baseline and follow-up IVUS assessments was analyzed in a blinded fashion.
Patients - Between November 2002 and October 2003, 507 patients had a baseline IVUS examination and received at least 1 dose of study drug. After 24 months, 349 patients had evaluable serial IVUS examinations.
Intervention - All patients received intensive statin therapy with rosuvastatin, 40 mg/d.
Main outcome measures - Two primary efficacy parameters were prespecified: the change in PAV and the change in nominal atheroma volume in the 10-mm subsegment with the greatest disease severity at baseline. A secondary efficacy variable, change in normalized total atheroma volume for the entire artery, was also prespecified. RESULTS: The mean (SD) baseline low-density lipoprotein cholesterol (LDL-C) level of 130.4 (34.3) mg/dL declined to 60.8 (20.0) mg/dL, a mean reduction of 53.2% (P<.001). Mean (SD) high-density lipoprotein cholesterol (HDL-C) level at baseline was 43.1 (11.1) mg/dL, increasing to 49.0 (12.6) mg/dL, an increase of 14.7% (P<.001). The mean (SD) change in PAV for the entire vessel was -0.98% (3.15%), with a median of -0.79% (97.5% CI, -1.21% to -0.53%) (P<.001 vs baseline). The mean (SD) change in atheroma volume in the most diseased 10-mm subsegment was -6.1 (10.1) mm3, with a median of -5.6 mm3 (97.5% CI, -6.8 to -4.0 mm3) (P<.001 vs baseline). Change in total atheroma volume showed a 6.8% median reduction;

with a mean (SD) reduction of -14.7 (25.7) mm3, with a median of -12.5 mm3 (95% CI, -15.1 to -10.5 mm3) (P<.001 vs baseline). Adverse events were infrequent and similar to other statin trials.
Conclusions - Very high-intensity statin therapy using rosuvastatin 40 mg/d achieved an average LDL-C of 60.8 mg/dL and increased HDL-C by 14.7%, resulting in significant regression of atherosclerosis for all 3 prespecified IVUS measures of disease burden. Treatment to LDL-C levels below currently accepted guidelines, when accompanied by significant HDL-C increases, can regress atherosclerosis in coronary disease patients. Further studies are needed to determine the effect of the observed changes on clinical outcome. **(*JAMA.* 2006 Apr 5;295(13):1556-65.)**

Hormone replacement therapy improves arterial stiffness in normotensive postmenopausal women

Sayaka Miura, Eiichi Tanaka, Akiko Mori, Mayumi Toya, Kazuhiro Takahashi, Kenji Nakahara, Masahide Ohmichi, Hirohisa Kurachi

Objectives - Aortic stiffness, determined by the pulse wave velocity (PWV), is an independent marker of cardiovascular risk. PWV is mainly influenced by age-associated alterations of arterial wall structure and blood pressure (BP). To determine the impact of hormone replacement therapy (HRT) on arterial compliance in normotensive, postmenopausal women, we examined the effects of HRT on PWV.
Methods - Fifty-six postmenopausal women aged 50-70 years were recruited into the present retrospective study from the patients visiting our menopause clinic. Twenty-seven women who were prescribed HRT (14 on estrogen alone and 13 on estrogen plus progestogen) for several months to 6 years and an age-matched group of 29 women not on HRT were studied (Study 1). Nine postmenopausal women were also studied before and at 4 weeks of the treatment of estrogen replacement therapy (ERT) (Study 2). Brachial to ankle PWV (baPWV), which is correlated with aortic PWV, was determined using an automatic device, BP-203PRE.
Results - In Study 1, PWV was significantly correlated with age in both groups (controls: r=0.392, P=0.035; HRT group: r=0.471, P=0.013), and HRT significantly lowered the PWV value at all ages examined (Mean+/-S.D. of baPWV in controls: 1382.2+/-114.1; HRT: 1245.3+/-124.8, P=0.0001). In Study 2, baPWV decreased significantly after ERT (P<0.05), without a significant change in systolic BP (P=0.851).
Conclusions - Estrogen appears to improve arterial compliance independently of BP within 4 weeks.
(*Maturitas,* 45 (2003) 293-298.)

Arterial stiffness in postmenopausal women: determinants of pulse wave velocity

Corinne E.I. Lebrun, Yvonne T. van der Schouw, Annette A.A. Bak, Frank H. de Jong, Huibert A.P. Pols, Diederick E. Grobbee, Steven W.J. Lamberts and Michiel L. Bots

Objective - To investigate the degree and potential cardiovascular determinants of arterial stiffness, assessed by aortic pulse wave velocity (PWV) measurements, and to relate arterial stiffness to absolute 10–12-year risks of stroke, coronary heart disease and death, as estimated by available risk functions, in postmenopausal women.
Method - We performed a cross-sectional study among 385 postmenopausal women, aged 50–74 years, sampled from the general population. Arterial stiffness was assessed non-invasively by measurement of aortic PWV using applanation tonometry. Information on health was obtained by medical history, registration of current medication, and physical examination. Height, weight, waist and hip circumferences, fasting glucose, total and high-density lipoprotein (HDL) cholesterol, triglycerides, resting blood pressure, and heart rate were measured. Three risk scores were used to estimate, for each individual, the absolute risk of stroke, coronary heart disease, and death within 10–12 years as a function of their cardiovascular risk factor profile. The relationship between PWV and these risk scores was subsequently determined.
Results - Significant positive relationships with PWV were found for body mass index, fasting glucose, diabetes mellitus, and triglycerides in analyses adjusted for age, mean arterial blood pressure, and heart rate. Height and HDL cholesterol were inversely related to PWV. The risks of stroke, coronary heart disease, and

death increased with increasing PWV in a linear graded manner.
Conclusions **-** This cross-sectional study among postmenopausal women provides evidence that most of the established cardiovascular risk factors are determinants of aortic PWV. Increased PWV marks an increased risk of stroke, coronary heart disease, and death within 10–12 years.
(*Journal of Hypertension,* 2002, 20:2165–2172.)

From Vulnerable Plaque to Vulnerable Patient - Part III: Executive Summary of the Screening for Heart Attack Prevention and Education (SHAPE) Task Force Report

Morteza Naghavi, MD, Erling Falk, MD, PhD, Harvey S. Hecht, MD, Michael J. Jamieson, MD, Sanjay Kaul, MD, MPH, Daniel Berman, MD, Zahi Fayad, PhD, Matthew J. Budoff, MD, John Rumberger, MD, PhD, Tasneem Z. Naqvi, MD, Leslee J. Shaw, PhD, Ole Faergeman, MD, Jay Cohn, MD, Raymond Bahr, MD, Wolfgang Koenig, MD, PhD, Jasenka Demirovic, MD, PhD, Dan Arking, PhD, Victoria L. M. Herrera, MD, Juan Badimon, PhD,r James A. Goldstein, MD,Yoram Rudy, PhD,t Juhani Airaksinen, MD, Robert S. Schwartz, MD, Ward A. Riley, PhD, Robert A. Mendes, MD, Pamela Douglas, MD, and Prediman K. Shah, MD, for the SHAPE Task Force

Screening for early-stage asymptomatic cancers (eg, cancers of breast and colon) to prevent late-stage malignancies has been widely accepted. However, although atherosclerotic cardiovascular disease (eg, heart attack and stroke) accounts for more death and disability than all cancers combined, there are no national screening guidelines for asymptomatic (subclinical) atherosclerosis, and there is no governmentor healthcare-sponsored reimbursement for atherosclerosis screening. Part I and Part II of this consensus statement elaborated on new discoveries in the field of atherosclerosis that led to the concept of the "vulnerable patient." These landmark discoveries, along with new diagnostic and therapeutic options, have set the stage for the next step: translation of this knowledge into a new practice of preventive cardiology. The identification and treatment of the vulnerable patient are the focuses of this consensus statement. In this report, the Screening for Heart Attack Prevention and Education (SHAPE) Task Force presents a new practice guideline for cardiovascular screening in the asymptomatic at-risk population. In summary, the SHAPE Guideline calls for noninvasive screening of all asymptomatic men 45-75 years of age and asymptomatic women 55-75 years of age (except those defined as very low risk) to detect and treat those with subclinical atherosclerosis. A variety of screening tests are available, and the cost-effectiveness of their use in a comprehensive strategy must be validated. Some of these screening tests, such as measurement of coronary artery calcification by computed tomography scanning and carotid artery intimamedia thickness and plaque by ultrasonography, have been available longer than others and are capable of providing direct evidence for the presence and extent of atherosclerosis. Both of these imaging methods provide prognostic information of proven value regarding the future risk of heart attack and stroke. Careful and responsible implementation of these tests as part of a comprehensive risk assessment and reduction approach is warranted and outlined by this report. Other tests for the detection of atherosclerosis and abnormal arterial structure and function, such as magnetic resonance imaging of the great arteries, studies of small and large artery stiffness, and assessment of systemic endothelial dysfunction, are emerging and must be further validated. The screening results (severity of subclinical arterial disease) combined with risk factor assessment are used for risk stratification to identify the vulnerable patient and initiate appropriate therapy. The higher the risk, the more vulnerable an individual is to a near-term adverse event. Because <10% of the population who test positive for atherosclerosis will experience a near-term event, additional risk stratification based on reliable markers of disease activity is needed and is expected to further focus the search for the vulnerable patient in the future. All individuals with asymptomatic atherosclerosis should be counseled and treated to prevent progression to overt clinical disease. The aggressiveness of the treatment should be proportional to the level of risk. Individuals with no evidence of subclinical disease may be reassured of the low risk of a future near-term event, yet encouraged to adhere to a healthy lifestyle and maintain appropriate risk factor levels. Early heart attack care education is urged for all individuals with a positive test for atherosclerosis. The SHAPE Task Force reinforces existing guidelines for the screening and treatment of risk factors in younger populations. Cardiovascular healthcare professionals and policymakers are urged to adopt the SHAPE proposal and its attendant cost-effectiveness as a new strategy to contain the epidemic of atherosclerotic cardiovascular disease and the rising cost of therapies associated with this epidemic. **(*Am J Cardiol*, 2006; 98[suppl]:2H15H)**

Expert consensus document on arterial stiffness: methodological issues and clinical applications

Stephane Laurent, John Cockcroft, Luc Van Bortel, Pierre Boutouyrie, Cristina Giannattasio, Daniel Hayoz, Bruno Pannier, Charalambos Vlachopoulos, Ian Wilkinson, and Harry Struijker-Boudier on behalf of the European Network for Non-invasive Investigation of Large Arteries

In recent years, great emphasis has been placed on the role of arterial stiffness in the development of cardiovascular diseases. Indeed, the assessment of arterial stiffness is increasingly used in the clinical assessment of patients. Although several papers have previously addressed the methodological issues concerning the various indices of arterial stiffness currently available, and their clinical applications, clinicians and researchers still report difficulties in selecting the most appropriate methodology for their specific use. This paper summarizes the proceedings of several meetings of the European Network for Non-invasive Investigation of Large Arteries and is aimed at providing an updated and practical overview of the most relevant methodological aspects and clinical applications in this area. (***European Heart Journal,* (2006) 27, 2588-2605.)**

Citations from this article

„... PWV. Carotid-femoral PWV is considered as the 'gold-standard' measurement of arterial stiffness."

„... Central pulse-wave analysis. Pulse-wave analysis should be optimally obtained at the central level, i.e. at the site of the carotid artery or the ascending aorta, and either directly recorded or computed from the radial artery waveform using a transfer function. Pulse wave should be analyzed through three major parameters: central pulse pressure, central systolic pressure, and the Aix."

„... In addition, aortic stiffness retains its predictive value for CHD events after adjustment to the Framingham risk score, suggesting that aortic stiffness has an added value to a combination of CV risk factors. One reason may be that aortic stiffness integrates the damage of CV risk factors on the aortic wall over a long period of time, whereas BP, glycaemia, and lipids can fluctuate over time and their values, recorded at the time of risk assessment, may not reflect the true values damaging the arterial wall. Another explanation may be that arterial stiffness shows the patients in which arterial risk factors were translated into real risk."

„... Predictive value of arterial stiffness and wave reflection for CV events. A large amount of evidence indicates that carotid-femoral PWV is an intermediate endpoint for CV events, either fatal or non-fatal. Aortic PWV has a better predictive value than classical CV risk factors entering various types of risk score. Central AIx and pulse pressure have shown an independent predictive value for all-cause mortality in ESRD patients and CV events in hypertensives and patients with coronary disease."

„... Several issues remain to be addressed. First, the predictive value of the attenuation of arterial stiffness and wave reflections for the reduction of CV events should be assessed in the long-term, large-scale therapeutic trials. As already noted, we urgently need to conduct clinical trials to determine whether a reduction in arterial stiffness is a desirable therapeutic goal in terms of hard clinical endpoints such as morbidity and mortality. To our knowledge, this has been done only once, in patients with ESRD, and not in a population of patients with hypertension or at low CV risk."

„... For instance, the predictive value of aortic PWV for primary CHD events in hypertensive patients was more marked for patients consideredas at low risk, i.e. belonging to the first and second tertiles of the Framingham risk score, than for patients at high risk (i.e. belonging to the third tertile of the score), indicating that this low-to-intermediate risk population benefited the most of risk assessment with PWV."

(2) ESH guidelines 2007

ESH Guidelines 2007 (Extract)

2007 Guidelines for the Management of Arterial Hypertension
The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Authors/Task Force Members: G. Mancia (Co-Chairperson); G. De Backer (Co-Chairperson); A. Dominiczak; R. Cifkova; R Fagard; G. Germano; G. Grassi; A. M. Heagerthy; S. E. Kjeldsen; S. Laurent; K Narkiewicz; L. Ruilope; A. Rynkiewitz; R. E. Schmieder; H. A.J. Struijker Boudier; A. Zanchetti

2. Definition and classification of hypertension
2.3 Total cardiovascular risk
2.3.2 Assessment

Estimation of total cardiovascular risk is simple in particular subgroups of patients such as those with 1) a previous diagnosis of cardiovascular disease, 2) type 2 diabetes, 3) type 1 diabetes, and 4) individuals with severely elevated single risk factors. In all these conditions the total cardiovascular risk is high, calling for the intense cardiovascular risk reducing measures that will be outlined in the following sections. However, a large number of hypertensive patients does not belong to one of the above categories and identification of those at high risk requires the use of models to estimate total cardiovascular risk so as to be able to adjust the intensity of the therapeutic approach accordingly.
Several computerized methods have been developed for estimating total cardiovascular risk, i.e. the absolute chance of having a cardiovascular event usually over 10 years. However, some of them are based on Framingham data which are only applicable to some European populations due to important differences in the incidence of coronary and stroke events. More recently, a European model has become available based on the large data-base provided by the SCORE project. SCORE charts are available for high and low risk countries in Europe. They estimate the risk of dying from cardiovascular (not just coronary) disease over 10 years and allow calibration of the charts for individual countries provided that national mortality statistics and estimates of the prevalence of major cardiovascular risk factors are known. The SCORE model has also been used in the HeartScore, the official ESC management tool for implementation of cardiovascular disease prevention in clinical practice. This is available on the ESC Web Site (www.escardio.org).

Fig. 1

	Blood pressure				
Other risk factors, OD or Disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP ≥ 180 or DBP ≥ 110
No other risk factors	Average risk	Average risk	Low added risk	Moderate risk	High added risk
1-2 Risk factors	Low added risk	Low added risk	Moderate risk	Moderate risk	Very high added risk
3 or more risk factors, MS, OD or Diabetes	Moderate risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

The 2003 ESH/ESC Guidelines classified the total cardiovascular risk based on the scheme proposed by the 1999 WHO/ISH Guidelines on hypertension with the extension to subjects with “normal” or “high normal” blood pressure. This classification is retained in the present Guidelines (Fig. 1 The stratification of CV Risk in four categories). The terms “low”, “moderate”, “high” and “very high” risk are used to indicate an approximate risk of cardiovascular morbidity and mortality in the coming 10 years, which is somewhat analogous to the increasing level of total cardiovascular risk estimated by the Framingham or the SCORE models. The term

"added" is used to emphasize that in all categories relative risk is greater than average risk. Although use of a categorical classification provides data that are in principle less precise than those obtained from equations based on continuous variables, this approach has the merit of simplicity. The 2003 WHO/ISH Guidelines have further simplified the approach by merging the high and very high risk categories which were regarded as similar when it came to making treatment decisions. The distinction between high and very high risk categories has be en maintained in the present guidelines, thereby preserving a separate place for secondary prevention, i.e. prevention in patients with established cardiovascular disease. In these patients, compared with the high risk category, not only can total risk be much higher, but multidrug treatment may be necessary throughout the blood pressure range from normal to high. The dashed line drawn in Fig. 1 illustrates how total cardiovascular risk evaluation inltuences the definition of hypertension when this is correctly considered as the blood pressure value above which treatment does more good than harm.

Table 2 Factors influencing prognosis

Risk factors - Systolic and diastolic BP levels - Levels of pulse pressure (in the elderly) - Age (M > 55 years;W > 65 years) - Smoking - Dyslipidaemia (TC > 5.0 mmol/l (190 mg/dl) or: LDL-C > 3.0 mmol/l (115 mg/dl) or: HDL-C: M < 1.0 mmol/l (40 mg/dl), W < 1.2 mmol/l (46 mg/dl) or: TG > 1.7 mmol/l (150 mg/dl) - Fasting plasma glucose 5.6-6.9 mmol/l (102-125 mg/dl) - Abnormal glucose tolerance test - Abdominal obesity (Waist circumference > 102 cm (M), > 88 cm (W) - Family history of premature CV disease (M at age < 55years, W at age < 65 years)	Subclinical Organ damage - Electrocardiographic LVH (Sokolow-Lyon > 38 mm; Cornell > 2440 mm*ms) - Echocardiographic LVH (LVMI M ≥ 125 g/m^2, W ≥ 110 g/m^2) - Carotid wall thickening (IMT > 0.9 mm) or plaque - Carotid-femoral pulse wave velocity > 12 m/s - Ankle/brachial BP index < 0.9 - Slight increase in plasma creatinine: M: 115-133 µmol/l (1.3-1.5 mg/dl) W: 107-124 µmol/l (1.2-1.4 mg/dl) - Low estimated glomerular filtration rate (< 60 ml/min/1.73m^2) or creatinine clearance (< 60 ml/min) - Microalbuminura 30-300 mg/24 h or albumin-creatinine ratio: ≥ 22 (M); or ≥ 31 (W) mg/g creatinine
Diabetes mellitus - Fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl) on repeated measurements, or - Postload plasma glucose > 11.0 mmol/l (198 mg/dl)	Established CV or renal disease - Cerebrovascular disease: ischemic stroke; cerebral haemorrhage; transient ischaemic attack - Heart disease: myocardial infarction; angina; coronary revascularization; heart failure - Renal disease: diabetic nephropathy; renal impairment (serum creatinine M > 133, W > 124 mmol/l); proteinuria (> 300 mg/24 h) - Peripheral artery disease - Advanced retinopathy: haemorrhages or exsudates, papilloedema

Note: the cluster of three out of risk factors among abdominal obesity, altered fasting plasma glucose, BP ≥ 130/85 mmHg, low HDL-Cholesterol and high TG (as defined above) indicates the presence of metaboloc syndrome.

M: man; W: woman; CV: cardiovascular disease; IMT: intima-media thickness; BP: blood pressure; TG: triglycerides; C: cholesterol.

Table 2 (Factors influencing prognosis) indicates the most common clinical variables that should be used to stratify the risk. They are based on risk factors (demographics, anthropometrics, family history of premature cardiovascular disease, blood pressure, smoking habits, glucose and lipid variables), measures of target organ damage, and diagnosis of diabetes and associated clinical conditions as outlined in the 2003 Guidelines. The following new points should be highlighted:

1. The metabolic syndrome has been mentioned because it represents a cluster of risk factors often associated with high blood pressure which markedly increases cardiovascular risk. No implication is made that it represents a pathogenetic entity.
2. Further emphasis has been given to identification of target organ damage, since hypertension-related subclinical alterations in several organs indicate progression in the cardiovascular disease continuum which markedly increases the risk beyond that caused by the simple presence of risk factors. A separate Section is devoted to searching for subclinical organ damage where evidence for the additional risk of each subclinical alteration is discussed and the proposed cutoff values are justified.

3. The list of renal markers of organ damage has been expanded, to include estimates of creatinine clearance by the Cockroft-Gault formula or of glomerular filtration rate by the MDRD formula, because of the evidence that these estimated values are a more precise index of the cardiovascular risk accompanying renal dysfunction.
4. Microalbuminuria has now been considered as an essential component in the assessment of organ damage because its detection is easy and relatively inexpensive.
5. Concentric left ventricular hypertrophy has been identified as the cardiac structural parameter that more markedly increases cardiovascular risk.
6. Whenever possible the recommendation is made to measure organ damage in different tissues (e.g. heart, blood vessels, kidney and brain) because multiorgan damage is associated with a worse prognosis.
7. Increased pulse wave velocity is added to the list of factors influencing prognosis as an early index of large artery stiffening, although with the caveat that it has a limited availability in the clinical practice.
8. A low ankle to brachial blood pressure ratio (<0.9) is listed as a relaltively easy to obtain marker of atherosclerotic disease and increased total cardiovascular risk.
9. Not only is assessment of organ damage recommended pre-treatment (in order to stratify risk) but also during therapy because of the evidence that regression of left ventricular hypertrophy and reduction of proteinuria indicate treatment-induced cardiovascular protection.
10. There may be reasons to include an elevated heart rate as a risk factor because of a growing body of evidence that elevated heart rate values relate to the risk of cardiovascular morbidity and mortality as well as to all cause mortality. Also, there is evidence that an elevated heart rate increases the risk of new onset hypertension and is frequently associated with metabolic disturbances and the metabolic syndrome. However because of the wide range of accepted resting heart rate normality values (60 to 90 beats/min), no cutoff heart rate can be offered presently to increase the accuracy of total cardiovascular risk stratification.
11. The major diagnostic elements for classifying subjects in the high or very high risk categories are summarized in Table 3. It is worth noticing that multiple risk factors, diabetes or organ damage invariably place a subject with hypertension, and even with high normal blood pressure, in the high risk category.

Table 3 High/Very high risk subjects

- BP ≥ 180 mmHg systolic and/or ≥ 110 mmHg diastolic
- Systolic BP > 160 mmHg with low diastolic BP (<70 mmHg)
- Diabetes mellitus
- Metabolic syndrome
- ≥ 3 cardiovascular risk factors
- One or more of te following subclinical organ damages:
  - Electrocardiographic (particularly with strain) or echocardiographic (particularly concentric) left ventricular hypertrophy
  - Ultrasound evidence of carotid artery wall thickening or plaque
  - **Increased arterial stiffness**
  - Moderate increase in serum creatinine
  - Reduced estimated glomerular filtration rate of creatinine clearance
  - Microalbuminuria or proteinuria
- Established cardiovascular or renal disease

3. Diagnostic evaluation

3.1 Blood pressure measurement

3.1.7 Central blood pressure

Due to the variable superimposition of incoming and reflected pressure waves along the arterial tree, aortic systolic and pulse pressure (i.e. the pressure exerted at the level of the heart, brain and kidney) may be different from the conventionally measured brachial pressure. Furthermore, the claim has long been made that peripheral and central systolic and pulse pressures may be differently affected by antihypertensive drugs. The need for invasive measurement of central blood pressure has confined this issue to research. However, recently a mehod has been described to non-invasively estimate aortic blood pressure by calculating the „augmentation index" from the pulse wave pressure contour recorded from a peripheral artery. Use of this method has confirmed that the effects of antihypertensive drugs on central systolic and pulse pressure do non invariably reflect those seen at the brachial artery level. Furthermore, the results obtained in a large substudy performed within a randomized trial have shown that **central pulse pressure as assessed from the „augmentation index" is significantly related to cardiovascular events**. However, the prognostic role of central as opposed to peripheral blood pressure needs to be further confirmed in more large-scale observational and interventional studies. **(*Journal of Hypertension,* 2007, 25:1105-1187.)**

(3) aortic blood pressure

Differential Impact of Blood Pressure Lowering Drugs on Central Aortic Pressure and Clinical Outcomes Principal Results of the Conduit Artery Function Evaluation (CAFE) Study

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Background - Different blood pressure (BP) lowering drugs could have different effects on central aortic pressures and thus cardiovascular outcome despite similar effects on brachial BP. The Conduit Artery Function Evaluation (CAFE) study, a substudy of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), examined the impact of 2 different BP lowering-regimens (atenolol±thiazide-based versus amlodipine±perindopril-based therapy) on derived central aortic pressures and hemodynamics.

Methods and Results - The CAFE study recruited 2199 patients in 5 ASCOT centers. Radial artery applanation tonometry and pulse wave analysis were used to derive central aortic pressures and hemodynamic indexes on repeated visits for up to 4 years. Most patients received combination therapy throughout the study. Despite similar brachial systolic BPs between treatment groups (0.7 mm Hg; 95% CI, 0.4 to 1.7; P=0.2), there were substantial reductions in central aortic pressures with the amlodipine regimen (central aortic systolic BP, 4.3 mm Hg; 95% CI, 3.3 to 5.4; P<0.0001; central aortic pulse pressure, 3.0 mm Hg; 95% CI, 2.1 to 3.9; P<0.0001). Cox proportional-hazards modeling showed that central pulse pressure was significantly associated with a post hocdefined composite outcome of total cardiovascular events/procedures and development of renal impairment in the CAFE cohort (unadjusted, P<0.0001; adjusted for baseline variables, P<0.05).

Conclusions - BP-lowering drugs can have substantially different effects on central aortic pressures and hemodynamics despite a similar impact on brachial BP. Moreover, central aortic pulse pressure may be a determinant of clinical outcomes, and differences in central aortic pressures may be a potential mechanism to explain the different clinical outcomes between the 2 BP treatment arms in ASCOT. **(*Circulation,* 2006;113:1213-1225.)**

(4) the research project

Dear Reader,

TensioMed™ Arteriograph is a Hungarian research success story .

The project began in 2001, within the framework of the National Research and Development Program, with the purpose of creating a fast, simple and reliable method for examining the flexibility of the arteries. At the time there was no technique that was widely used for routine examination and screening of the arteries; examinations of arterial stiffness were carried out only at special laboratories and mainly with research objectives.

The Research Consortium was a cooperation of numerous acknowledged Hungarian institutions, such as the Hungarian Academy of Science, Semmelweis University and St.Imre Hospital, under the guidance of TensioMed Ltd.

The reason for the project was based on the fact that the decrease in elasticity, the stiffening of the arteries is the earliest sign of arteriosclerosis. In recent years, research has proven that if arteriosclerosis is recognized at an early stage, there is a good opportunity to slow down desease progress in the patient by administering proper treatment. Since cardiovascular disease of atherosclerotic origin (e.g. stroke, heart attack) is the cause of one in two deaths, it is clear that early diagnosis could assist in decreasing cardiovascular mortality and increasing life expectancy.

During the research we introduced special devices to the homes of over 650 patients. These not only measured blood pressure and pulse rate, but also stored complete oscillation pulse curves. Using telemedicine, these data were transferred automatically to our research computer system. In this way we created the world's biggest oscillometric database, in which we could store over 1,700,000 pulse curves with clinical and laboratory data. This database was the basis of the research, and by modern, mathematical analysis of these recorded data we were able to gain further factual information and to explain these diverse and heterogenic oscillation pulse curves in point of hemodynamic principles.

As a result of our work, the method and the device TensioMed™ Arteriograph itself has been created. The parameters measured - Augmentation Index (Aix), Pulse Wave Velocity (PWV) - are validated by both invasive and non-invasive methods, and the correlation is high in all cases.

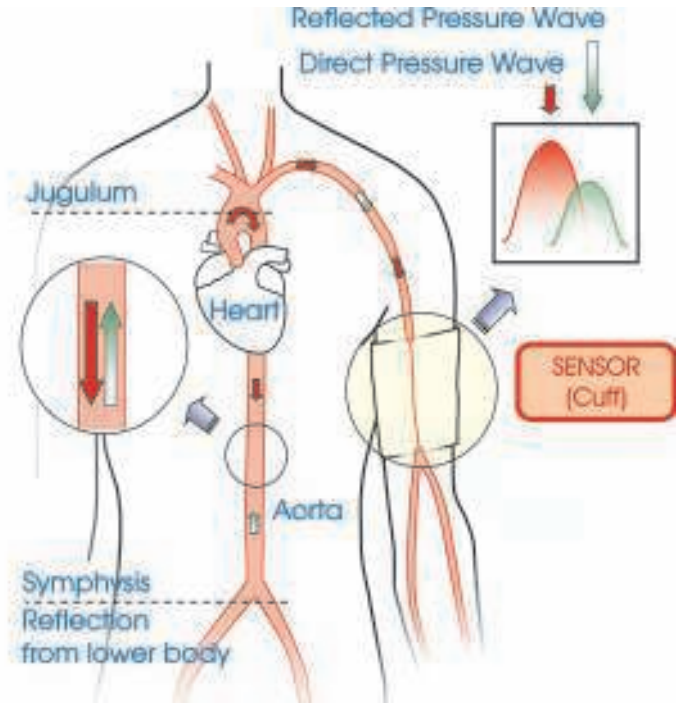
With the invention of TensioMed™ Arteriograph a simple, quick, and userindependent method is now available for cardiovascular prevention.
The introduction of the device as a means of population screening would improve the patients' cardiovascular risk stratification, and due to the detection of an early stage of atherosclerosis the appropriate therapy can be initiated.

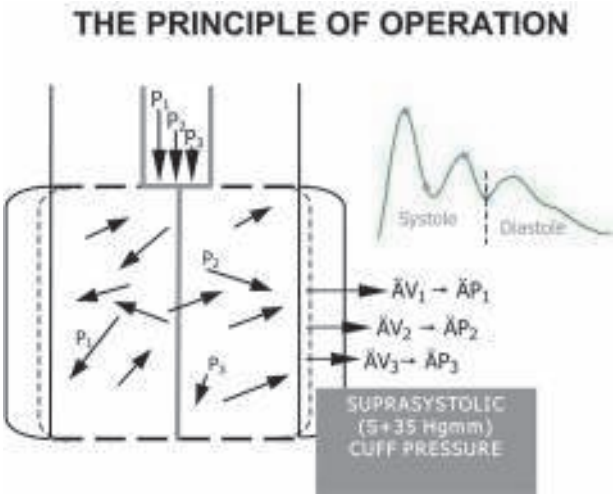
Illyés Miklós MD, Phd
Head of the research consortium

(5) measuring and parameters

The principle of operation and the parameters measured

The novelty of the Arteriograph device is that a simple upper arm cuff is used as a sensor, but in a unique manner; the device first measures the actual blood pressure and then immediately the cuff is pressurized at least 35 mmHg over the actual systolic pressure (S35). The recording time at suprasystolic pressure can be set between 8-20 seconds (8 seconds is generally used). By creating this stop-flow condition a small diaphragm will develop in the brachial artery at the level of the upper edge of the over-pressurized cuff. The central pressure changes as early (direct) systolic wave (P1), late (reflected) systolic wave (P2) and diastolic wave (P3) reach this point and cause beats, one after one, like a drumstick on the membrane. Because the upper arm tissues are practically incompressible, the pressure wave propagates and reaches the skin - over-pressurized cuff edge without any distortion, where it causes a very small volume/pressure change in the cuff, which can be recorded by a high-fidelity pressure sensor and then amplified and filtered in the special tonometer. In this situation the conduit arteries (subclavian, axillary, brachial) act like a cannula to transfer the central pressure changes to the edge-position sensor (similar to the central pressure measurement during catheterization). It is noteworthy to mention that in this set-up the influence of the characteristics of the brachial artery's wall is eliminated, and the received curves are determined by the central hemodynamics.





On the upper figure it can be seen that the recorded pulse wave (on the right upper side of the picture) measured with the Arteriograph at suprasystolic pressure includes the earlier (P1) and the later (P2) systolic wave. The valley caused by the closing of the aorta valve is clearly recognizable as well as the diastolic wave (P3).

All of the signals received by the tonometer are transmitted wirelessly via infrared to notebook or desktop PC providing a complete electric isolation of the patient from the computer. The data analysis is performed by the software designed for this purpose.

Parameters provided by the Arteriograph

- Brachial Augmentation Index (Aix brachial) - measured
- Aortic Augmentation Index (Aix aortic) - calculated
- Aortic Pulse Wave Velocity (PWVao) - measured
- Standard Deviation (SD) of the beat to beat PWVao (quality control)
- Return Time (from aortic root to bifurcation and back - RT) - measured
- Peripheral (brachial) SBP, DBP, MAP, PP, HR - measured
- Central (aortic) Systolic Blood Pressure (SBPao) - calculated
- Systolic and Diastolic Area Index (SAI, DAI) - measured
- Diastolic Reflection Area (DRA) - measured

SAMPLE REPORT 1 - HEALTHY PATIENT

TensioMed™ Arteriograph

Arterial Stiffness Report

Patient details

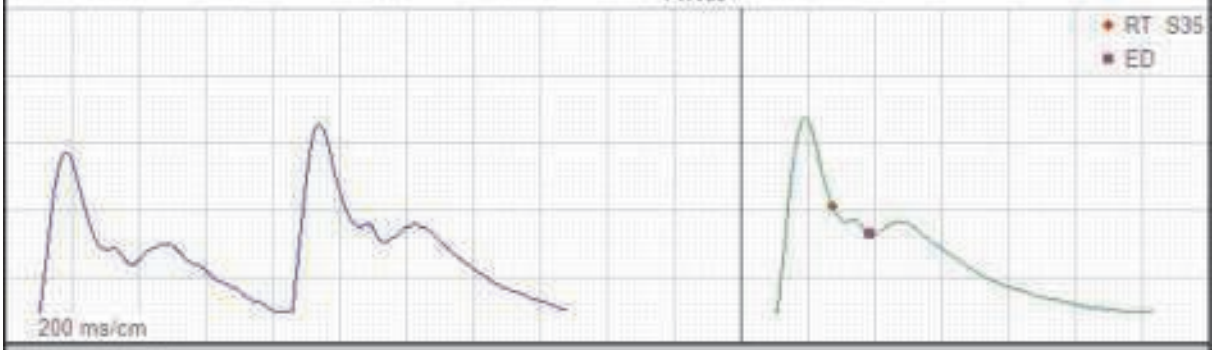
Name:
Date of Birth: 29.03.1974. Height: 178 cm BMI: 23.36 Cholesterol: 4.00 mmol/l
Sex: Male Weight: 74 kg Smoker: Yes
Comment:

Study data

Examination date and time: 27.05.2007. 16:12 JUG-SY: 54 cm
Operator's name: ARTERIOGRAM
Sys: 147 mmHg Dia: 81 mmHg HR: 81 /min MAP: 103 mmHg PP: 66 mmHg

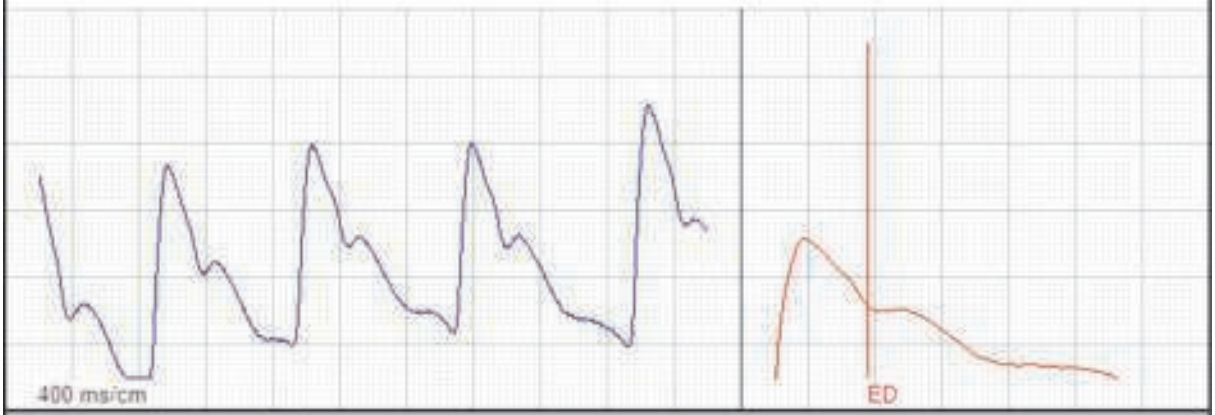
Results S 35

Aix brachial: -53.38 % ED: 285 ms PWVao: 6.25 m/s SBPao: 129.85 mmHg
Aix aortic: 9.94 % RT: 173 ms SD_{PWVao}: 0.33 m/s



Results D

DRA: 39 SAI: 44.97 % DAI: 55.03 %



Automatic analysis

Aix brachial: -53.38 % optimal PWVao: 6.25 m/s optimal

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TensioMed™ Software v.1.9.9.4

SAMPLE REPORT 2 - ILL PATIENT

TensioMed™ Arteriograph

Arterial Stiffness Report

Patient details

Name:	BK						
Date of Birth:	23.04.1956.	**Height:**	158 cm	**BMI:**	20.03	**Cholesterol:**	
Sex:	Female	**Weight:**	50 kg	**Smoker:**	Yes		

Comment:

10 year risk of fatal CVD (EHRC score):

Study data

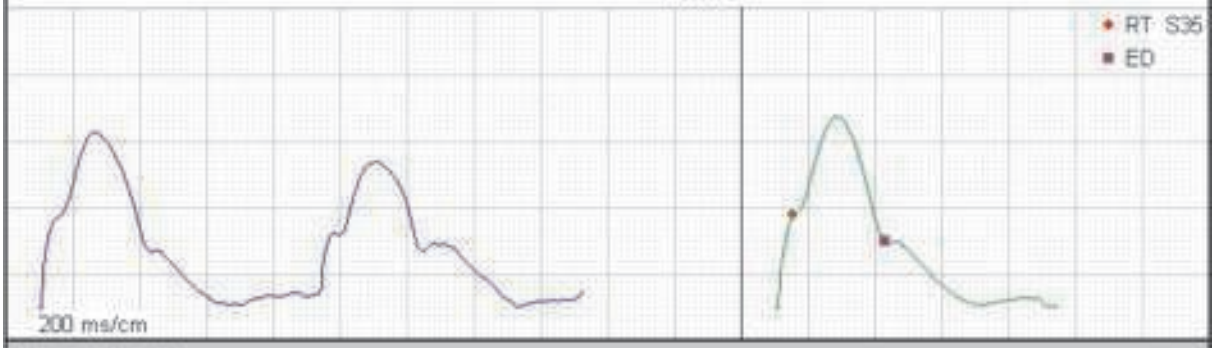
Examination date and time: 25.05.2006. 14:33 **JUG-SY:** 47 cm

Operator's name: ARTERIOGRAM

Sys: 147 mmHg **Dia:** 85 mmHg **HR:** 78 /min **MAP:** 106 mmHg **PP:** 62 mmHg

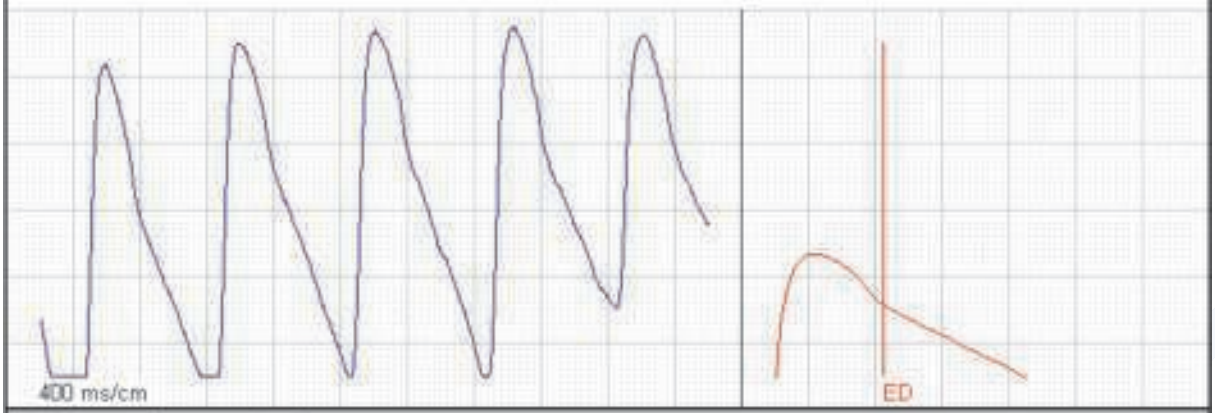
Results S 35

Aix brachial:	50.26 %	**ED:**	330 ms	**PWVao :**	17.29 m/s	**SBPao:**	154.35 mmHg
Aix aortic:	53.88 %	**RT :**	54 ms	**SD_{PWVao} :**	1.45 m/s		



Results D

DRA: 39 **SAI:** 56.95 % **DAI:** 43.05 %



Automatic analysis

Aix brachial: 50.26 % abnormal **PWVao :** 17.29 m/s abnormal

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(7) publications and validation

A new and fast screening method for measuring complex hemodynamical parameters and arterial stiffness noninvasively with a simple arm cuff

Miklos Illyes. TensioMed Ltd., TensioMed Ltd, Budapest, Hungary.

Aims - In a project of the National Research Program of Hungary, we studied if oscillometric signals received during an oscillometric BP measurement contain any information about arterial hemodynamics.
Materials, Methods - We have developed a research tool by which not only SBP, DBP, HR data, but the complete oscillometric signals were stored and transmitted telemedically to our computer center from the home of 650 patients who performed BP measurements at least 4 times a day, for at least 1 month. Through this a large database was collected, containing more than 1,700,000 oscillometric pulse curves and the relevant clinical data of patients. For data mining we used Kohonen's self-organising map method. Non-invasively recorded oscillometric curves from the upper arm cuff were validated by the simultaneously recorded intraarterial pressure curve of brachial artery.
Results - Our researches showed that oscillometric pulse curve of the brachial artery is identical to the intraarterial pressure curve if the cuff was inflated to suprasystolic pressure, preferably 35 mmHg above the SBP. Thus the early and the late systolic pressure peak, the closing incisure of the aortic valve can be recognizable, and several hemodinamical parameters could be calculated. By using the mentioned results of basic researches, a new instrument, the TensioClinic Arteriograph was developed, by which the following parameters could be measured within 2 minutes, by using a simple upper arm cuff: SBP, DBP, HR, MAP,PP, augmentation index (AIx), normalized augmentation index to 80/min heart rate (AIx80), return time of the pulse wave of the aorta (RT), pulse wave velocity (PWV) of the aorta, length of the cardiac cycle, area of systolic (SAI) and diastolic (DAI) part of pulse curve. Validation studies of the new method to control the accuracy of measured AIx and PWV showed high correlations (R = 0,76 and R = 0,8) with values measured with other noninvasive methods (Sphygmocor and Complior) respectively.
Conclusions - Due to the swiftness, simplicity and good reproducibility of this method and apparatus, the non-invasive assessment of the most important hemodynamical parameters and arterial stiffness had become available for population screening, opening a new window in the detection of the early phase of the athero- and arteriosclerosis, and thus it can play an important role in the reduction of the CV morbidity and mortality.
(*American Journal of Hypertension,* May 2005-VOL. 18, NO. 5, PART 2)

Blood pressure and arterial stiffness

A comparison of two devices for measuring augmentationindex and pulse wave velocity

Magometschnigg D., Institut für Hypertoniker, Wien, Österreich

Augmentationindex (AIx) and Pulse Wave Velocity (PWV) give much more information on the function of the arterial tree than that obtained by blood pressure recordings. The rediscovered value of arterial stiffness measured by means of AIx or PWV is now proven as an independent cardiovascular risk factor and helps to differentiate patients at risk and their cardiovascular treatment offer. In the last decade, the methods to measure and to calculate AIx and PWV have become increasingly simple. But as the different methods use different strategies for measuring and calculating these parameters, the results concerning the same term vary, depending on the device used. We undertook nearly simultaneous recordings of AIx in 400 and of PWV in 100 treated hypertensive patients with the very new TensioClinic device developed by M. Illyés, and compared those data with measurements obtained by the SphygmoCor device. The absolute values of m (mean) and SD (standard deviation) of AIx were when TensioClinic was used m: -6.2 % +/- SD:37.9 % and by SphygmoCor m: 26,2 % +/- SD: 11,8 %. The differences were caused by the different methods. As both devices measure the same quality of vascular function, the results correlate closely with a correlation coefficient r = 0.77. In PWV the results of Aortic PWV measured by TensioClinic were

m: 9.1 +/- SD: 1.8m/sec and of brachial PWV measured by SphygmoCor: 8.4 +/- SD: 1.5 m/sec. As in AIx, these results were also different, but in contrast to AIx they did not correlate (r = -0.04) because PWV depend on the artery and its physical characteristics, and we measured once the aorta (TensioClinic) and once predominantly the arteria brachialis (SphygmoCor).
(*Wien Med Wochenschr*, 2005; 155/17-18; 4040-410.)

Eine neue oszillometrische Methode zur Bestimmung der arteriellen Gefäßsteifigkeit Vergleich zu tonometrischer und piezo-elektronischer Methode

J Baulmann, U Schillings, S Rickert, S Uen, R Düsing, H Vetter, T Mengden,
Medizinische Poliklinik der Universität Bonn, Bonn

Hintergrund und Fragestellung - Pulswellen-Geschwindigkeit (PWV) ist ein direkter Parameter der arteriellen Gefäßsteifigkeit und ein starker Indikator erhöhten kardiovaskulären Risikos. Ziel der Studie ist, das neue einfach anzuwendende oszillometrische System (Arteriograph) zur Bestimmung von PWV gegen 2 klinisch validierte, breit akzeptierte tonometrische und piezo-elektronische Systeme (SphygmoCor und Complior) zu validieren.
Patienten und Methodik - PWV wurde bei 51 Patienten jeweils bis zu 5 mal mit SphygmoCor und Arteriograph (PWV und AIx) und Complior (PWV) gemessen. 36 von ihnen in einer 2.Sitzung gleichen Protokolls erneut.
Ergebnisse - Im Vergleich der jeweiligen tonometrischen und piezo-elektronischen zur oszillometrischen Methode korrelieren diePWVs von Arteriograph zu SphygmoCor r=0,67 und Arteriograph zu Complior r=0,69 jeweils hochsignifikant (p<0,001).
Schlussfolgerung - Mit dem Arteriograph steht eine neue, sehr einfach anzuwendende, Untersucherunabhängige und kostengünstige oszillometrische Methode zur Messung der arteriellen Gefäßsteifigkeit und der Pulswellen-Reflexion zur Verfügung. **(*Dtsch med Wochenschr,* 2006; 131 DOI: 10.1055/s-2006-956701)**

Varianz und Reproduzierbarkeit einer neuen oszillometrische Methode zur Bestimmung der arteriellen Gefäßsteifigkeit Vergleich zu tonometrischer und piezo-elektronischer Methode

J Baulmann, U Schillings, S Rickert, S Uen, R Düsing, H Vetter, T Mengden,
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Hintergrund und Fragestellung - Pulswellen-Geschwindigkeit (PWV) ist ein direkter Parameter der arteriellen Gefäßsteifigkeit und ein starker Indikator erhöhten kardiovaskulären Risikos. Ziel der Studie ist, das neue oszillometrische System (Arteriograph) zur Bestimmung von PWV gegen 2 klinisch validierte, breit akzeptierte tonometrische und piezo-elektronische Systeme (SphygmoCor und Complior) hinsichtlich der Varianz und Reproduzierbarkeit zu validieren.
Patienten und Methodik - PWV und AIx wurde bei 51 Patienten jeweils bis zu 5 mal mit SphygmoCor und Arteriograph (PWV und AIx) und Complior (PWV) gemessen. 36 von ihnen in einer 2.Sitzung gleichen Protokolls erneut. Die Varianz wurde als Schätzung der Messfehler für die Wiederholungsmessungen innerhalb einer Sitzung gemäß Bland-Altman in m2/s2 berechnet; die Reproduzierbarkeit für die Wiederholungsmessungen zwischen 2 Sitzungen.
Ergebnisse - Die Varianz der PWV ist für den Arteriograph am niedrigsten (0,18 m2/s2), gefolgt von Complior (0,31 m2/s2) und SphygmoCor (0,36
m2/s2). Die Reproduzierbarkeit ist ebenfalls am geringsten in der Reihenfolge Arteriograph (1,18 m2/s2), Complior (1,55 m2/s2) und SphygmoCor (1,67 m2/s2).
Schlussfolgerung - Mit dem Arteriograph steht eine neue, sehr einfach anzuwendende, Untersucher-unabhängige und kostengünstige oszillometrische Methode zur Messung der arteriellen Gefäßsteifigkeit und der Pulswellen-Reflexion zur Verfügung. **(*Dtsch med Wochenschr,* 2006; 131 DOI: 10.1055/s-2006-956702)**

Arteria brachialis flow-mediated vasodilatation, carotis intima-media thickness and augmentation index (AIx) - comparative studies

Dr. Dér Henrietta, Dr. Kerekes György, Dr. Veres Katalin, Dr. Szomják Edit, Dr. Soltész Pál

Summary - Authors developed a prospectiv methodical study to investigate the relationship between brachial artery flow-mediated vasodilation, nitrate-mediated vasodilation, carotid artery intima-media thickness and the augmentation index measured by TensioClinic arteriograph and pulse wave velocity. 90 patients with different type of vasculopathy (primary antiphospholipid syndrome, hypertony, diabetes mellitus, progressiv systemic sclerosis, rheumatoid arthritis) were investigated. Brachial arterial flow-mediated dilation was assessed using high-resolution ultrasonography (10 MHz linear transducer) in patients. The flow- mediated values (FMD) were measured by offline method with AVITA softver. Authors found strong negativ linear correlation between augmentation index and flow mediated-vasodilation (R= -0,4413; p<0,001) and middle strong significant correlation between intima-media thickness and augmentation index (R= -0,3013; p=0,013). The correlation is also significant between pulse wave velocity, flow-mediated vasodilation (R= -0,3207; p=0,008) and carotid artery intima-media thickness (R= 0,2829; p<0,0001). Patients who had impaired flow-mediated vasodilation had simultaneously pathological increased augmentation index and pulse wave velocity. **(Lecture on the 16th Congress of the Hungarian Atherosclerosis Society, Sopron, 13.10.2006.)**

Invasive validations of a new oscillometric device (Arteriograph) for measuring arterial stiffness

I. Horvát, A. Cziráki, L. Papp
Heart center and 1st department of Internal Medicine, University of Pécs, Hungary

Objective - To validate invasively a new apparatus (Arteriograph), which can measure augmentation index (Aix) and aortic pulse wave velocity (PWVao) simultaneously, within 2-3 minutes. According to the available literature data not any non-invasive device for measuring PWVao was validated with invasive method.
Design and method - Our comparative study was performed on 36 patients who underwent routine coronarography for diagnostic purposes. In 10 cases we measured the brachial Aix and aortic Aix with catheter and the brachial Aix with Arteriograph on identical pulses. In 26 cases the invasively and non-invasively measured PWVao were compared. In 11 cases we used 2 catheters (inserted from radial and femoral artery) positioned to the aortic root and to the aortic bifurcation and the transit time of the pulse wave was measured on identical heart cycles. In the remnant cases the PWVao was determined with one catheter with pull back from the aortic root to the bifurcation and the transit time was measured using ECG gating. All of the invasively measured transit time were determined by intersecting tangent algorithm on te pulse waves recorded in the aortic root and bifurcation. The aortic root-bifurcation distance was measured by marking the cannula in the aortic root and after its pull back to the bifurcation, and was compared to the non-invasively measured sternal notch-pubic bone distance.
Results - The R values (Pearson's correlation) between invasively and Arteriograph measured Aix brachial/brachial, Aix aortic/brachial and PWVao were 0.92 (p<0.001), 0.92 (p<0.001) and 0.78 (p<0.001) respectively. With Bland-Altman plots te differences were within 2SD in all of the compared parameters and no significant deviation from the zero line was found in different ranges of the measured values. The aortic root-bifurcation and sternal notch-pubic bone distance strongly correlated to each other (R=0.75, p<0.001) and the difference (0.4 cm) between their means did not prove to be significant (0.36).
Conclusions - The new oscillometric Arteriograph device can measure accurately the central (aortic) and the peripheral (brachial) Aix and aortic PWV. The simplicity (due to oscillometric principle) of the use of this new method to determine stiffness parameters may help to spread more widely, even in primary care the measurement of the arterial stiffness parameters, of which importance is gaining ground rapidly nowadays in the detection of asymptomatic arterial disease. **(ESH Milan Meeting - *Seventeenth European Meeting on Hypertension, Milan*, 18.06.2007; Poster Session 31 - Blood pressure measurement)**

Arterial stiffness and coronary artery disease

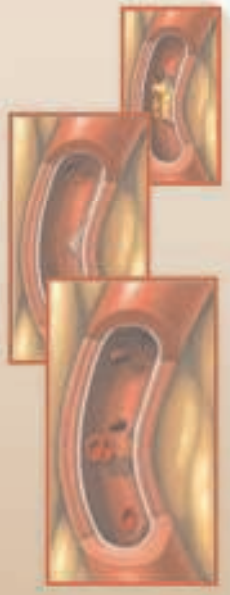
A. Cziráki, M. Illyés, L. Papp

Objective - Although classical risk factors are responsible in about 90% for the development of the coronary artery disease (CAD) their predictive value is weak, because of the very different susceptibility of the subjects to the risk factors. For this reason newer methods are sought to improve te risk assessment. Aortic pulse wave velocity (PWVao) and aortic augmentation index are known to relate with the adverse cardiac outcome. However, few studies measure both parameters together and even fewer the brachial augmentation index (Aix-br). Our aim was to assess the relationship between Aix-br and PWVao with CAD proven by coronarography.
Design and method - Aix-br and PWVao were measured simultaneously with a new oscillometric device (Arteriograph) in 110 patients on the same day, but in time before of the diagnostic coronarography. The coronarography was considered to be positive if at least 1 vessel was narrowed with 50%. The control group was recruited from patients with negative coronarography and from asymptomatic aged matched general population group (n=399).
Results - Out of the 110 patients coronarography proved to be positive (C+) in 73 and negative (C-) in 37 cases. In the C+ group the mean Aix-br was 4.6±25.9%, the mean PWVao 10.7±2 m/s, while in the C- group these parameters were significantly lower (Aix-br -5.8±24.7%, PWVao 8.8±1.6 m/s, $p<0.05$ and $p<0.001$ respectively). We did not find any statistical difference between these groups concerning classical risk factors. If we compared the C+ group with the age matched general population we also found significantly lower values in the control group (Aix-br -10.9±23.8%, PWVao 9.5±1.9 m/s, $p<0.001$). If we compared the mean Aix-br (1.1±25.9%) and PWVao (10.1±2.1m/s) values of the total number of the patients who underwent coronargraphy (C+ and C-) with the general population control, the differences proved to be also significant ($p<0.001$). The classical risk factors did not show any statistical difference in this comparison, as well.
Conclusions - Our results showed that increased Aix-br and PWVao were independent markers from the classical risk factors for CAD. The mean difference in PWVao between C+ and C- groups reached as much as 1.9m/s, which higlights the relationship between the stiffened aorta and macrovascular atherosclerotic (e.g. coronary) lesions. We can conclude that the measurement of the stiffness parameters with Artetriograph (even Aix-br) provides additive information for revealing CAD. (**ESH Milan Meeting - *Seventeenth European Meeting on Hypertension, Milan*, 18.06.2007; Poster Session 33 - Large Arteries)**

Invitation
to the

4th International Symposium on Arterial Stiffness
and
2nd Congress of the Hungarian Arterial Stiffness Society

22-23 February, 2008
Danubius Health Spa Resort Margitsziget,
Budapest, Hungary



Organizing committee:
Hungarian Arterial Stiffness Society
Chairman: *Miklós Illyés MD, Phd*
Secretary-general: *Béla Benczúr MD*

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