CLINICAL **ARTERIOGRAPH**





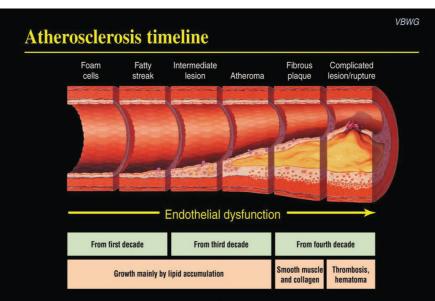
MEASURE YOUR ARTERIAL AGE WITH ARTERIOGRAPH

Pulse Wave Analysis (PWA) and Aortic Pulse Wave Velocity (PWVao) measurements are basic tests to reveal loss of arterial elasticity due to asymptomatic atherosclerosis and vascular calcification.

It has also been proven that central, aortic systolic blood pressure (SBPao), augmentation index (AlXao), and PWVao measured by Arteriograph during the 11-13th weeks of gestation, are higher in pregnant women who develop preeclampsia compared to those who remain normotensive.

MEASUREMENTS BEFORE ARTERIOGRAPH

Formerly the PWA and PWV measurements were generally accepted by applanation tonometry and piezoelectic methods. These methods, however, were used mostly in scientific research, because they are not suitable for clinical practice due to their time consuming and sophisticated manner. In addition, these methods require trained personnel to perform the measurement.

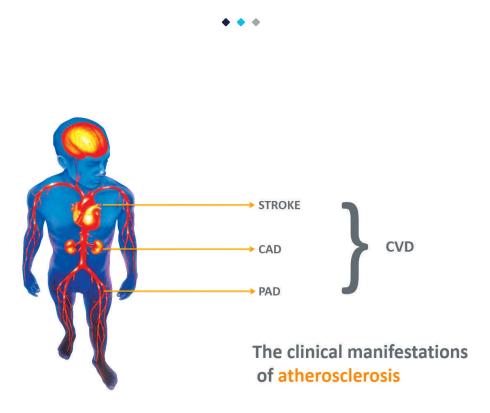


THE ARTERIOGRAPH SOLUTION

Arteriograph became the first, patented and pioneering method and apparatus (US Patent Number 20070106162) providing a single upper arm cuff based oscillometric measurement of PWA and PWV.

Its user independent, fast (only 3 minutes), and simple operation allows the implementation of the arterial function measurement broadly in routine clinical practice.

The device's software provides a comprehensive report with detailed explanation of all the measured parameters and their threshold values for cardiovascular morbidity and mortality.







ACCURATE

The Arteriograph parameters are accurate compared to invasively measured counterparts.

Journal of Hypertension 2010, 28:2068–2075 High Blood Press Cardiovasc Prev DOI 10.1007/s40292-017-0238-8



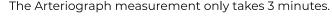
REPRODUCIBLE

Reproducibility and variability (repeatability) of aortic PWV measured with Arteriograph are better than the applanation tonometric or piezoelectric method.

Journal of Hypertension 2008, 26:523-528



FAST





EASY

The single upper arm cuff-based operation is completely user independent. Performing the measurement does not require trained personnel.



COST EFFECTIVE

The Arteriograph device is portable and lightweight allowing the use from outpatient clinic to the bedside. The device requires only 4 AA type alkaline or rechargeable batteries.

WHEN SHOULD ARTERIAL STIFFNESS MEASUREMENT BE DONE

Close to 300 studies have been performed in cardiology and other medical areas using Arteriograph in different clinical conditions. Here are the most relevant ones.

Cardiology

"We found measurement of arterial stiffness to be a convenient, inexpensive and reliable method for predicting mortality in patients with advanced heart failure (HF). In addition, it could also be used in outpatients with HF to optimize treatment and thus avoid hospitalization. Arterial stiffness was assessed noninvasively with the arteriograph (TensioMed, Budapest, Hungary)."

Demir, S. et al.: The prognostic value of arterial stiffness in systolic heart failure.

Cardiology Journal 2013, Vol. 20, No. 6, pp. 665-671.

"Arterial stiffness was assessed noninvasively by using TensioMed Arteriograph.

...The independent prognostic indicator aortic PWV may be an easy and reliable method for determining the risk of future events in patients hospitalized with acute MI.

Akkus, O., et al.: Evaluation of Arterial Stiffness for Predicting Future Cardiovascular Events in Patients with ST Segment Elevation and Non-ST Segment Elevation Myocardial Infarction.

The ScientificWorld Journal Volume 2013, Article ID 792693, 6 pages,

http://dx.doi.org/10.1155/2013/792693

"In the present study, we found a strong correlation between the stiffness parameters measured with the Arteriograph and those obtained using the echo-tracking method."

"Our findings encourage the implementation of regional and local arterial stiffness and function measurements in daily clinical routine in patients suspected of having CAD."

Gaszner, B., et al: Comparison of Aortic and Carotid Arterial Stiffness Parameters in Patients With Verified Coronary Artery Disease

Clin. Cardiol. 35, 1, 26–31 (2012)

"Our results confirm the importance of measuring arterial elasticity in patients with CAD predisposition. Also, we have found that an elevated PWV is associated with ISR (In-Stent Restenosis) suggesting its measuring before the procedure which contributes for a better selection of the stent implant. This study confirms the value of Arteriograph in cardiovascular risk assessment as a broadly applicable method for screening the general population."

Prskalo et al.: Arterial stiffness in patients with coronary artery disease: relation with in-stent restenosis following percutaneous coronary intervention

BMC Cardiovascular Disorders (2016) 16:128

"The Pulse Wave Velocity and Augmentation Index were measured using the TENSIOMED Arteriograph (TensioMed Ltd., Hungary)....

....As a result of our research we conclude that this type of analysis can provide a simple inexpensive and noninvasive means for studying changes in the elastic properties of the vascular system in patients with the coronary heart disease."

Hlimonenko, I. et al.: Assessment of Pulse Wave Velocity and Augmentation Index in different arteries in patients with severe coronary heart disease.

Proceedings of the 29th Annual International

Conference of the IEEE EMBS, Cité Internationale, Lyon, France

August 23-26, 2007. FrA07.4

"Assessment of arterial wave reflections was performed non-invasively with the commercially available Arteriograph apparatus (TensioMed Budapest Hungary, Ltd) by analysis of the oscillometric pressure curves registered on the upper arm with a single pressure cuff."

"Indeed, in our study, we found that DAI (Diastolic Area Index) and DRA (Diastolic Reflection Area), two markers that reflect the contribution of reflected waves to perfusion of the coronary circulation, were closely associated with CFR (Coronary Flow Reserve), even after adjustment for other factors influencing CFR."

Tritakis, V., et al.: Association of arterial stiffness with coronary flow reserve in revascularized coronary artery disease patients.

World J Cardiol 2016 February 26; 8(2): 231-239.

"Oscillometric aortic PWV (Arteriograph, TensioMed Ltd, Budapest, Hungary) was assessed....

...Aortic pulse wave velocity assessed by a simple oscillometric method using an arm cuff only, independently predicted all cause mortality and major CV events in a large cohort of subjects attending health screening."

Kahan, T. et al.: Aortic stiffness measured by a novel oscillometric method independently predicts cardiovascular morbidity and mortality: a study of 4146 subjects.

Journal of Hypertension Volume 31, e-Supplement A, June 2013, e102. 7B.12

Nephrology

"Subjects underwent monitoring with the TensioMed Arteriograph24 ambulatory arterial stiffness pulse wave velocity (PWV) monitor (TensioMed Ltd, Hungary) for 24 hours.

...day and night PWV did not differ between chronic kidney diseased and control groups. Whereas PWV fell at night in control subjects, it did not in those with CKD"

Dhaun, N. et al: Diurnal Variation in Blood Pressure and Arterial Stiffness in Chronic Kidney Disease.

Hypertension. 2014;64:296-304.

"The Arteriograph device (TensioMed Ltd, Budapest, Hungary), which has recently been validated against the Complior and SphygmoCor devices, was used to determine indices of arterial stiffness, that is, PWV, Alx, and central SBP before revascularization and at the end of the follow-up period."

"In conclusion, this study is the first to show that arterial stiffness is higher in patients with refractory aRVH (atherosclerotic RenoVascular Hypertension) than in those with essential hypertension."

Fodor, L., et al: Arterial stiffness in atherosclerotic renovascular hypertension.

Journal of Hypertension 2014, 32:2238-2245.

"A non-invasive oscillometric method Tensiomed Arteriograph was applied to assess arterial stiffness parameters...

...Our findings suggest that arterial stiffness monitoring is a reliable method to assess global cardiovascular risk among kidney-transplanted patients. The oscillometric method is convenient, fast, painless technique to monitor arterial function, which, in the case of pathological findings, proposes more frequent cardiovascular control."

Kovács, D., et al.: Three-Year Longitudinal Clinical Trial of Arterial Function Assessed by a Oscillometric Non-Invasive Method in Comparison With Carotid Sclerosis and Transferrin Kidney-Transplanted Patients.

Transplantation Proceedings, 46, 2168e2170 (2014)

Diabetology

"In our study we applied a simple, feasible oscillometric method. We have revealed a significant impairment of arterial stiffness, measured as increased PWVao in patients with CAD and T2DM, which reflects premature arterial damage. The cut-off value for PWVao measured by Arteriograph is in good correlation with the recently published recommendation of cfPWV recording.

....Our findings encourage the implementation of arterial stiffness and function measurements in daily clinical routine in high cardiovascular risk patients with CAD and T2DM."

Lenkey, Zs. et al.: Comparison of Arterial Stiffness Parameters in Patients With Coronary Artery Disease and Diabetes Mellitus Using Arteriograph. Physiol. Res. 63: 429-437, 2014

"The Arteriograph24 is applicable for research purpose. PVW in type 2 diabetes is modestly reduced during the night."

Krogager, C. et al.: 24-h ambulatory pulse wave velocity and central blood pressure in type 2 diabetes.

Artery Research (2014), http://dx.doi.org/10.1016/j.artres.2014.04.004

Obstetrics

"The Arteriograph (TensioMed Ltd, Budapest, Hungary) was used to measure the Alx, PWV and SBPAo.

Compared with women who remain normotensive, women who develop preeclampsia have higher SBPAo and arterial stiffness, which is apparent from the first trimester of pregnancy."

Khalil, A. et al.: Maternal hemodynamics at 11–13 weeks' gestation and risk of preeclampsia. Ultrasound Obstet Gynecol 2012; 40: 28–34.

"The patients' Alx and PWV were measured with the TensioClinic TL1 Arteriograph and TENSIOCLINIC software (TensioMed Ltd.)....

...After pregnancy, early-onset and late-onset pre-eclamptic patients exhibit differences in vascular function. This result indicates the presence of a higher cardiovascular risk in patients after early-onset pre-eclampsia."....

Franz MB, et al: Augmentation index and pulse wave velocity in normotensive and pre-eclamptic pregnancies.

Acta Obstet Gynecol Scand. 2013; 92:960-966.

"Pulse wave velocity (PWV) and augmentation index (Alx) were recorded using the Arteriograph...

Multiple consecutive noninvasive measurements of vascular stiffness, CO, SV and TPR were highly correlated confirming repeatability of measurements in the third trimester of uncomplicated pregnancy, so these haemodynamic measurements do not need to be undertaken at a specific time period of the day.

Osman, W. et al.: Diurnal variation and repeatability of arterial stiffness and cardiac output measurements in the third trimester of uncomplicated pregnancy.

Journal of Hypertension 2017, 35:2436-2442.

"Pulse wavevelocity (PWV) and central BP were measured at 14–18 and 18–24 weeks gestation using a Tensioclinic arteriograph.

"....PWV is a marker of vascular compliance and is a likely indicator of the degree of maternal vascular adaptation to pregnancy. Higher PWV in this cohort was associated with a significantly increased risk of preterm delivery indicated by maternal and/or fetal disease."

Cockerill, R. et al.: Prediction of iatrogenic preterm delivery in women with chronic vascular disease and/or previous early onset preeclampsia.

Abstracts / Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health 5 (2015) 53–156

Gynaecology

"Aortic PWV as a measure of arterial stiffness was assessed using an oscillometric device, Arteriograph (TensioMed, Budapest, Hungary).

...This study among postmenopausal women provides evidence that increased arterial stiffness as measured by aortic PWV and not carotid IMT may be a marker or a risk factor for LVDD, independent of other classical risk factors."

Albu, A. et al.: Arterial stiffness, carotid atherosclerosis and left ventricular diastolic dysfunction in postmenopausal women.

European Journal of Internal Medicine 24 (2013) 250-25

Paediatrics

"A noninvasive, occlusive, oscillometric device (Arteriograph; TensioMed Ltd, Budapest, Hungary) was used for the PWVao measurements...."

"Our study provides the largest database to date concerning arterial stiffness in healthy children and adolescents between the ages of 3 and 18 years, and the technology adopted proved easy to use in large paediatric populations, even at a very young age."

 $\mbox{Hidv\'egi, E.V., et al.:}$ Reference values of aortic pulse wave velocity in a large healthy population aged between 3 and 18 years.

Journal of Hypertension 2012, 30:2314-2321

"A noninvasive, occlusive, oscillometric device (Arteriograph, TensioMed Ltd, Budapest, Hungary) was used for measurement of arterial function."

"This paper provides the first description of the reference values of Aixao as applied to genders, based on a large cohort of healthy children and adolescents aged between 3 and 18 years."

Hidvégi, E.V., et al.: Influence of body height on aortic systolic pressure augmentation and wave reflection in childhood.

J Hum Hypertens. 2015 Aug;29(8):495-501

Sports medicine

"Aortic, brachial hemodynamics and arterial stiffness were measured (Arteriograph, TensioMed®, Hungary) before and after a standardized exercise test.

... Professional rowers showed higher chronic aortic pulse pressure and arterial stiffness. Given the risk associated with elevated aortic pulse pressure and Alx for development of cardiovascular diseases, longterm observations of professional rowers are needed with respect to arterial stiffness and prognosis.

Acute and chronic effects on central hemodynamics and arterial stiffness in professional rowers.

Physiol Meas. 2016 Mar 21;37(4):544-553.

"Aortic pulse wave velocity (PWVao), as a measure of arterial stiffness and augmentation index (AIX%), as a measure of peripheral arterial tone, were assessed by a non-invasive oscillometric tonometry device

(Arteriograph; TensioMed Ltd., Budapest, Hungary) from the right arm."

"Poor cardiorespiratory fitness and higher waist circumference were associated with increased arterial stiffness in children and adolescents with chronic diseases and physical disabilities."

Haapala, E.A., et al.: The associations of cardiorespiratory fitness, adiposity and sports participation with arterial stiffness in youth with chronic diseases or physical disabilities.

Eur J Prev Cardiol. 2017 Jul;24(10):1102-1111.



PARAMETERS MEASURED BY ARTERIOGRAPH

SBP = brachial systolic blood pressure (normal under 140 mmHg)

DBP = brachial diastolic blood pressure (normal under 90 mmHg)

PP = brachial pulse pressure (normal under 60 mmHg)

MAP = mean arterial pressure

HR = heart rate

SBPao = aortic (central) systolic blood pressure. SBPao physiologically lower than the peripheral (brachial) SBP.

SBPao is normal under 140 mmHg.

PPao = aortic (central) pulse pressure. PPao is the difference between the central systolic and diastolic pressure.

PPao is normal under 50 mmHg.

Aix aortic = aortic (central) augmentation index. Aix aortic is mainly determined by the peripheral arterial tone (resistance) of the small arteries and arterioles, which is influenced by endothelial NO synthesis. Aix aortic is normal under 33%.

ED = Ejection (systole) duration of the left ventricle of the heart. ED is influenced by the heart rate. This parameter is not taken account in the evaluation of Arteriograph report. Normal values are described by Weissler AM, Harris LC, White D: "Left ventricular ejection time index in man" J Appl Physiol 18 (5) 919-923;1963.

RT = return time of the aortic pulse wave. RT reflects to the characteristics of the aortic wall. The stiffer the aortic wall, the lower the RT. RT is normal above 124 msec.

PWVao = Pulse Wave Velocity of the aorta. PWVao is determined by the characteristics of the aortic wall (see RT). The stiffer the aortic wall, the faster the PWVao. PWVao is normal under 9.0 m/s. Increased PWVao values are related to increased CV risk and atherosclerotic organ damage. Vascular (arterial) age assessment is based on the PWVao values. Higher SBP and/or HR can increase PWVao causing enhanced lateral tension (i.e. stiffness) on the aortic wall and can lead to false arterial age assessment. For this reason in case of hypertension and/or high heart rate the examination should be repeated as the elevated parameters are normalized.

SD = Standard deviation of the beat to beat measured aortic pulse wave velocity values. The lower the SD the better the quality of the recording. SD should be in the green range (0.0-0.7 m/s). Yellow (>0.7 <1.0 m/s) is still acceptable but with caution and with supervision by medical doctor. Red range (>=1.0 m/s) cannot be accepted and the examination must be repeated.

DRA = diastolic reflection area. The left coronary artery provides blood and oxygen supply to the left ventricle of the heart; however this artery is perfused mainly during diastole. Thus the diastolic perfusion pressure and the duration of diastole are playing determinant role in the blood supply of the left ventricle of the heart. DRA is a complex dimensionless parameter, describes the diastolic wave reflection intensity and the duration of diastole. The higher the DRA is the better the left coronary perfusion. The DRA is normal above 40.

SAI = systolic area index, DAI = diastolic area index. Pressurizing the cuff to the diastolic blood pressure volumetric signals can be obtained. The area under the curve is taken as 100%, and then it is divided into systolic (SAI) and diastolic (DAI) area and expressed as the percentage of the total (100%). In normal, resting situation with normal heart rate the SAI used to be less than 50% and the DAI more than 50%. The lower third of the DAI is under 46%, which could be considered abnormally low.

ABI = ankle-brachial index. This is the ratio of the systolic blood pressure of the ankle to the systolic blood pressure of the brachial artery. Persons who have an ABI of 0.9 or less, or 1.4 or greater, are at increased risk of cardiovascular events and mortality, regardless of the presence of PAD symptoms or other cardiovascular risk factors. An ABI between 0.91 and 1.0 is considered borderline for cardiovascular risk.

*Threshold values are obtained from a hard end-point follow-up study using receiver operating curve to determine the optimal threshold with the best sensitivity and specificity. (Kahan, T. et al.: Aortic stiffness measured by a novel oscillometric method independently predicts cardiovascular morbidity and mortality: a study of 4146 subjects. ESH Congress 2013 Milan. Oral presentation, Large Arteries Session. Monday 17 June).

*Threshold values for ABI: Measurement and Interpretation of the Ankle-Brachial Index. A Scientific Statement From the American Heart Association. Circulation. 2012;126:2890-2909.

*Arterial age assessment is based on the age related median of the percentiles curves of aortic PWV values derived from a database of 10,000 normotensive, apparently healthy patients



THE VALUE OF THE MEASURED DATA - CLINICAL EXAMPLES

47 years old apparently healty, non-smoker male, BMI 20.3 kg/m²

Sys: 129 mmHg

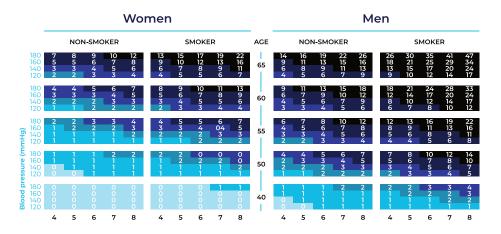
Dia: **77** mmHg

PP: **52** mmHg

MAP: 94 mmHg

HR: **68** /min

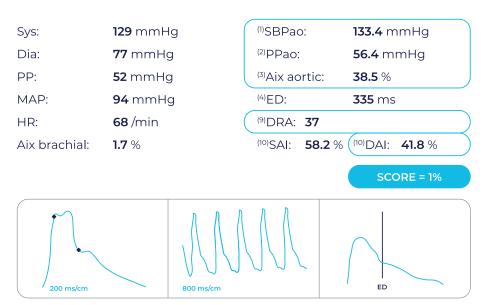
SCORE - European High Risk Chart



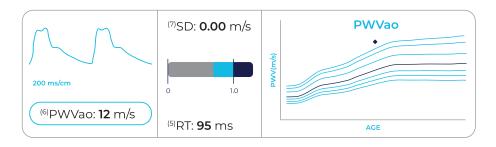
SCORE = 1% Cholesterol 6.0 mmol/l

A 47 years old asymptomatic, apparently healthy patient with no any prior CV history was evaluated due to his own initiative for CV check-up. The normotensive subject had a slightly elevated total cholesterol level. However, the SCORE analysis showed only low (1%) risk, thus this patient was considered, according to the recent CV prevention strategy, to be a "normal" patient with low CV risk. In this case no intervention is suggested by the relevant Guidelines only to repeat the CV risk evaluation later.

47 years old apparently healty, non-smoker male, BMI 20.3 kg/m²

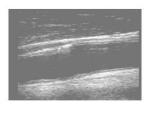


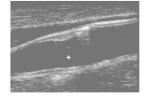
However, the performed Arteriograph examination revealed increased central systolic blood pressure (SBPao), increased aortic pulse pressure (PPao), increased aortic augmentation index (Aix), decreased diastolic reflection area (DRA) and decreased diastolic area index (DAI).

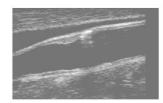


The aortic pulse wave velocity turned to be very high, 12 m/s, exceeding the normal range. Also, the patient's PWVao was beyond the 95th percentiles and exhibited early vascular ageing (EVA).

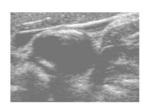
Taking into consideration that the high PWVao is a sign of vascular calcification and our scientific results showed 76% sensitivity of >9m/s PWVao for asymptomatic carotid atherosclerosis (plaques), we performed carotid ultrasound examination.

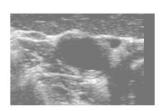






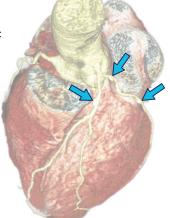






The carotid ultrasound revealed atherosclerotic plaques and proved asymptomatic atherosclerosis. Considering that the atherosclerosis is a systemic disease of the medium and large size arteries, consequently we can expect that the coronary arteries could also be affected by atherosclerosis, we suggested to perform computer tomographic examination of the coronary arteries.

The cardio-CT revealed multiple plaques on the coronary arteries (marked by arrows).



CONCLUSIONS

Blood pressure measurement is a standard routine procedure during each medical check-up. The Arteriograph examination takes no more time and no more work, because its operational procedure does not differ from a standard oscillometric BP measurement. Expanding the BP measurement with the use of Arteriograph we can detect hidden, asymptomatic CV damages. Having discovered these pathological changes, the duly implemented interventions can save many lives in active, young and middle aged population.

