

Beyond the Cuff

Using Arterial Elasticity Indices in the Early Assessment
and Management of Cardiovascular Disease

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Summary

The development of vascular disease appears to be initiated by one or more environmental or genetic factors such as aging, diet, smoking, inactivity, diabetes, elevated lipids, elevated blood pressure and/or oxidative stress. Other factors such as clinical obesity and/or chronic inactivity may also exacerbate vascular disease. Relatively early in the progression of vascular disease, these factors cause a dysfunction of the endothelial lining of primarily the small arteries and arterioles.^{1, 2} This change may be identified clinically as a premature reduction in arterial elasticity relative to arterial elasticity values for normal, healthy individuals of the same age and gender.

These reductions in arterial elasticity occur in the presence of endothelial dysfunction as detected by a reduction in small artery elasticity (C_2). A decreasing C_2 -small artery elasticity leads to elevated blood pressure as well as to arteriosclerosis and atherosclerosis.^{3, 4} It is important to note that atherosclerosis only occurs in the presence of endothelial dysfunction and this change can be detected by a reduction in C_2 -small artery elasticity. Somewhere during this stage of the disease progression, a patient may be diagnosed with diabetes and/or hyperlipidemia. In time, if treatment is not provided or if treatment is not effective, the walls of the artery thicken, clinical hypertension becomes apparent and plaque will form on the lining of the large arteries, i.e. the aorta and its main tributaries including the coronary arteries. These large artery wall changes may be identified clinically as a premature reduction or loss of C_1 -large artery elasticity relative to arterial elasticity values for normal, healthy individuals of the same age and gender. Due to the pathologic nature and irreversibility of these late stage changes, other clinical parameters may also be altered such as an increase in blood pressure, pulse pressure and/or pressure wave velocity, elevated calcium scores and reduced ankle-brachial indices. It is at this point that a patient may experience a

morbidity clinical event such as a heart attack or stroke and require life-saving treatments including angioplasty, stenting and/or coronary artery by-pass grafting.

The CVProfilor[®] non-invasively detects early changes in vascular tone through its non-invasive collection and analysis of blood pressure waveforms. The C_2 -small artery elasticity index describes the current status or condition of the very small arteries and arterioles just before the capillary bed – providing a surrogate marker for endothelial function.^{5, 6} A premature loss of arterial elasticity has extensively been shown in medical literature to be correlated with early macro- and micro-vascular complications indicative of increased risk for cardiovascular disease morbidity and mortality. A premature reduction in C_2 -small artery elasticity, left untreated, has been shown to be a sensitive and early predictor of cardiovascular disease morbidity and mortality. One such study indicated that a reduced C_1 -large artery elasticity and a reduced C_2 -small artery elasticity were univariate predictors of events and, after adjusting for age, indicated that for every 2-unit decrease in C_2 -small artery elasticity there was a 50% increase in cardiovascular events.³ To make a determination as to the status of the blood vessels, individual patient C_1 -large and C_2 -small artery elasticity parameters are compared to a database of “normal” and “abnormal” categories for similar age and gender-matched individuals. This process of comparison allows the physician a parameter to better understand the status of the patient’s blood vessels relative to the patient’s medical history, risk factors, disease diagnoses and/or the effectiveness of various treatment therapies. An abnormal C_2 -small artery elasticity value coupled with a normal C_1 -large artery elasticity value is typically indicative of early underlying vascular disease. Subsequent diagnostic tests will typically identify contributing factors to this condition. The aggressiveness of therapy may be dependent on the severity of the C_2 -small artery elasticity parameter relative to other medical knowledge. An abnormal C_2 -small artery elasticity

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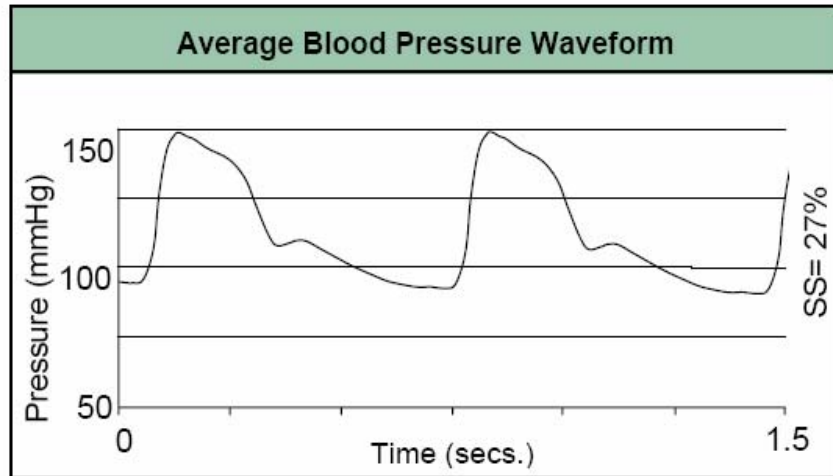


ID#:
DEMO DATA

Profile by: DR RICHARDS
4123 HEALTHWAY METROPOLIS
PHONE NUMBER

Name:
SMITH,
MIKE M

SSN:
Date: Jun 17, 2004
Time: 13:52
Age: 40 years
Gender: Male
Height: 5 ft 9 in
Weight: 148 lbs
BSArea: 1.82 meters²
Body Mass Index: 21.9



PARAMETER		VALUE
Systolic Blood Pressure	(mmHg)	148
Diastolic Blood Pressure	(mmHg)	90
Mean Arterial Blood Pressure	(mmHg)	128
Pulse Pressure	(mmHg)	58
Pulse Rate	(beats/min)	87
C1 – Large Artery Elasticity Index	(ml/mmHg x 10) (Capacitive Arterial Compliance)	6.9
C2 – Small Artery Elasticity Index	(ml/mmHg x 100) (Oscillatory or Reflective Arterial Compliance)	2.0
MEDICAL HISTORY		CLINICAL COMMENTS: SAMPLE REPORT Hypertensive – Elasticity Abnormal
CV Disease:	N	
CV Medications:	N	
Diabetes:	N	
Relatives CV Disease:	Y	
Tobacco:	N	
Race:	Caucasian	

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value coupled with an abnormal C₁-large artery elasticity value is an indication of vascular disease that has progressed to the point where aggressive and immediate diagnostic testing and/or therapy is warranted.

The Meaning of C₁-Large Artery Elasticity and C₂-Small Artery Elasticity

The C₁-large artery elasticity measurement includes predominantly the aorta and large conduit arteries (femoral, brachial, carotid, etc.). The elasticity decreases with age, its decrease is accelerated in individuals with atherosclerosis, and it is inversely related to blood pressure. This decrease is an important reason why pulse pressure increases with age. Since the C₁-large artery elasticity is very sensitive to blood pressure, one will find that when the blood pressure is higher the C₁ will be lower.⁷

The C₂-small artery elasticity resides predominantly in the arterial branch points and in the microcirculation where reflected waves are generated. The C₂-small artery elasticity also decreases with age, in large part because of the decline in endothelial function and the loss of nitric oxide synthase. A low C₂-small artery elasticity has been shown to be a surrogate marker for endothelial dysfunction and can be an early marker for subsequent atherosclerosis.^{4, 5, 6, 8}

When C₁-Large Artery Elasticity and C₂-Small Artery Elasticity Differ From All Other Data Collected on the Patient

When C₁-large and/or C₂-small artery elasticity values differ from all other data known or collected on the patient, these differences may either be associated with early signs of underlying vascular disease that would normally go unnoticed or an errant reading. In this situation, the best solution is to repeat the test. While no diagnostic tool is absolutely perfect 100% of the time, the CVProfilor[®] measurements are highly reproducible – with intra-visit measurements taken five minutes

apart differing by less than 3% and inter-visit measurements taken 1 to 4 weeks apart differing by less than 4%.⁹ Nonetheless, interpretation of results needs to be based on professional judgment that combines test results, patient history, medical condition, and the influence of vasoactive substances.

Should an errant test result be suspected, one should retest and ensure that: (a) the sensor is properly placed within 2 centimeters toward the patient's elbow from the base of the right thumb; (b) the wrist stabilizer is used; (c) the waveform is properly obtained and there are no artifacts; (d) the signal strength is at least 10% or higher and is optimized through a process of increasing hold-down pressure in ¼ turn increments until the highest possible signal strength is achieved; and (e) the patient remains motionless for the duration of the waveform data capture. In addition, test results should be discarded if the patient's medical condition matches CVProfilor contraindications of: (a) weight less than 50 pounds or more than 330 pounds; (b) age younger than 15 years; (c) non-ambulatory patients, or (d) patients with a diagnosis of heart failure, arrhythmia or cardiac valve abnormality.

Procedures for Handling Variations of C₁-Large and C₂-Small Artery Elasticity Scores When Performing Multiple Tests on the Same Patient

All physiologic measurements, such as blood pressure, vary with repeated assessments. There are also technical reasons why some readings may be aberrant. Modest differences in numbers that fall within the same diagnostic category for age (normal, abnormal) should be viewed as consistent readings within the same category, e.g., variations on a "normal" result.

Results that cross the boundary between "normal" and "abnormal" should be repeated. Often one can identify in the aberrant reading a lower signal

strength or an artifact on the wave form that disqualifies it. If one does three or more recordings, the outlier should be discarded, the others averaged, and the dominant category viewed as the appropriate assessment.

Do Patients Need to be Fasting For the Measurement?

Food, time of day, smoking, caffeine and alcohol all may affect arterial elasticity, much as they do blood pressure. Individually the magnitude of their effect is usually so small that it will not change the diagnostic category of the reading. Collectively, the impact can be more significant. If one is reassessing an individual for changes over time, however, strict control of these variables is important and adherence to a generalized fasting protocol is recommended.

Clinical Use of C₁-Large and C₂-Small Artery Elasticity Measurements

The C₂-small artery elasticity measurement, as an early marker for risk, can also be used as a guide in assessing aggressiveness of therapy. A patient with a borderline blood pressure or a borderline elevated cholesterol who has a normal C₂-small artery elasticity might be advised about lifestyle adjustment, whereas a similar patient with a low C₂-small artery elasticity should more likely be treated with drugs. A low C₁-large artery elasticity is usually a marker for more advanced aging of the arteries and is often associated with a high systolic blood pressure. Therapy to slow progression of disease is usually warranted.

Relationship of C₁-Large and C₂-Small Artery Elasticity to Other Measures of Vascular Disease

A low C₂-small artery elasticity may be the earliest marker for future disease and may be detected before any other abnormalities are seen. Clinical trials incorporating early treatment of vasoactive

drugs show a significant improvement in reducing and preventing morbid cardiovascular events.^{10, 11} Both lifestyle adjustments and pharmaceutical therapy demonstrate improvements in arterial elasticity within 12 to 16 weeks with some appearing to reverse vascular wall damage.^{12, 13, 14, 15}

Ultimately, in combination, a low or abnormal C₂-small artery elasticity and a low or abnormal C₁-large artery elasticity will be associated with other abnormalities (elevated blood pressure, thickening of the carotid artery, A:V nicking in the retina, calcium in the coronary arteries by EBCT) and are later manifestations of disease that justify treatment to slow progression. The earlier abnormality of C₂-small artery elasticity may allow more effective intervention at an earlier stage of the disease, changing the paradigm from that currently held, i.e. disease management, to that of slowing or arresting the progression of disease.

Treatment of Patients With an Abnormal C₂-Small Artery Elasticity but No Other Symptoms of Cardiovascular Disease

Since the small arteries can become abnormal years prior to the actual manifestation of cardiovascular disease symptoms and/or events, it is not uncommon to identify asymptomatic patients with an abnormal C₂-small and a normal C₁-large artery elasticity. With these patients, it is always important to identify the factors that may be contributing to the abnormal C₂-small artery elasticity prior to initiating treatment. Vasoconstrictive substances such as nicotine^{16, 17} and caffeine,¹⁸ as well as a high fat meal, can all decrease endothelial function and, therefore, decrease C₂-small artery elasticity. Retesting under your generalized fasting protocol is typically the best way to measure the influence of these vasoconstrictive substances in a patient's vascular assessment. Treatment options for these patients would include smoking cessation, caffeine reduction, reduced dietary fat intake and increased levels of physical activity; all of which

have been associated with improvements in C₂-small artery elasticity.

In addition to lifestyle changes, foods and nutritional supplements that increase nitric oxide or reduce oxidative stress appear to show promise in improving small artery elasticity, thus providing a low-risk alternative to pharmaceutical therapy in early stage disease. Dietary supplements might include nuts, such as walnuts and almonds, fish-oil (1-2 grams), or L-arginine (3-9 grams daily), all of which may improve the bioactivity of nitric oxide. Other nutraceuticals have been claimed to have benefit without documentation including Coenzyme Q10 (30-150 mg), garlic (10 mg), Ginkgo Biloba (160-320 mg), and Grape Seed Extract (150-300 mg).¹⁹ Not all supplements are harmless and it is, therefore, important to know the specific benefits of the supplements used as well as the potential for negative reactions when used in combination with other pharmaceutical medications. It is also important to keep in mind that nothing can take the place of a healthy diet, regular exercise, risk reduction and weight management in restoring endothelial function. But, for patients who are doing everything right and still demonstrating an abnormal C₂-small artery elasticity measurement, such dietary supplements could be a first step in an effort to slow progression of disease.

Other Measures of Arterial Elasticity that May be Useful

The CVProfilor[®] is the most user-friendly,

reproducible and sensitive FDA-cleared device for assessing arterial elasticity or stiffness. Furthermore, it is the only device that provides an independent assessment of large and small artery elasticity validated through correlation with age, cardiovascular disease, cardiovascular disease progression, drug effects, magnetic resonance imaging (MRI), intima-media thickness (IMT), ankle-brachial index (ABI), and flow-mediated vasodilatation (FMD).

Pulse wave velocity is a cumbersome method and only assesses large artery stiffness, which means it can only assess late stage disease. A device is available for transforming a radial waveform into a central waveform for analysis of the reflected wave, but this device relies on a mathematical “transfer function” that has been shown to be unreliable. Still other devices utilize a blood pressure waveform derived from pulsatile volume changes in the fingertip, but variations in fingertip blood flow due to environmental changes such as heat and cold, make these measurements quite unpredictable.

Reflected waves can sometimes be visualized in the systolic portion of the arterial pressure waveform recorded by the CVProfilor.[®] One can often, but not always, detect a second wave in systole that tends to be higher when the C₂-small and C₁-large artery elasticity values are low. It tends to confirm that the low C₂-small artery elasticity index is dependent on the reflection or oscillation in the waveform, but the second peak in systole is not as specific or sensitive a measurement.

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