Pulse Dynamics

The Essentials of DynaPulse Noninvasive Blood Pressure and Hemodynamic Monitoring

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The Essentials of DynaPulse Noninvasive Blood Pressure and Hemodynamic Monitoring & Pulse Wave Analysis

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Preface

Hypertension, or high blood pressure, affects about one-quarter of the U.S. population and is known to link directly to heart attack, stroke, and kidney problems. The causes of nearly 80% of hypertension, known as “essential hypertension,” are still unknown. In the past two decades, many researchers worldwide have been focused on looking for a new marker or index, other than the systolic and diastolic numbers, to monitor and diagnose hypertension. Arterial compliance and distensibility (specific compliance), both of which describe the elastic characteristics of the arteries, were found to be strong “markers” that correlate well with hypertension. Different methods of analyzing the pulse waveform to determine arterial compliance, including catheterization, use of the Windkessel C1 and C2 model, or from echo Doppler using blood flow methods, were all found too difficult to use and not very reproducible. The reliability of each method, the complexities of the human hemodynamic system, and the difficulty in defining and separating the arterial structural and functional properties are topics of constant debates among researchers.

During the past ten years, we have developed and improved a new non-invasive method, Pulse Dynamics, which measures the arterial compliance, peripheral resistance, and left ventricular contractility through the analysis of pulsation signals obtained by a
cuff sphygmomanometer. This method and its clinical application to genetic risk of hypertension and the effects of hypertensive drugs were studied and published in Hypertension 1996; 28:599-603 (DT O’Connor, University of California at San Diego/VA). The development of the Pulse Dynamics methodology, the physical model, the determination of arterial compliance, and its clinical validation were also published in the American Journal of Cardiology 1997; 80:323-330 (AN DeMaria, UCSD). Most recently, under the guidance of Dr. DeMaria at UCSD, our researchers have further developed a method of deriving cardiac output from the Pulse Dynamic brachial arterial pulse waveform, which was validated against the Doppler ultrasound method with good correlation, (r=0.84, p<0.001, n=113). The preliminary results were presented at the Heart Failure Society of America meeting, and to be published in Clinical Cardiology, 2008. With the help of professor TD Li at 301 Hospital in Beijing, this method has also been evaluated against both the Doppler method and the Fick method with good correlations (r=0.76, p<0.01, n=45 for Doppler and r=0.61, p<0.001, n=26 for Fick). The ability to evaluate a patient’s hemodynamic profile, both cardiac and vascular functions, during routine clinic examination or home monitoring is essential for physicians to effectively manage and treat patients with hypertension and related cardiovascular diseases.

A new 24-hour ambulatory blood pressure and compliance monitoring method, using the DynaPulse 5000A device and Pulse Dynamic analysis, was presented and published in “Time-Dependent Structure and Control of Arterial Blood Pressure,” Annals of the New York Acad. of Sciences, 1996; 783:310-312 (MA Weber, UCI). The ability to record 24-hour ambulatory hemodynamics should allow physicians to further understand the circadian regulation mechanisms of human physiology, and to provide even better care, especially during drug treatment, to patients with hypertension and cardiovascular diseases.

Since 1994, the Pulse Dynamic method has been made available to researchers, medical centers, and hospitals, both in the US and overseas, in support of important clinical research programs. This Pulse Dynamics booklet summarizes these studies and findings. We are pleased to share this important information with those physicians and researchers who have a special interest in hemodynamics and clinical applications for prevention, treatment and management of hypertension and cardiovascular disease.

I would like to thank those who have supported me and Pulse Metric in the past, and I sincerely hope that continuous research and development of new technologies and new clinical applications in these areas will someday provide a better solution for the diagnosis, treatment, and even prevention of this No. 1 killer - “Hypertension”.

In this 2nd edition Pulse Dynamics booklet, we added new clinical studies published since March 2002, reorganized the contents, and included background materials on human cardiovascular circulation system and blood pressure measurement and a chapter of “The Physics of Pulse Dynamics” that describes the technology and methodology developed since 1988.

(By, Shiu-Shin Chio, Ph.D., Inventor of Pulse Dynamics, and founder of Pulse Metric, Inc.)
Comments and Letters from Physicians and Researchers

By, Todd J. Brinton, M.D., Stanford University Hospital

Over the past thirty years, the mortality rate due to cardiovascular disease has significantly declined. Major advancements have been made in the detection and treatment of cardiovascular disease. However, cardiovascular disease continues to be the number one killer in the United States.

Hypertension is a major risk factor for the development of cardiovascular disease. High blood pressure screening has become an integral component of preventive care. However, high blood pressure and hypertension are not synonymous. Recent studies have demonstrated that hypertension is a syndrome of abnormalities in lipid and glucose metabolism, cardiac enlargement, and vascular stiffening, which may develop many years prior to the onset of high blood pressure.

Although blood pressure measurement is a time-honored method for the detection of hypertension, many measurement techniques are plagued with problems in observer bias and reproducibility. In addition, recent studies have also found that approximately 30% of those individuals with elevated blood pressures in the clinic have normal blood pressures at home. The identification of this large number of patients with “white coat hypertension” poses the question: Does blood pressure truly reflect the presence of hypertensive disease? The development of new methods for the early detection of hypertension based on our current understanding of the pathophysiology of the disease are needed. New technologies to evaluate target organ disease such as left ventricle hypertrophy or vascular compliance may represent advancements in not only the detection but also the monitoring of the progression of disease. In addition, these target organs may provide ideal indices for the development of new anti-hypertensive therapies. Current anti-hypertensive therapies target reduction of blood pressure as a surrogate endpoint for the reduction of cardiovascular mortality. The evaluation of current anti-hypertensive therapies and the development of new therapies that utilize target organ indices such as left ventricle hypertrophy or vascular compliance to assess the efficacy of hypertension treatment would represent a new paradigm in disease management and the prevention of cardiovascular disease.

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By, Peixoto, A.J., MD, Professor of medicine, Yale University:

“Our group has had an excellent experience with DynaPulse devices for both research and clinical care. We have used DP5000A ambulatory BP devices since 2000
and have found it to be a reliable instrument that not only provides accurate ambulatory BP data but also offers the possibility of hemodynamic assessment through the DAC. We have also used DP500G device for research projects since 2002. It has proven to be a very versatile device, with excellent performance in a wide variety of patient groups, including hemodialysis (Motiwala, et.al., Blood Press Monitorig 2005:in press) and chronic kidney disease (Yarlagadda et al, Am J Nephrol 2005; 25:451-8). Overall, we are most pleased with the data obtained through the DynaPulse devices in our unit.”

By, Kyriazis, et.al., from the Letter, title “The (dP/dt)max derived from arterial pulse waveforms: prospective applications in the haemodialysis setting”, published in Nephrol Dial Transplant (2001) 16: 1087-1088, quote:

“A new non-invasive, pulse-dynamic technology [1] can provide not only automated systolic and diastolic pressures, but also measurements of the rate of pressure change during the cardiac cycle. Measurements of the maximum rate of BP increase in systole are derived from the brachial pulsation signal, obtained with the use of an inflated cuff, after converting it into its first derivative (dP/dt)max with respect to time. These peripheral (dP/dt)max calculations are in good agreement (r=0.87) with invasive measurements of left ventricular (dP/dt)max [1]. Recently, Germano et al. [2] reported that the (dP/dt)max of normal subjects was significantly greater (P<0.05) than that of cardiac patients with ejection fraction <40%. In the present study, we (i) further investigated the associations between brachial pulse (dP/dt)max and other haemodynamic parameters in a chronic haemodialysis population and (ii) examined the potential role of (dP/dt)max as a tool to track effectively haemodynamic changes during HD. ………

These findings raise the hypothesis that brachial pulse's derivative can be adopted as an additional representative of cardiac function. Given that each arterial pulse waveform obtained during a 24 h BP oscillometric recording can be converted to its first derivative (dP/dt)max, the latter would be extremely useful to monitor cardiac performance during daily activities, or to outline the nycthoemeral rhythm [3]. Furthermore, owing to its satisfactory reproducibility in the HD setting, (dP/dt)max may be adopted in the evaluation of the effects of therapeutic interventions on cardiac function.”

By, Gutkin, M, MD, FACP, Specialist in clinical hypertension:

“We have found the measurement of systemic hemodynamics by the Pulse Metric apparatus highly useful in our practice. Our practice consists of patients with hypertension and dyslipidemia, and your method (Pulse Dynamics) has enabled us to determine hemodynamic variables (cardiac output and blood pressure, with the derived value of peripheral resistance), and the rigidity of the muscular (brachial) vessels. In addition, we are able to estimate dP/dt MAX as an index of the effect of beta-blockade.
These measurements often prove pivotal in determining the proper combination of drug therapy for a resistant hypertensive patient, give us an assessment of cardiovascular risk based on the rigidity of the central vessels, and provide an estimate of vasomotion in the muscular vessels that helps adjust drug therapy.

We look forward to expanding the application of this technique and to growing a community of interest. We feel these measurements should be applicable universally in medical practice in the United States.”

By, Antonio Delgado-Almeida, M.D., Hypertension research specialist:

For more than a century, measurement of blood pressure has been considered the key factor for the detection, evaluation and management of hypertension. Unfortunately, arterial pressure as the hemodynamic determinant of left ventricular function, vascular compliance, and regional blood flow has never been suitable in understanding the normal or altered hemodynamics in hypertension. Back in the 1980’s and until the 1990’s, arterial waveform analysis, disclosing the incident forward and reflectance waves and pulse wave velocity (PWV), was the first clinical approach to a clearer explanation of hemodynamics, including the significance of arterial stiffness and pulse pressure on target organ damage. However, even with such technological advances, many LV functional parameters could not be assessed from arterial waveform analysis.

Since 1996, new non-invasive measures of left ventricular function (LVET, contractility, dP/dt, SV, CO) along with systemic arterial compliance, peripheral resistance and brachial artery flow, were made possible through the work of S.S. Chio and coworkers on a sophisticated method for analysis of the arterial waveform (Pulse Dynamics methodology). Since then, on-line cardiovascular hemodynamic profiles of each patient became available to several research centers around the world. With the refinement of this technique, it was possible, for the first time, to assess LV parameters and vascular functions in a 24- hour fashion, from normal to hypertensive subjects up to heart failure cases, providing one of the most fascinating opportunities to evaluate daily hemodynamic regulation in cardiovascular disease.

In our laboratory, we have used the Pulse Dynamics technique in the evaluation and study of other hemodynamic parameters (aortic augmentation index, aortic wave reflectance) and measures of SV/CO with simultaneous M mode and 2D echocardiograms, while the LV functional parameters are expressed as Isovolumic Pressure Index, Ejection Phase Index and Pressure-Volume relationship. Currently, PWV between brachial and radial artery and PEP/LVET ratios are being explored with this novel technique. However, probably the best results have been found in hemodynamic studies of normotensive subjects with a family history of hypertension and a possible genetic defect in cell K transport, since they showed abnormal vascular compliance in the presence of this proposed intermediate phenotype of hypertension. Also, the recording of a backward reflection wave early in systole during a handgrip test strongly suggests the presence of an intermediate phenotype for the vascular bed.
In summary, the application of this technology on cardiovascular hemodynamics should not be limited to the advanced clinical research sector, but should play an important role in providing a large number of practicing physicians with a powerful tool to assess and treat cardiovascular disease.

By, Hyman, M.H., MD, GP in hypertension & CVD/CHF patient management:

“We have been using the DynaPulse noninvasive hemodynamic monitoring system for patients with hypertension, diabetes and heart failure, for the past four years.

With fluctuations in blood pressure during a twenty-four hour period, and patient’s with “white coat syndrome”, the information we receive from the DynaPulse System assists me in the diagnosis and treatment of patients.

From a technical standpoint, my technicians have found the instrument easy to use. The uploading of information to web-base system is clear-cut and fast. We are able to get the results the same day. The technical support we get from Pulse Metric has been very good.

From the patient’s standpoint, once the patient understands the importance of monitoring their blood pressure for twenty-fours, the information that is obtained to help in controlling and treating their hypertension, and that the monitor works automatically, they are easily assured.

Based on these last four years, the DynaPulse Monitoring System has improved the management of patients in our practice. We anticipate many more years of using this approach in our office for the management of these diseases.”

By, Lee, Y.T., M.D., Professor & Chief Cardiologist, NTU Hospital*:

Recent advances in biomedical engineering and electronic and computer technologies are making a “dream come true” for cardiovascular physicians: to be able to measure and analyze, non-invasively, a blood pressure contour or waveform to obtain useful hemodynamic parameters, such as arterial compliance or distensibility, and vascular resistance. For many years physicians have wanted a non-invasive method to capture these derived parameters so they would be able to monitor a patient’s condition more precisely, and to evaluate and assess a problem to determine the best treatment. For all of these reasons, we are glad to have this opportunity to invite Professor Anthony DeMaria, Chief of Cardiovascular Medicine at the University of California at San Diego Medical Center, Dr. Shiu-Shin Chio, the inventor of DynaPulse and Pulse Dynamics, and his clinical research team, Professor Urbina of Tulane University Medical School and Professor Sutton-Tyrrell of Pittsburgh University Medical School to join the professors and doctors of Taiwan Medical Centers, including Dr. Lian-Yu Lin, Dr. Chau-Chung
Wu and Dr. Ta-Chen Su of National Taiwan University (NTU) Hospital, Professor Chen-Huan Chen of Taipei General VA Hospital, Professor Chung-Sheng Lin, superintendent of Chung-San Medical School and Dr. Chun-Hsiung Wang, Chief Cardiologist of Zen-I Hospital to share their research studies in non-invasive hemodynamic monitoring and clinical applications. I hope that through this conference we will encourage our physicians and researchers in Taiwan to further participate in studies of non-invasive hemodynamic monitoring and develop clinical applications for screening, early diagnosis, prevention, and disease management to improve the future patient healthcare in Taiwan.

(* Dr. Y.T. Lee, professor of NTUH and the Chairman of the Taiwan Society of Atherosclerosis & Vascular Disease. This is an English translation of the “Preface” of Dr. Lee, presented at “The First International Conference on Non-invasive Hemodynamic Monitoring for Cardiovascular Disease and Management”, July 21, 2001 in Taipei, Taiwan, hosted by “Taiwan Society of Atherosclerosis & Vascular Disease”.)

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By, Xie, Q.Y., M.D., M.P.H, clinical researcher:

In order to more effectively manage patients with cardiovascular diseases such as hypertension and heart failure, it is critical that clinicians be able to assess the effects of therapy on the underlying pathophysiology associated with the patient’s given disease state. In fact, objective physiologic data, which can be monitored during the course of treatment, is often unavailable to the clinician, frequently requiring treatment decisions to be made based on subjective information provided by the patient. Readily available hemodynamic information, such as cardiac output, systemic vascular resistance, ventricular contractility, and arterial/systemic compliance, in concert with subjective information from the patient, has been demonstrated to improve the management and treatment of cardiovascular diseases.

During the course of the past decade DynaPulse arterial waveform analysis technology has been used to noninvasively monitor the hemodynamics of thousands of individuals. As a result, Pulse Metric, Inc. has been able to establish baseline hemodynamic data in a normal population as well as patients with various disease states along with medical histories and pharmacological treatment data. Through the efforts of numerous worldwide clinical studies, collaborations, and independent patient participation, Pulse Metric, Inc. has also identified many interesting cases in which the DynaPulse hemodynamic monitoring technology has enabled clinicians to more effectively manage and treat patients with cardiovascular disease.

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**Backgrounds: Cardiovascular circulation and blood pressure monitoring**

**Introduction:**

Blood pressure is the most common index of cardiovascular performance utilized today. Currently, blood pressure is used in the diagnosis of a wide variety of complications associated with the cardiovascular system. However, certain disorders may not be detectable, or quantifiable, by conventional blood pressure measurement. Therefore, the potential for further advances in cardiovascular monitoring lies in determining the presence and severity of these disorders by monitoring not only blood pressure, but also additional cardiovascular parameters. The Pulse Dynamic waveform may be used to determine some of these parameters, possibly providing the physician with more information regarding cardiovascular health.

This section provides a brief review of the cardiovascular system, outlines some of the major disorders that may impair system function, and describes the latest advances in this area using Pulse Dynamics.

**The Heart**

The heart, lungs, and associated vasculature comprise the cardiovascular system. These components work together to fulfill the primary function of the cardiovascular system: to deliver oxygen to the body. Impairment of any component affects the rest of the system, so most disorders of the cardiovascular system have widespread effects. Therefore, each of those individual components, and the interaction that occurs within the vasculature needs to be described.

Central to the cardiovascular system is the heart, which pumps blood through the body in a pulsatile fashion. The cardiovascular cycle consists of a complex pumping process that occurs during each heartbeat. This pumping takes place in four separate chambers, each with their own function and structure. A description of each step in the process is included below (approximate pressures and volumes are in units of mmHg and mL, respectively):

**Ventricular Diastole (End)**
Passive Filling: The ventricle fills with blood.
Aortic Pressure: Decreases from 100
Ventricular Pressure: Increases slightly from 0
EKG: P wave
Ventricular Volume: Increases slightly from 100

Atrial Contraction: The atrium contracts, forcing more blood into the ventricle.
Aortic Pressure: Continues to decrease
Ventricular Pressure: Increases rapidly
EKG: QRS complex begins
Ventricular Volume: Increases

### Ventricular Systole

![Heart diagram]

Isovolumetric Contraction: The ventricle increases contractile tone, but there is no change in volume.
Aortic Pressure: Decreases to 80
Ventricular Pressure: Increases rapidly to 80
EKG: QRS complex main spike
Ventricular Volume: Increases to maximum of 150

Ejection: When ventricular pressure exceeds aortic pressure, the aortic valve opens and blood is ejected into the aorta.
Aortic Pressure: Increases rapidly to maximum of 120
Ventricular Pressure: Increases rapidly to maximum of 120
EKG: QRS complex ends, T wave begins
Ventricular Volume: Decreases rapidly to minimum of 50

### Ventricular Diastole (Beginning):

Isovolumetric Relaxation: The ventricle relaxes its tone, but remains at the same volume. The dicrotic notch (see below) may be observed in pressure waveforms, and is caused by closure of the aortic valve. This notch may provide information regarding aortic valve regurgitation. The valve closes once ventricular pressure falls below aortic pressure.
Aortic Pressure: Dicrotic notch may be observed in waveforms, followed by a pressure decrease.
Ventricular Pressure: Decreases rapidly
EKG: T wave ends  
Ventricular Volume: Begins to increase

Oxygenated blood is driven through the aorta into the complex network of arteries that carry blood into the systemic circulation. The flow of blood through an artery can be compared to the flow of water through a tube. This analogy has allowed the application of fundamental fluid dynamic principles for the development of mathematical models of the circulation, in order to better understand the interaction between arterial properties such as compliance (elasticity) and peripheral resistance.

In fluid mechanics, the two poles that characterize the spectrum of flow classification are laminar and turbulent flow. Ideal laminar flow is described as slow velocity, uniform flow without disturbances such as ripples or waves. At the other extreme is turbulent flow, in which waves created by high velocity flow increase flow resistance. Disturbances caused by turbulent flow generate vibrations in the arterial wall. The Korotkoff sounds may actually be audible vibrations created by systolic turbulent
flow, and the periodic silences may be characteristic of laminar flow occurring during diastole. In the body, systolic blood flow in the central arteries is generally turbulent, whereas flow in the arterioles and capillaries is usually laminar.

The interdependence of flow and cardiovascular activity may be seen in the case of arterial remodeling. If the heart generates an abnormally high velocity flow over a sufficient length of time, hypertrophy of the arterial wall occurs, increasing peripheral resistance. The heart can respond by increasing pressure to overcome the additional resistance. A long term increase in pressure can lead to a vicious cycle that causes a decrease in arterial elasticity and increasing resistance to blood flow. This may lead to further, more serious, cardiovascular disorders.

Heart failure is often the ultimate result of cardiovascular complications, and occurs when either the left or right ventricle fails to pump blood into the circulation at a sufficient rate to meet body requirements. Failure of one ventricle (right heart or left heart failure) may result in ischemia (inadequate perfusion of tissues), edema (blood congestion in one branch of the circulation), total heart failure (failure of both right and left ventricles), or ultimately, death. Some of the causes of heart failure are described below.

Ischemic heart disease is characterized by occurrence of ischemia in the myocardium (heart muscle). This may be due to any one of several factors, and indicates insufficient coronary perfusion. Common causes of ischemic heart disease are coronary atherosclerosis, aortic valvular disease, or coronary embolism. If perfusion is not restored quickly, an acute myocardial infarction may occur. An infarction is an ischemic area of cells that has not received oxygenated blood flow for some time, and is characterized by massive cell necrosis (cell death) in the ischemic area, in addition to severe impairment of tissue function in the regions surrounding the afflicted zone. In the case of acute myocardial infarction, the subsequent impairment of cardiovascular function may lead to heart failure.

Another cause of heart failure may be valvular disease. There are many potential causes for heart valve impairment, including congenital factors, bacterial infection, and other events that propagate structural or functional heart valve damage.

Valve dysfunction commonly involves the mitral or aortic valves. Failure for both of these types of valves is similar, and so a description of aortic valve failure should be sufficient to characterize the disorder.

Aortic valve failure may occur by either stenosis or regurgitation, or a combination of the two. Stenosis refers to an impairment of the valve opening, resulting in dysfunction. Regurgitation, on the other hand, occurs when the valve itself does not open or close correctly. Regurgitation often causes significant backflow, or reflux, into the ventricle during systole. A sufficiently large reflux will result in incomplete ventricular emptying.

Aortic stenosis is characterized by a narrowing of the aortic opening, and may be due to calcification caused by an abnormally-shaped valve (congenital case), by time and use (degenerative case), or by an externally caused disease such as rheumatic fever. Degenerative aortic stenosis occurs exclusively in the elderly. If the opening deteriorates sufficiently, cardiac output drops, followed by left heart failure.
Aortic regurgitation, on the other hand, is characterized by a reflux of blood from the aorta to the left ventricle during diastole. There are many causes of aortic regurgitation, including rheumatic fever, bacterial infection, and blunt chest trauma. Chronic regurgitation causes decreases in cardiac output and ventricular elasticity, and may lead to low cardiac output, edema, and heart failure. A sudden, severe, occurrence of regurgitation (due to trauma, for example) results in an immediate decrease in cardiac output. The decrease in cardiac output results in insufficient blood flow to adequately perfuse all tissues. The body responds to this situation by initiating widespread peripheral vasoconstriction, to maintain adequate perfusion to vital organs such as the brain and heart. The increased resistance created by peripheral vasoconstriction may lead to ischemia and shock. The decreased cardiac output also can cause sudden-onset pulmonary edema.

Peripheral Circulation

In addition to providing information regarding cardiac function, Pulse Dynamics may also be used to obtain properties of the peripheral circulation. Peripheral resistance and arterial compliance both describe properties of the peripheral circulatory system.

Arterial compliance, which is the inverse of the elastic modulus, measures the degree of arterial wall stiffness. Arterial compliance (or simply "compliance") is affected by a wide variety of circumstances, including age and certain cardiovascular diseases, such as hypertension. Therefore, a determination of a patient's compliance may facilitate the diagnosis of hypertension.

Peripheral resistance is a property common to all fluid filled "pipe" systems. There will always be a downstream resistance to the flow of a fluid through a pipe. This resistance is due to a number of properties, including properties of the fluid, the diameter of the pipe, and any turns or branching that takes place in the system. For the purposes of circulation the pipe would be the arteries and other associated vessels and the fluid would be blood.

Recently, a technique has been validated for the quantitative determination of arterial compliance. This was accomplished by comparing the Pulse Dynamic waveform compliance values to those values derived in the invasive catheterization laboratory. A method for determining peripheral resistance from the waveform is currently under development, as well. These parameters will provide the physician with additional information to diagnose hypertension and determine cardiovascular performance, without taking any additional measurements.

The History of Blood Pressure Monitoring

The first well-documented instance of blood pressure measurement was in 1733 by Reverend Stephen Hales, who inserted a long glass tube upright into an incision made in a horse's carotid artery. The pumping action of the heart generated a pressure force, causing the blood level to rise in the tube.

The need for a noninvasive method for blood pressure determination arose due to the danger of infection and the amount of blood loss involved in these early invasive procedures. In 1905, Korotkoff described the auscultatory sounds which became the foundation for the auscultatory (Riva-Rocci) technique. Later in the twentieth century
came the development of oscillometric devices, which determine blood pressure using empirically generated pressure-sensitive algorithms.

With the advent of computers and the move towards increased automation, many monitors utilizing new technologies and methodologies have recently been developed. In 1989, Dr. Shiu-Shin Chio patented the Pulse Dynamic technology used exclusively in DynaPulse monitors. This technology is the first to utilize a graphical display of the brachial artery pulsation signal to noninvasively determine blood pressure and cardiovascular performance.

**Blood Pressure Monitoring Today**

Blood pressure may be measured using direct or indirect techniques. Direct measurements use catheters to invasively determine blood pressure, whereas indirect methods utilize a variety of noninvasive techniques.

Direct measurements utilize one of two different types of sensors, in conjunction with a catheter, to determine blood pressure. Extravascular sensors are located outside of the body and use the principle of wave propagation to transmit vascular pressure from the measurement site to the sensor via a fluid-filled catheter. In contrast, intravascular sensors, such as fiber-optic pressure sensors, are positioned on the tip of the catheter and inserted into the artery. Catheter systems are often used for direct, continuous measurement of intra-arterial blood pressure in the aorta, which is considered the "gold standard" for blood pressure measurement.

The need for this type of continuous, highly accurate reading of a patient's central blood pressure is commonly found in critical care surgical settings. However, the invasive nature of catheter procedures prohibits them from being a viable option for routine blood pressure measurement. Instead, physicians use noninvasive methods for casual measurements. Therefore, a major goal in the field of noninvasive blood pressure monitoring has been the development of a method which correlates with "gold standard" catheter measurements.

The noninvasive measurement of blood pressure may be performed in several different ways. Many methods use an air filled cuff to temporarily occlude blood flow through the artery, and then apply a particular technique to obtain blood pressure data while the cuff deflates. The most common indirect technique is the auscultatory method, in which a clinician determines systolic and diastolic pressures by listening to the characteristic Korotkoff sounds of the blood flow during cuff deflation. The Korotkoff sounds have been categorized into five phases (descriptions taken from ANSI/AAMI 1987 guidelines):

- **Phase I** - begins with the sudden appearance of a faint, clear, tapping or thumping sound that gradually increases in intensity.
- **Phase II** - phase I ends and phase II begins when the sounds change to a loud "swishing" murmur.
- **Phase III** - the beginning of Phase III occurs when the sounds assume a loud, distinct, knocking quality. These sounds are less intense than those of Phase I.
- **Phase IV** - begins when the sounds suddenly become muffled and have a faint murmur-like or "swishing" quality.
- **Phase V** - begins when silence develops.
The beginning of Phase I corresponds to SBP. The actual point of DBP based on these Korotkoff sounds is less clear. The ANSI/AAMI 1987 report suggests that the pressures at the beginnings of both phases IV and V be recorded, since there may be some debate as to which value best represents DBP. The phase IV values tend to be higher than catheter measurements, while phase V values are usually lower. The DBP criteria is further complicated by the fact that some patients may not have audible phase IV sounds, whereas in others, the beginning of phase V (silence) may be difficult to determine.

Since the auscultatory technique is based on the ability of the human ear to detect and distinguish sounds, there is a possibility for measurement error due to individual levels of auditory acuity and sensitivity. Although a fully-qualified clinician can consistently obtain accurate blood pressure measurements, unqualified or inexperienced personnel may be more susceptible to outside noise interference, or inconsistent assessment of the actual points of Phase I and Phase IV or V.

In an attempt to increase reproducibility, some automated devices have replaced the human ear with a microphone. These devices apply sound-based algorithms to estimate SBP and DBP. In addition to noise-artifact sensitivity, these sound-dependent algorithms may not adequately compensate for patient conditions such as hypotension (i.e. low blood pressure), where the Korotkoff sounds may be muted.

There is no way to determine mean arterial pressure (MAP) solely by the use of Korotkoff sounds, and that is a strong limitation of auscultation. In order to provide an estimation of MAP a formula has been developed, which is quite commonly used in auscultatory devices:

$$\text{MAP} = \frac{\text{SBP}}{3} + \frac{2\times\text{DBP}}{3}$$

Oscillometric blood pressure determination is the other common noninvasive method of blood pressure monitoring. The term "oscillometric" refers to any measurement of the oscillations caused by the arterial pulse. These oscillations are the direct result of the coupling of the occlusive cuff to the artery. This technology was originally designed as an alternative to the auscultatory technique, allowing blood pressure measurement of critical care and intensive care unit (ICU) patients whose Korotkoff sounds were inaudible (usually due to hypotension caused by massive hemorrhage or shock).

In oscillometric techniques, the cuff is first inflated until the artery is fully occluded. Then, the monitor takes measurements while the cuff deflates. Most oscillometric devices examine the pulsatile pressure generated by the arterial wall as it expands and contracts against the cuff with each cardiovascular cycle. An electrical signal is generated by the pressure transducer based on the distension of the artery. Over the course of the measurement process, the magnitude of the pulsatile signal increases, reaches a maximum amplitude, and then decreases.

A common algorithm used by many oscillometric devices sets MAP equal to the point of maximum amplitude. SBP and DBP are then determined by the application of predetermined systolic and diastolic ratios. In the height-based approach, for example, ratios of pulse amplitude to maximum amplitude are used. For this type of algorithm, the maximum amplitude is defined as MAP.
An oscillation that satisfies the systolic ratio and occurs before the MAP point, is considered SBP. An oscillation that satisfies the diastolic ratio and occurs after the point of MAP determination, is considered DBP. The determination of both systolic and diastolic ratios are based on the correlation to auscultatory or catheter measurements. Unfortunately, an erroneous determination of MAP, due to any form of artifact, may produce inaccurate values for SBP and DBP.

The majority of the monitors on the market today are either auscultatory or oscillometric in nature, however, there are other types of devices. In addition, some monitors employ both auscultatory and oscillometric methods, using one method as a primary measurement and the other as a secondary measurement for verification.

Not all techniques yield both SBP and DBP. For example, the palpatory method only measures SBP. In this technique, the artery is occluded with a cuff. Then, the cuff is allowed to deflate, and SBP is determined by measuring the cuff pressure at which a radial or finger pulse is first detected. Most techniques, however, provide both SBP and DBP. The infrasound method, for example, attempts to improve on the auscultatory method by detecting low frequency Korotkoff vibrations below about 50 Hz, including sub-audible vibrations.

The ultrasound method is quite different from infrasound, because it measures Doppler shifts to determine blood pressure. Ultrasound waves generated from a transmitter located distal to the cuff are projected towards the artery. These waves contact the arterial wall and are reflected back to the receiver. Distension of the wall causes phase shifts in the reflected waves (known as Doppler shifts). From these phase shifts the opening and closing of the artery can be determined. Systolic pressure is the point at which the artery can remain open with the largest cuff pressure. Diastolic pressure is determined by a similar algorithm.

Another method, known as impedance plethysmography, also measures the volumetric change associated with arterial distension. The volume changes cause changes in the electrical conductivity (impedance) of the measurement site. The pulsatile nature of the volume changes (due to the cardiovascular cycle) is reflected in the measurement of impedance pulses. When graphed over time, these pulses produce a waveform similar to the pressure-generated oscillometric waveform. Pressures are then estimated in a manner similar to the oscillometric technique.

Arterial Tonometry utilizes a very different approach. The artery is flattened and the pressures required to maintain that flat region are measured. This is accomplished by using an array of sensors, each of which measures pressure. This array ensures that the maximal pressure being exerted on the arterial wall by the blood is felt. The result of this method is a waveform similar to catheter measurements, and some type of algorithm must be used to calculate pressures from that waveform.

There are several limitations to tonometry. First, it is a measure of the peripheral circulation, with much different values for pressure than are felt closer to the heart. A second limitation of tonometry is its high sensitivity to sensor location and angle. With each relocation of the sensor, there can be varying values for pressure. Measurement errors may be minimized by experienced, well trained operators. However, inter-operator reproducibility may still be lack consistency. Lastly, tonometry requires a blood pressure measurement for calibration by an independent technique.
Pulse Dynamic Blood Pressure Measurement

DynaPulse monitors are classified as oscillometric devices because they measure the oscillations (due to the arterial pulse) that occur from the coupling of a cuff to an artery. However, while other oscillometric devices use empirically-derived algorithms, DynaPulse monitors utilize Pulse Dynamic technology to measure blood pressure and to obtain additional cardiovascular information.

An inherent element of Pulse Dynamic technology is the graphical display of the waveform. That waveform, displayed with each measurement, is a digitally accurate record of the measurement which plots arterial pressure oscillations against both cuff pressure and time. SBP, DBP, and MAP are then determined based on the physical principles of blood flow, not empirically-generated criteria.

In order to perform a blood pressure measurement, the cuff is first inflated to occlude the artery. Next, the cuff is allowed to deflate over a span of approximately thirty seconds. The physical events that correspond to particular sections of the waveform are outlined below, in chronological order:

1. Cuff pressure exceeds SBP. This is considered the "super-systolic" portion of the waveform. During this period, the artery remains fully occluded. Pressure waves generated by cardiovascular activity create pulsatile arterial distention proximal to the occlusion. This distention is sensed by the transducer, producing the initial oscillations displayed on the waveform (see diagram above). Unlike later oscillations, the occlusion prevents blood flow from contributing to the measured pressures (i.e. the pressures are dominated by forces directly generated by the heart). Therefore, these oscillations represent aortic activity and may be a source of additional cardiovascular information.

When cuff pressure decreases to a point just below SBP, the pressure built up from previous heartbeats forces blood through the artery at a high velocity,
creating a Bernoulli effect: a force acting inward on the arterial wall. This inward force creates a measurable shift in the pressure wave, that shift causes the transducer to generate a signal. The shift is a time-dependent signal which exhibits different time-dependent characteristics from the original, pulsatile signal. The time dependent signal may be detected by visually inspecting the waveform and observing the gradual pulse-to-pulse change in trough shape over time. SBP is determined by using a digital pattern-recognition algorithm to identify the time-dependent signal characteristic of SBP (marked by the first triangle icon on the waveform).

2. As the cuff deflates, an increasing portion of the cardiovascular cycle generates pressures that exceed cuff pressure, resulting in an increasing volume of blood flow through the artery. The increase in blood flow volume causes an increase in oscillometric amplitude and a progressive shape change in the time-dependent signal.

When cuff pressure reaches MAP, the forces produced by the Bernoulli effect balance the cuff pressure, and the corresponding time-dependent signal results in a symmetrically-shaped triangular trough (marked by the second triangle icon).

3. Cuff pressure continues to decrease, and is no longer sufficient to occlude the artery. The resultant alleviation of the driving pressure causes the magnitude of the arterial wall distention to decrease. This is reflected in the decreasing magnitude of the waveform oscillations.

When the time-dependent signal reaches a characteristic DBP point, the pattern recognition algorithm identifies DBP (marked by the third triangle icon).

4. At pressures lower than diastolic, the cuff does not occlude the artery. Therefore, blood flow is no longer impeded. This final portion of the waveform is known as the sub-diastolic range of measurement. In this region, the forces on the arterial wall are dominated by hemodynamic factors. Therefore, any arterial wall distention can be used for calculations of arterial compliance (change in volume/change in pressure), or blood flow based on changes in hemodynamic parameters.

Since DynaPulse blood pressures are determined by a physical consequence of blood flow (i.e. the time-dependent signal), as opposed to the abstract criteria used in traditional oscillometric techniques, blood pressures measured using oscillometric Pulse Dynamics correlate very well to invasive, "gold standard" catheter measurements taken at the aorta. For further information on the correlation of the Pulse Dynamic technique to both catheter and auscultatory blood pressure please refer to DynaPulse Clinical Data. (link to research/validation)

Another advantage of the waveform is the high degree of confidence provided by its measurements. While most monitors provide final measurements, without any indication of measurement quality, DynaPulse monitors provide "full disclosure" by displaying a waveform for each measurement. Signal noise (artifact) due to patient movement, inadequate cuff placement, or other
factors will produce waveform irregularities that may be visually detected. This allows the operator to quickly establish the quality of individual measurements for validation.

The occlusion applied by the cuff during the measurement process causes the brachial and associated central arteries (including the aorta) to completely fill with blood. In this state, the arteries transmit cardiovascular pressure waves and fluctuations from the heart to the brachial artery, where they result in an output signal from the transducer. This allows additional cardiovascular information to be extracted from the waveform. For example, ectopic arrhythmia and other cardiac rhythm abnormalities may be detected by visually examining the waveform for missing or distorted oscillations.

The above plot is a graphical display of arrhythmia from the Pulse Dynamic technology. With this information, the physician could refer to traditional diagnostic techniques to determine the actual nature of the arrhythmia.
The above plot is a graphical display of arrhythmia from the Pulse Dynamic technology. With this information, the physician could refer to traditional diagnostic techniques to determine the actual nature of the arrhythmia.

**Ambulatory Monitoring**

Ambulatory blood pressure monitors periodically measure patient blood pressure over a predetermined length of time (typically 24 hours) as the patients go about their normal daily routines. The purpose of ambulatory blood pressure monitoring (ABPM) is to obtain data that reflects the cardiovascular state of the patient under conditions more representative of their normal everyday lifestyle than those inherent in a clinical environment.

The need for an ambulatory device was first recognized by Dr. Maurice Sokolow, head of the hypertension section of the San Francisco General Hospital during the 1950’s. He conducted a study demonstrating that there were persons with highly elevated blood pressures who lived a normal life span, whereas others with modest hypertension died at an early age due to cardiovascular complications. From these findings, Dr. Sokolow theorized that the clinic pressures of patients were not always representative of their everyday pressures.

In order to monitor patients outside of the clinical environment, Dr. Sokolow designed and constructed an ambulatory device. By using the ambulatory monitor, he was able to show that blood pressure varied throughout the day, and that "clinic pressures tended to be higher than ambulatory pressures in the majority of patients". Since the 1950’s, there has been a great deal of research in the area of ABPM. As a clinical procedure, ABPM has played a major role in the discoveries of white coat syndrome and the circadian rhythm of blood pressure, as well as the development of hypertension-relieving chronotherapeutics. ABPM has also been found to provide good correlative information regarding end-organ damage, such as left ventricular hypertrophy.

White coat hypertension is generally defined as "a persistently elevated clinic blood pressure and a normal pressure at other times," The elevation in blood pressure may be due to several factors, including nervousness, stress, or increased sympathetic activity associated with the clinical environment. It should be noted that it is not unusual for patients to exhibit high blood pressure in a new clinical environment. Therefore, elevated blood pressure may constitute a more significant symptom of hypertension once the patient has become acclimated to the clinical site.

Although the general description of white coat hypertension is agreed upon, the exact definition varies. Somewhere between 20% to 40% of patients with mild to moderate hypertension in a clinical setting may actually be white coat hypertensive. There are two salient issues that arise from white coat hypertension: the effects of anti-hypertensive drugs on normotensive individuals, and also the cost of administering those drugs. In order to avoid administering unnecessary hypertension management therapy to white coat hypertensives, these "white coat hypertensives" must be identified. Therefore, an increasing number of physicians are implementing ABPM into their hypertension diagnosis procedures.

There are three major mechanisms to explain white coat hypertension. The first is that it characterizes an exaggerated alerting response and, therefore, a heightened
response to stressful stimuli. The second explanation is that white coat hypertension is a learned, or conditioned, response. The third theory is that it is a precursor of sustained hypertension. Since the mechanisms responsible for white coat hypertension are not completely agreed upon, the question of whether the condition is benign or malevolent is also a matter of some debate. Currently, research is being conducted to determine whether white coat hypertensives should be classified for treatment purposes as normotensives, hypertensives, or as a completely new category with separate risks, characteristics, and treatment guidelines.

In addition to identifying "white coat hypertensives," ABPM is also extremely helpful in the development of chronotherapeutics (time-released medication) for hypertension management. Chronotherapy varies drug delivery rates throughout the day, either by automated delivery devices or by manual regulation. This can be used to account for periodic variations in patient conditions caused by circadian rhythms and periodically conducted activities. By examining individual time intervals, the physician is able to determine how much medication is required for each interval. Chronotherapeutics are then prescribed, allowing the patient to be treated with a minimum of medication. ABPM may prove to be extremely helpful in identifying the time periods when medication is required for chronotherapeutic treatment of hypertension. Once treatment has been initiated, subsequent ambulatory sessions would allow the physician to optimize the treatment program.

ABPM has also directly led to the discovery of the circadian rhythm of blood pressure: a decrease in blood pressure levels from periods of wakefulness to periods of sleep (for convenience, daytime and nighttime will be used for wakefulness and sleep, respectively). Many people exhibit this circadian rhythm, which consists of a blood pressure decrease of approximately 15%-25% during the evening, with increases to daytime levels again in the morning. Clinical studies have shown that people may be classified as either "dippers" or "non-dippers", depending on whether their blood pressure exhibits the circadian rhythm or remains close to its daytime level during nighttime hours. Since hypertensive "dippers" may be normotensive during nighttime hours, ABPM may prove helpful in optimizing treatment programs for hypertension.

An important characteristic of the circadian rhythm is a sharp increase in blood pressure early in the morning. This is accompanied by increases in heart rate, catecholamine levels, a-adrenergic receptors, corticosteroids, and platelet aggregation. Together, these sudden changes may result in early morning myocardial ischemia/infarction, stroke, and sudden death. ABPM may be a key factor in discovering the causes of such early morning cardiovascular complications.

ABPM data provides the best correlation between blood pressure and left ventricular hypertrophy (LVH), a measure of cardiac end-organ damage. White et. al. found a correlation between average daily blood pressure obtained by ABPM and LVH, whereas no relationship could be found between clinically obtained blood pressure data and LVH. This correlation has already been used in several important discoveries. For example, Verdecchia et. al. found that non-dippers have significantly higher degrees of LVH than dippers. This led to support for the hypothesis that non-dippers, when compared with dippers, also have a significantly greater number of strokes.
Clinical research in the field of ABPM has led to the application of additional analysis techniques that may allow the physician to obtain a clearer assessment of a patient's hypertensive condition. For example, the large volume of data collected from one ambulatory session allows the calculation of blood pressure and heart rate averages based on an entire day, as opposed to measurements taken during the limited time span of a visit to a clinic. This may give the physician additional information regarding a patient's overall cardiovascular condition.

Another technique now used with ABPM is load analysis. Load analysis quantifies the degree of patient hypertension by determining the total duration of patient blood pressure elevation as a percentage of the ambulatory period. Physicians may also graphically determine when during the ambulatory period a patient's blood pressure was elevated, to validate alternative explanations to hypertension for blood pressure elevation (food consumption, exercise, stressful situations, etc.). Load analysis is a potentially powerful tool that enables the physician to more specifically assess the severity and the nature of hypertension, and has already been used to quantitatively characterize the likelihood of LVH occurrence.

An important factor in any medical procedure is cost. ABPM may be cost effective by reducing the number of patients who are mislabeled as hypertensive and subsequently undergo hypertension management therapy. ABPM is also useful for long-term patient tracking, to allow earlier detection of cardiovascular changes. In addition, one twenty-four hour ABPM session using Pulse Dynamic technology may provide reliable information regarding blood pressure, arterial compliance, peripheral resistance, white coat classification, dipper/non-dipper classification, and cardiac end-organ damage evaluation. This decreases the need for exhaustive testing and allows quicker, easier diagnosis and treatment program development.

**Glossary of Cardiovascular Terms**

**Aneurysm:** Widening of a portion of an artery, due to disease or congenital abnormality.

**Angina Pectoris:** Pain in the central front of the chest brought about by effort. Usually a symptom of ischaemic heart disease.

**Anoxia:** Lack of oxygen. The condition which causes the death of tissue when arteries are blocked.

**Antihypertensives:** Drugs which reduce high blood pressure.

**Aorta:** The main trunk artery, receiving blood from the left ventricle.

**Aortic insufficiency:** Improper closing of the aortic valve, allowing a back flow of blood.

**Aortic valve:** The valve between the left ventricle and the aorta.

**Apex:** Lower portion of the heart, tip of the ventricles. The apex points leftward, downward, and forward.

**Arrhythmia:** Abnormal rhythm of the heart. May refer to rate, rhythm, or propagation sequence of depolarisation. Some are harmless. some are very serious.

**Arterial Compliance:** An index of the stiffness of the arterial wall.

**Arterioles:** The smallest arterial vessels resulting from repeated branching of the arteries. They conduct the blood to the capillaries.

**Arteriosclerosis:** Thickening, hardening, and loss of elasticity to the arterial wall.

**Artery:** Blood vessel carrying blood away from the heart.

**Artifact:** Noise which distorts a recording. For example, physical noise on a pressure tracing, or electrical noise on an ECG.
Asystole: A period during which the heart does not contract. Recorded on a tracing as a straight line.

Atherosclerosis: Deposits, usually fatty, on the inside of the artery.

Atrial septum: The wall separating the left and right atria.

Atrioventricular (AV) Node: The small bundle of specialised conductive cells which transmits electrical impulses from the atria to the ventricles.

Atrium: One of the two upper chambers of the heart.

Auscultation: The act of listening to sound from within the body. In cardiology usually with a stethoscope or automatic microphone based system.

Automaticity: The inherent property of myocardial cells to generate an electrical impulse by spontaneous depolarisation.

Autonomic nervous system: The system which controls tissues not under voluntary control such as the heart muscle. Divided into the sympathetic and parasympathetic systems.

Bradycardia: Low heart rate (usually defined as below 60BPM).

Bundle branch: Either of the branches of the specialised conduction system just below the His Bundle.

Bundle of His: The bundle of conduction fibres linking the AV node to the bundle branches.

Capillaries: The very narrow tubes forming the network between the arterioles and the veins.

Cardiac Arrest: Cessation of Ventricular activity. Absence of heartbeat.

Cardiac Cycle: One complete heart beat, contraction and relaxation. Normally takes about 0.85 seconds.

Cardiac Output: Volume of blood pumped by the heart per minute.

Cardiomyopathy: Disease of the heart muscle from various causes.

Chordae Tendinae: The fibrous cords which anchor the atroventricular valves to prevent them being turned inside out by ventricular contractions.

Collateral circulation: Circulation of the blood through nearby smaller vessels when a main vessel has been occluded.

Conduction: The transmission of an electrical impulse.

Coronary arteries: The small arteries supplying blood to the tissue of the heart.

Cor Pulmonale: Heart disease caused by impairment of blood flow through the lungs. Ultimately can cause failure of the right ventricle among other problems.

Depolarisation: The sudden change in electrical potential from negative to positive. In normal circumstances usually results in a contraction.

Diastole: The relaxation period of the heart.

Electrocardiogram (ECG or EKG): Graphic representation of the electrical activity of the heart as detected by electrodes on the skin or internally.

Embolism: Occlusion of a blood vessel by particles such as fat or air.

Embolus: A substance in a blood vessel which may be carried to a smaller vessel to become an obstruction to the flow.

Endocardium: The thin smooth membrane lining the inner surface of the heart. A specialised form of endothelial tissue.

Epicardium: The outer layer of tissue of the heart.

Essential hypertension: Hypertension of unknown origin, the commonest form of consistently elevated blood pressure.

Extrasystole: A premature contraction of the heart, in most cases harmless.

Fibrillation: Chaotic, high rate unsynchronised vibrations of the myocardium, resulting in absent or ineffectual pumping.

Haemodynamics: The study of blood flow and the forces involved.

Heart attack: A non-specific term relating to disturbance of heart function in coronary and other cardiac diseases.
Heart block: Total or partial blocking of electrical impulse travel from atria to ventricles resulting in slow or irregular pumping action.

Hypertension: High blood pressure, can relate to systolic, mean, or diastolic pressures.

Hypertrophy: The enlargement of a body due to increase in size of the cells. In the heart it is usually a result of increased demand for output.

Hypotension: Low blood pressure.

Idioventricular rhythm: Relatively slow rhythm arising from a ventricular focus, normally during heart block.

Infarction: Area of tissue which is dead or severely damaged, usually due to lack of blood supply.

Inherent rate: The rate of impulse formation in the various areas of the conduction system.

Ischemic tissue: Tissue with inadequate blood supply to maintain normal function.

Korotkoff sounds: The sounds heard via stethoscope or microphone during release of pressure in the arm cuff. The basic principle of auscultatory BP measurement.

Lumen: The passageway inside a blood vessel.

Malignant hypertension: Severe high blood pressure causing rapid damage to other organs such as the eyes and kidneys.

Mean Arterial Pressure (MAP): The time-weighted average of systolic and diastolic pressures.

Mitral valve: The valve between the left atrium and the left ventricle.

Murmur: An abnormal heart sound heard between the normal heart sounds.

Myocardium: The muscular wall of the heart, lying between the endocardium and the epicardium.

Normotensive: Having normal blood pressure.

Oscillometry: Measurement of changes in magnitude of arterial pressure pulses.

Pulmonary valve: The valve between the right ventricle and the pulmonary artery.

Purkinje Fibres: Network of electrical conducting fibres at the end of the specialised ventricular conducting system.

Refractory period: The length of time after depolarisation during which the muscle is incapable of another depolarisation.

Renal Hypertension: High blood pressure caused by kidney disease.

Repolarisation: Electrical recovery of heart when cell returns to a negative state.

Sino-Atrial (SA) Node: The small bundle of specialised cells high in the right atrium which initiates the regular cardiac depolarisation cycle.

Sphygmomanometer: An instrument for measuring arterial blood pressure.

Stroke volume: The amount of blood pumped out of the heart at each contraction.

Supraventricular tachycardia: A tachycardia originating in the atria, AV node, or His Bundle.

Systole: The period of contraction of the heart muscle. The depolarisation period.

Tachycardia: Rapid heart rate, usually defined as in excess of 100BPM.

Thrombosis: Occlusion of a blood vessel by clotting of the blood within the vessel itself at the site of the occlusion

Tricuspid valve: The valve between the right atrium and the right ventricle.

Vein: Any vessel in the body carrying blood back to the heart.

Vena Cava: The superior and inferior venae cavae carry the blood from the body back into the right atrium.

Ventricle: one of the two lower chambers of the heart.

Ventricular septum: (or Interventricular septum). The muscular wall separating the ventricles.

Waveform: Shape and/or structure of a pressure or electrical pulse recording cardiac activity.
Introduction to Pulse Dynamics: The DynaPulse Hemodynamic Monitoring

Understanding hemodynamics, the dynamic, physical relationships among blood pressure, blood flow and volume, the heart, vessels, and circulatory system, is essential for physicians to have a complete picture of the circulatory system so that they may more effectively diagnose and treat patients with cardiovascular complications. For the past 40 to 50 years, both invasive catheterization methods and non-invasive methods using ultrasound, sound, electrical, pressure coupling and sensing, or IR methods were developed and used for obtaining hemodynamic information, either directly or indirectly via waveform analysis.

Hemodynamic parameters, such as the viscosity of blood plasma, blood pressures, blood flow, cardiac output and stroke volume, resistance and compliance, have been defined and used for the evaluation of circulatory systems. “Normal” ranges for the human population were studied, reported, and used in clinical applications. For example, values of 140/90 (Systolic/Diastolic) for high blood pressure or 40% ejection fraction for systolic dysfunction in heart failure serve as guidelines for clinical decisions. However, due to the extreme complexities of not only the cardiovascular system, but also the associated diseases, both quantitative measurement of physical parameters and qualitative evaluation of the pulse waveform were used for the proper diagnosis of associated cardiovascular problems. Echocardiography and catheterization techniques were developed and became “gold standards” for the monitoring of hemodynamics and diagnosing complicated cardiovascular problems.

In the 1980’s, with the booming popularity of the personal computer, communication systems, and the Internet and information industries led by advanced technologies, the healthcare system was facing challenges of coping with an extremely large, aging population, the baby boomers, and their increased associated risks for developing or suffering cardiovascular diseases. Unfortunately, both catheterization and echocardiography are expensive, time consuming, and require professionally trained operators. Pulse Dynamic technologies, in contrast, are designed as non-invasive, low-cost, and effective methods for monitoring hemodynamics in the clinical setting, or even at a patient’s home. Pulse Dynamics allows wider access to important cardiovascular monitoring for a population increasingly at risk for cardiovascular disease.

This “Pulse Dynamics” booklet summarizes the physics of its methodology, the hemodynamic parameters derived from it, clinical validation and application studies since 1988. It’s intended to be used as references for 1) physicians using DynaPulse profiling for evaluating patient’s hemodynamics, 2) researchers to use Pulse Dynamic parameters for studies on hypertension and related cardiovascular diseases, risks and managements, and 3) educators to apply DynaPulse blood pressure monitoring and its online hemodynamic analysis for teaching physiology, circulation and cardiovascular system, other health related educational programs as well as Vital sign monitoring in Bioengineering. To learn more about Pulse Dynamics, its device and software, and online hemodynamic analysis operations, a quick guide for DynaPulse-5200A/Pathway is provided in Appendix A.
The Physics of Pulse Dynamics:

Pulse Dynamics, based upon the physical model of Shiu-Shin Chio’s invention (see reference patents and publications sited below), is a non-invasive method that measures blood pressures and other hemodynamic parameters. It analyzes the pulse waveform obtained from a cuff placed over brachial artery during routine blood pressure measurement, the **DynaPulse waveform**, which is similar to pulsation signals obtained from the so-called oscillometric. Hemodynamic parameters, systolic, diastolic, mean arterial pressure (MAP), heart rate, cardiac output, arterial compliance and resistance, etc. were derived from analyzing the DynaPulse waveform using the Chio’s methodology. Following chapters describe and illustrate the Pulse Dynamics (DynaPulse) technologies and physical models employed in the method.

**Chapter 1: The concept of Pulse Dynamics**

**Fig.1** shows the fundamental physics approach to describe the pulse-wave obtained from an inflated cuff coupled to a section of artery (brachial as an example) of a circulation system.
Chapter 2: Cuff – the pressure coupler

Cuff with a bladder, made of natural rubber material (latex), inside it, when inflated, has very good frequency response of 10Hz and below, which has been used in most ausculatatory and oscillometric blood pressure monitors. Following figure, Fig. 2, illustrate the common use of an inflated cuff on arterials, include upper arm (brachial), for occluding blood flow and measuring blood pressures. This cuff-artery pressure coupling system enable the transferring of arterial pulse signals from artery to the cuff, and then be recorded by DynaPulse device.

Fig. 2. Using cuff on human artery system

The Pulse Dynamic Cuff-based Physical System:
“Interaction” between Cuff & Arterial Circulation

- Cuff = A good low frequency (0-10 Hz) pressure sensor and its interaction with artery is “dynamic”.
- Arterial System = A dynamic, complicate and multi-component closed circulation system.
Chapter 3: DynaPulse device – the pressure signal detection, amplification and digital data acquisition via personal computer (PC)

DynaPulse is the electronic device that couples to the cuff with a silicone pressure sensor, amplifies, digitizes and records the cuff-pulse signals for further analysis by the Pulse Dynamics methodology. Silicon pressure was used because it has better linearity than other cheaper capacitance-coupled sensor used in most home blood pressure monitor in the pressure range of 30 to 300 mmHg. It's more sensitive than most home blood pressure monitors, with signal/noise ratio of 50-60 times better. The cuff pressure pulse signals were then recorded digitally at 50 Hz sampling rate. 50 Hz sampling allows up to 25-Hz resolution on pulse signals, which is essential for determination of systolic and diastolic pressure points, since the systolic/diastolic phenomena associated to the K-1 and K-4 of Korotkoff sounds are normally in 10-20 Hz range. Figure 3 below is an example of the recorded DynaPulse pulse waveform.

![Fig. 3 The DynaPulse (oscillometric) pulse waveform](image)

Chapter 4: DynaPulse blood pressure measurement method

The Pulse Dynamic method first determines the systolic, diastolic and mean arterial pressure (MAP) via analyzing the recorded DynaPulse pulse waveform (Fig. 3) by pattern recognition their associated pressure points. Illustrated in Fig 3, at the lower portion and above the “Cuff Pressure” axis, three triangular icons marked the DynaPulse determination of Systolic, MAP and Diastolic points. Their patterns represent the negative-going pressure, the phenomena know as Bernulli principle, (Bernulli/Venturi diagram illustrated in Fig. 4) are results from various velocities of blood flow caused by the occlusion of cuff to artery during blood pressure measurement. It’s different from other oscillometric blood pressure measurement methods that analyzed the amplitude changes instead. With this method, DynaPulse may be used to measure arterial blood pressure other than brachial. DynaPulse, with its higher sensibility, detects the very moments of pressure changes at systolic and diastolic points, which has been noticed closer to the invasive (catheterization) measurements, and different from the Korotkoff’s K-1, K-4 and K-5 sounds according to many studies sited in the booklet. Fig. 5 illustrates the comparison of DynaPulse blood pressure vs. K-sounds. In addition, DynaPulse pulse
waveform, records the entire information during a blood pressure measurement of 20-50 seconds, allow user to identify irregular heartbeats and artifacts due to arm movement. Fig. 6 illustrates some sample recordings.

Fig. 4 The Bernulli/Venturi diagram

Fig. 5 DynaPulse blood pressures vs. Korotkoff sounds
Fig. 6 Sample DynaPulse waveforms (one normal and two with irregular beats)
Chapter 5: DynaPulse brachial artery compliance and resistance measurement method

In order to derive other hemodynamic parameters beyond systolic and diastolic, Pulse Dynamic method further analyzes the complicated cuff-pressure dependent DynaPulse pulse waveform at three areas of cuff-pressure, the **supra-systolic** area at systolic and above, the **sub-diastolic** area at diastolic and below, and the area between systolic and diastolic, the blood pressure measurement, or blood flow **Dynamic**, area. At supra-systolic, where cuff pressure exceeds the systolic and occluded the brachial artery, therefore cuff can sense up to the aortic point (T-sensing), and at sub-diastolic, where full blood flow through a “straight tube” artery section is assumed, and pulse is sensed by the cuff (S-sensing). Fig. 7 is the conceptual illustration of Pulse Dynamic model, and compared to other measurement methods, catheter, ultrasound and tonometer. Fig. 8 showed the comparison of DynaPulse supra-systolic and sub-diastolic waveforms to simultaneously recorded catheterization pressure pulses. Where supra-systolic waveform resembles the cath-waveform at up-stroke area, and the sub-diastolic resembles the down stroke area. This observation is the fundamental principle of Pulse Dynamics, which made possible to treat the pressure inside an artery section independently for perpendicular and parallel components, as illustrated in Fig. 9. Arterial (brachial) compliance and distensibility, and resistance were derived, independently from the perpendicular and parallel pressure components separately (reference to Chio patents and publications sited below). The derived equations were summarized in the “Pulse Dynamic parameters and their definitions” section of this booklet.

**Fig. 7** The conceptual physical model of Pulse Dynamic method

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The Pulse Dynamic Cuff-based Physical Model:
The “T” and Straight tube model vs. other sensors

- “T” Sensing = Cuff at Supra-systolic pressure
- “Straight” Sensing = Cuff at Sub-diastolic pressure
- “Dynamic” Sensing = Cuff pressure varies from systolic to diastolic pressures
Chapter 6: DynaPulse cardiac output measurement method

As described above, Pulse Dynamics determines systolic, diastolic and MAP closer to the aortic pressure values. By further analyzing the normalized DynaPulse pressure waveform, and assuming that it closely resembles the central aortic pressure, which
superimposes to the top portion of an LV pressure contour (Fig. 10 illustrates the concepts), using Gaussian transformation from aortic-to-LV pressure pulse waveforms, The (LV dP/dt )max was derived according to following equation:

\[
LV\frac{dP}{dt}_{\text{max}} = BA\frac{dP}{dt}_{\text{max}} \frac{Tr}{Tr} \cdot \frac{e^{\frac{Tr^2}{2}}}{2}, \text{ and}
\]

\[
LVC = \frac{BA}{Tr} \frac{dP}{dt}_{\text{max}} \cdot \frac{e^{\frac{Tr^2}{2}}}{SBP}
\]

Where,

\[
1 \cdot T_{pp,BA}^L = T_{pp,BA}^L = \sqrt{1 + \frac{DBP}{SBP - DBP} \cdot \sqrt{e}}, \text{ and}
\]

Tpp = time interval between \( \frac{dP}{dt} \) to \( \frac{dP}{dt} \) for brachial artery (BA) and left-ventricular (LV) pressure contours

Cardiac output (CO) was then obtained using equation \( CO \propto LVC \cdot HR \cdot BSA \) and an empirically determined scaling factor obtained by comparing to thermo-dilution (TD) CO. Where, BSA (body surface area) is defined by standard DuBois equation, a function of weight and height. Fig.11 shows a typical normalized DynaPulse waveform.

**Fig. 10** (Right): The concept of Aortic-to-LV pressure contour fitting for transformation
(Left): Comparison of a convoluted DynaPulse pulse to a Cath-aortic pulse
Chapter 7: DynaPulse hemodynamic profiling and report

In summary, the Pulse Dynamic method analyzes the entire pulse waveform of 20 –50 seconds recorded during a cuff blood pressure measurement. It identifies the subtle pressure changes due to cuff restriction to the blood flow when its pressure decreased from above systolic to below diastolic to determine the blood pressures. It further analyzes the normalized pressure waveform (normalized to systolic and diastolic obtained above), and independently, derives brachial arterial (BA) compliance and distensibility from the systolic cycle pulse wave (pressure above MAP), and BA resistance from the diastolic cycle. Cardiac output (CO) was derived, also independent to the above described parameters, from systolic cycle pulse wave with its dP/dt max (up stroke), transferred to LV dP/dt max, together with other factors, heart rate (HR) and body surface area (BSA). Other hemodynamic parameters, such as stroke volume (SV), systemic vascular compliance (SVC) and resistance (SVR) were calculated according to following equations:

\[ SV = \frac{CO}{HR}, \]

\[ SVC = \frac{SV}{PP}, \text{ where PP (pulse pressure) = systolic – diastolic, and} \]

\[ SVR = \frac{MAP}{CO} \]

Their indexes were calculated by dividing them by body surface area (BSA), obtained by using weight and height with standard DuBois equation.

DynaPulse user may upload the Pulse Dynamic waveform, via Internet, to DynaPulse Data Analysis Center (DAC) to obtain hemodynamic profile report. This allows a cost-effective, safe and consistent, and worldwide application of Pulse Dynamics. Fig. 12 is an example DynaPulse Hemodynamic profile report.
Fig. 12 Sample of DynaPulse Hemodynamic Profile Report

Hemodynamic Report

DynaPulse - Physician Name: Physician Name

Patient ID: 647
Patient Name: Nathan Linn
Age/SEX: 47/Male
Ethnicity: (Unspecified)
Cuff Size/ASLA: M/1.76 m²
Height/Weight: 167 cm/68 kg
BA Diameter: 0.46 cm
Measurement Time: 3/26/1997 15:40

153
Systolic

112
Mean

90
Diastolic

70
HR

The morphology of the waveform should be considered when interpreting the numbers below.

CARDIAC PARAMETERS
LV Ejection Time (sec) 0.307 [0.207 - 0.388]
LV dP/dt Max (mmHg/s) 1,056 [847 - 1505]
LV Contractility (1/6) 11.36 [12.59 - 19.08]
Cardiac Output (L/min) 4.84 [3.59 - 7.9]
Cardiac Index (L/min/m²) 2.74 [1.95 - 3.74]
Stroke Volume (mL) 68.3 [57.7 - 100.7]
Stroke Vol Index (mL/m²) 39.7 [31.0 - 48.0]

SYSTEMIC VASCULAR PARAMETERS
SV Compliance (mL/mmHg) 1.08 [1.02 - 2.0]
SV Resistance (dynas/sec/cm⁵) 23.13 [871 - 1902]

BRACHIAL ARTERY PARAMETERS
BA Compliance (mL/mmHg) 0.076 [0.056 - 0.132]
BA Distensibility (kPa/mmHg) 5.18 [4.35 - 9.26]
BA Resistance (kdyns/sec/cm⁵) 2.435 [80 - 317]

*These “normal” ranges of Pulse Dynamic parameters are based on data analyzed using Male (n=916) normotensive subjects (Systolic <140 and Diastolic<90) between 18-40 years of age. The range is defined as the Mean +/- 2SD. Am. J. Hypertension 2000; Vol 13, No. 4, Part 2, pp. 257A.

PulseMetric has received FDA clearance to market their devices as blood pressure monitors and are registered some of the hemodynamic parameters listed herein may not have yet received clearance from the FDA and may be limited to investigational use. Contact PulseMetric for an update.

Format for Print
Chapter 8: Clinical application and limitation of Pulse Dynamics

Blood pressures and other hemodynamic parameters are physical values or indicators that represents the dynamic nature of artery blood circulation system. They are not a "constant" like body temperature, but may vary minute-to-minute or even beat-to-beat. Clinical applications using hemodynamic monitoring is complicated, and would require fully understanding of the dynamic nature and physics of human circulation system, functions of connected organs, and a closely examination of all parameters and the directions of their changes against each related parameters. Pulse Dynamics obtained all hemodynamic parameters, including blood pressures, within 20-50 seconds during a cuff-blood pressure measurement, which provides the closest possible of obtaining a "simultaneous" of hemodynamic monitoring. The DynaPulse hemodynamic profile demonstrates its unique ability to clinical and sub-clinical applications. In addition, clinical application user shall also understand the limitations of Pulse Dynamic method to fully utilize the derived hemodynamic data. In the course of our past validation and clinical application studies with Pulse Dynamics, following are limitations of this method:

1. Sever irregular heart beat or artifacts that make impossible to determine accurate blood pressures,
2. Obesity, overweight, subject with upper arm of cone shape that difficult to put on a cuff,
3. Systolic blood pressure of right and left arm are different of more than 10 to 20 points, possibility of blockage at one side, the higher systolic side shall be based,
4. Heart rate over 120 and the patient is not at rest (unstable hemodynamics), and
5. Patient with pulmonary hypertension, aortic regurgitation, and other sever heart problems that may affect the accuracy in cardiac output estimation, especially when compare to thermo-dilution method.

References to the technologies of Pulse Dynamics:

[Patents]:

[Publications]:
1. Chio SS, DeMaria AN, et.al., Development and Validation of a Non-invasive Method to Estimate Cardiac Output using Cuff Sphygmomanometry, accepted and to be published at Clinical Cardiology in 2008.


Clinical Validation of DynaPulse Hemodynamic Parameters:

Pulse Dynamics is an easy-to-use and reproducible non-invasive method, developed by Pulse Metric R&D team, for monitoring hemodynamics. It is based on the biophysics of direct pressure coupling between a blood pressure cuff and a section of artery (brachial), a technology protected by patents from Dr. S-S. Chio. The physical model and validation of blood pressure, waveform and compliance were conducted with the help of Dr. AN DeMaria and Dr. DT O’Connor at UCSD, and published in Am. J. of Cardiology 1977; 80:323-330, and other papers published after. The following table is a summary of the results of our validation studies on Pulse Dynamic parameters.

Table I: Summary of Clinical Validation of the Pulse Dynamic Parameters

<table>
<thead>
<tr>
<th>DynaPulse Parameters</th>
<th>Reference Method</th>
<th>Reference Parameter</th>
<th>N</th>
<th>R</th>
<th>P</th>
<th>SEM (+/-)</th>
<th>Bias (Ref-D)</th>
<th>SD (SE)</th>
<th>Ref. [*]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic pressure</td>
<td>Catheterization</td>
<td>Ao end systolic</td>
<td>36</td>
<td>0.94</td>
<td>&lt;0.01</td>
<td>145</td>
<td>5</td>
<td>-1</td>
<td>9.5</td>
</tr>
<tr>
<td></td>
<td>2. Auscultation</td>
<td>K1 systolic</td>
<td>132</td>
<td>0.97</td>
<td>&lt;0.001</td>
<td>127</td>
<td>21</td>
<td>-5</td>
<td>5.3</td>
</tr>
<tr>
<td>Diastolic pressure</td>
<td>Catheterization</td>
<td>Ao end diastolic</td>
<td>36</td>
<td>0.91</td>
<td>&lt;0.01</td>
<td>77</td>
<td>2</td>
<td>-3</td>
<td>5.3</td>
</tr>
<tr>
<td></td>
<td>2. Auscultation</td>
<td>K4 diastolic</td>
<td>132</td>
<td>0.89</td>
<td>&lt;0.001</td>
<td>72</td>
<td>10</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Pulse Pressure</td>
<td>Catheterization</td>
<td>Ao (SBP-DBP)</td>
<td>36</td>
<td>0.93</td>
<td>&lt;0.01</td>
<td>68</td>
<td>4</td>
<td>2</td>
<td>7.3</td>
</tr>
<tr>
<td></td>
<td>2. Auscultation</td>
<td>K4 (SBP-DBP)</td>
<td>132</td>
<td>0.9</td>
<td>&lt;0.001</td>
<td>72</td>
<td>10</td>
<td>1</td>
<td>7.8</td>
</tr>
<tr>
<td>Mean Arterial Pressure</td>
<td>Catheterization</td>
<td>Ao MAP</td>
<td>36</td>
<td>0.95</td>
<td>&lt;0.01</td>
<td>100</td>
<td>3</td>
<td>0</td>
<td>5.6</td>
</tr>
<tr>
<td>Ejection Time</td>
<td>Catheterization</td>
<td>Ao &quot;tpp&quot; time</td>
<td>14</td>
<td>0.85</td>
<td>&lt;0.001</td>
<td>0.25</td>
<td>0.01</td>
<td>0</td>
<td>0.02</td>
</tr>
<tr>
<td>dP/dt Max (Aortic)</td>
<td>Catheterization</td>
<td>Ao dP/dt max</td>
<td>14</td>
<td>0.87</td>
<td>&lt;0.001</td>
<td>508</td>
<td>37</td>
<td>-92</td>
<td>82</td>
</tr>
<tr>
<td>dP/dt Max (LV)</td>
<td>Catheterization</td>
<td>LV dP/dt max</td>
<td>22</td>
<td>0.75</td>
<td>&lt;0.01</td>
<td>1279</td>
<td>241</td>
<td>182</td>
<td>7</td>
</tr>
<tr>
<td>Cardiac Output</td>
<td>Doppler ultrasound #1</td>
<td>CO/LVOT+DB stress</td>
<td>113</td>
<td>0.84</td>
<td>&lt;0.001</td>
<td>-0.74</td>
<td>0.8</td>
<td>[3]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Doppler ultrasound #2</td>
<td>CO/resting</td>
<td>45</td>
<td>0.76</td>
<td>&lt;0.01</td>
<td>4.74</td>
<td>0.77</td>
<td>0.03</td>
<td>[4]</td>
</tr>
<tr>
<td></td>
<td>3. FICK</td>
<td>CO</td>
<td>26</td>
<td>0.61</td>
<td>&lt;0.001</td>
<td>5.01</td>
<td>1.09</td>
<td>0.28</td>
<td>[4]</td>
</tr>
<tr>
<td></td>
<td>4. Thermo-dilution CO (11 NPH+9 PH)</td>
<td>20</td>
<td>0.47</td>
<td>0.04</td>
<td>4.29</td>
<td>1.21</td>
<td>-0.83</td>
<td>1.12</td>
<td>[6]</td>
</tr>
<tr>
<td></td>
<td>CO (11 NPH)</td>
<td>11</td>
<td>0.63</td>
<td>0.04</td>
<td>4.84</td>
<td>0.95</td>
<td>-0.07</td>
<td>0.76</td>
<td>[6]</td>
</tr>
<tr>
<td></td>
<td>CO (9 PH)</td>
<td>9</td>
<td>0.81</td>
<td>0.01</td>
<td>3.62</td>
<td>1.18</td>
<td>-1.76</td>
<td>0.71</td>
<td>[6]</td>
</tr>
<tr>
<td>Arterial Compliance</td>
<td>Catheterization</td>
<td>SVC</td>
<td>20</td>
<td>0.83</td>
<td>&lt;0.001</td>
<td>0.036</td>
<td>[1]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arterial Resistance</td>
<td>1. Indirect with drug #1</td>
<td>ACE pre/post treat.</td>
<td>10</td>
<td>0.003</td>
<td>593.8</td>
<td>34.8</td>
<td>141</td>
<td>[5]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Indirect with drug #2</td>
<td>Ca. Ch. Blockade</td>
<td>8</td>
<td>0.006</td>
<td>650.5</td>
<td>41.6</td>
<td>108.5</td>
<td>[5]</td>
<td></td>
</tr>
</tbody>
</table>

[*] References:
3. Tsai, J, .. DeMaria AN, 2001; Abstract at Heart Failure Meeting (see page 15)
4. Li, TD, et. al., Medical J. of Chinese PLA, 2001; 26: 189-190 (see Appendix B, page 62)
5. Brinton, TJ, .. O’Connor, DT, Hypertension, 1996; 28:599-603 (see page 28)
6. Chio, SS, .. DeMaria, AN, (accepted and to be published in Clinical Cardiology 2008)
7. Brinton TJ,.. Liu, CP, Abstract, Am. Society of Hypertension annual meeting, 1997 (see page 28)
DynaPulse Hemodynamic Report: Sample Figure and explanations

After taking a complete recording of blood pressure and pulse waveforms with a DynaPulse device, and transmitting the waveforms for analysis through Internet/web based algorithms via the DynaPulse Analysis Center (DAC), see Appendix A for a quick overview of operations, Pulse Dynamic (hemodynamic) parameters and pulse waveforms can be reported in the following (1-5 area) arrangement, as shown in the figure below:

Area 1: Showed auscultatory (K-sound) equivalent Systolic, diastolic and heart rate, and the Pulse Dynamic pulse waveform for visual identification of a good pulse signal or bad signal with irregular heart beat or motion artifacts.

Area 2: Showed Pulse Dynamic blood pressures, systolic, diastolic and MAP that are closely related to central aortic pressures, and pulse pressure.

Area 3: Showed cardiac or heart functions, which include heart rate, ejection time, contractility, cardiac output, stroke volume and their indexes, according to the equations described below.

Area 4: Showed systemic vascular compliance and resistance as derived from cardiac output and other pressure parameters, according to the equations described below.

Area 5: Showed brachial artery compliance, distensibility and resistance, according to the equations described below.
Hemodynamic Report

PMI - Physician Name: Dr. Robert Smith

<table>
<thead>
<tr>
<th>Patient ID: 01010101</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Name: John Doe</td>
</tr>
<tr>
<td>Age/Sex/Ethnicity: 24/Male/(Unspecified)</td>
</tr>
<tr>
<td>Height/Weight: 177 cm/63 kg</td>
</tr>
<tr>
<td>CuffSize/BSA/BA Diam: M/1.78 m²/0.38 cm</td>
</tr>
</tbody>
</table>

Auscultatory eq. Syst.(K1)/Dia.(K4)

117 / 77 mmHg
HR: 68 bpm

The morphology of the waveform should be considered when interpreting the numbers below.

**CENTRAL BP PARAMETERS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Normal Range (Male)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>End Systolic (mmHg)</td>
<td>122</td>
<td>[105 - 143]</td>
</tr>
<tr>
<td>End Diastolic (mmHg)</td>
<td>78</td>
<td>[54 - 83]</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>89</td>
<td>[70 - 101]</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>44</td>
<td>[39 - 72]</td>
</tr>
</tbody>
</table>

**CARDIAC PARAMETERS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Normal Range (Male)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV Ejection Time (sec)</td>
<td>0.293</td>
<td>[0.207 - 0.388]</td>
</tr>
<tr>
<td>LV dP/dt Max (mmHg/s)</td>
<td>1,186</td>
<td>[847 - 1506]</td>
</tr>
<tr>
<td>LV Contractility (1/s)</td>
<td>16.02</td>
<td>[12.39 - 19.08]</td>
</tr>
<tr>
<td>Cardiac Index (L/min/m²)</td>
<td>3.71</td>
<td>[3.59 - 7.90]</td>
</tr>
<tr>
<td>Stroke Volume (mL)</td>
<td>240</td>
<td>[195 - 3.74]</td>
</tr>
<tr>
<td>Stroke Volume Index (mL/m²)</td>
<td>76.3</td>
<td>[57.7 - 100.7]</td>
</tr>
</tbody>
</table>

**SYSTEMIC VASCULAR PARAMETERS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Normal Range (Male)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV Compliance (mL/mmHg)</td>
<td>1.74</td>
<td>[1.02 - 2.00]</td>
</tr>
<tr>
<td>SV Resistance (dyne/sec/cm²)</td>
<td>1925</td>
<td>[871 - 1902]</td>
</tr>
</tbody>
</table>

**BRACHIAL ARTERY PARAMETERS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Normal Range (Male)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BA Compliance (mL/mmHg)</td>
<td>0.114</td>
<td>[0.056 - 0.132]</td>
</tr>
<tr>
<td>BA Distensibility (%/mmHg)</td>
<td>8.97</td>
<td>[4.38 - 9.28]</td>
</tr>
<tr>
<td>BA Resistance (kdyne/sec/cm²)</td>
<td>185</td>
<td>[80 - 317]</td>
</tr>
</tbody>
</table>
Pulse Dynamic Parameters and their Definitions

The hemodynamic parameters measured by the DynaPulse monitors are based on the patented methodologies of Pulse Metric, Inc., using innovative technology to acquire an arterial pressure waveform generated by brachial artery pulsation signals through a non-invasive cuff sphygmomanometer. At the DynaPulse Analysis Center, various proprietary algorithms are applied to the pressure waveform to extract detailed characteristics, and through extensive clinical research, derive certain hemodynamic parameters. The definitions for these parameters are described below:

I. BLOOD PRESSURE

• **Systolic** is the measurement of standard clinical systolic blood pressure. Measured using standard oscillometric algorithms, and closely represents values taken by auscultatory techniques using mercury cuff sphygmomanometry and Korotkoff sounds (K1).

• **Diastolic** blood pressure is the measurement of standard clinical diastolic blood pressure. Measured using standard oscillometric algorithms, and closely represents values taken by auscultatory techniques using mercury cuff sphygmomanometry and Korotkoff sounds (K4).

• **End Systolic** blood pressure measures central arterial blood pressure at end-systole. Measured using proprietary Pulse Dynamics waveform pattern-recognition algorithms.

• **End Diastolic** blood pressure measures central arterial blood pressure at end-diastole. Measured using proprietary Pulse Dynamics waveform pattern-recognition algorithms.

• **Mean Arterial Pressure** is the average blood pressure over time, measured using proprietary Pulse Dynamics pattern-recognition algorithms. It can also be estimated using MAP = 1/3 Systolic + 2/3 Diastolic.

• **Pulse Pressure** = Systolic – Diastolic

II. CARDIAC PARAMETERS

• **Heart Rate (HR)** is determined by the DynaPulse monitor

• **LV Ejection Time** is the duration of the systolic cycle

• **LV dp/dt max** is the maximum rate of pressure change in the LV, derived from arterial dp/dt max

• **LV Contractility** is an index of cardiac contractility derived from LV dp/dt max

• **Cardiac Output (CO)** is the volume of blood ejected by the left ventricle per minute. It is calculated using proprietary algorithms and a model based on LV dp/dt, HR, and an empirically derived scaling factor. Validation has been performed using thermo-dilution and echocardiography.

• **Cardiac Index = CO / BSA** Where, BSA = Body Surface Area
• **Stroke Volume (SV)** = \( \frac{CO}{HR} \)
• **Stroke Volume Index** = \( \frac{SV}{BSA} \)

III. SYSTEMIC VASCULAR PARAMETERS
• **Systemic Vascular Compliance (SVC)** = \( \frac{SV}{PP} \)
• **Systemic Vascular Resistance (SVR)** = \( \frac{MAP}{CO} \)

IV. BRACHIAL ARTERY PARAMETERS
• **Brachial Artery Compliance** is defined as \( \frac{dV}{dP} \), derived using a physical model of the brachial artery segment
• **Brachial Artery Distensibility** is defined as the compliance divided by the arterial volume \( \left[ \frac{dV}{dP} \right] / V \), or the percentage change in volume per mmHg change in pressure
• **Brachial Artery Resistance** = \( \frac{(MAP-DBP)}{(Diastolic volume flow)} \)

V. ANTHROPOMETRIC PARAMETERS
• **Body Surface Area (BSA)** is defined by the standard DuBois equation
• **Brachial Artery Diameter** for the reference volume was estimated using an empirically derived model based on gender, height, weight, and MAP, and validated using B-Mode ultrasound \( (n = 1,250, r = 0.63, P < 0.05) \)

The DynaPulse technology is based on simple concepts of physics applied to the human system. It acquires a biological signal, and using advanced algorithms and engineering, is able to calculate parameters describing the cardiovascular system and blood flow properties, called hemodynamics. These hemodynamics are then provided to physicians to help care for their patients.

The device records and displays the oscillometric pressure waveform signal from the brachial artery using a blood pressure cuff wrapped around the upper arm. As the cuff deflates from high to low pressures, a pressure waveform is generated, first at low amplitudes because at high pressures the artery is occluded and there is very little blood flow (near systolic blood pressure), then steadily increasing to wider amplitudes as the blood flow resumes reaching a high point around the mean arterial pressure, then finally decreasing again in amplitude (near diastolic blood pressure) as the coupling between the cuff and the artery weakens making it harder for the cuff to detect the pulse signal. These changes of blood flowing through a dynamically changing artery create differences in Bernoulli’s flow effects at each stage, creating what can be described as a phase change in the waveform. For example at the systolic blood pressure, as the artery just begins to open after being occluded, blood spurts through in turbulent flow, creating an early suction effect on the wall. This suction effect translates into the phase change of the waveform, which is then detected by proprietary algorithms and interpreted as the systolic blood pressure. Similar phenomenon happens for mean arterial and diastolic.
blood pressures, each with a unique flow pattern. For more details see our website at http://www.dynapulse.com

The most clinically significant and primary parameters of DynaPulse are systolic, diastolic and mean arterial blood pressures, heart rate, brachial artery compliance and distensibility, cardiac output and systemic vascular resistance. Many other parameters can be derived from these parameters.

Cardiac output is the volume amount of blood ejected per minute, and is defined as CO = SV x HR. Stroke volume is estimated by assuming that the amount of blood ejected per beat is related to the left ventricular contractility, with adjustments for weight and height to account for body size. The faster and more forcefully the left ventricle contracts (dP/dt), the more blood is ejected out. This technique has been validated with good correlations against thermo-dilution, Fick, and echocardiography.

Arterial compliance and distensibility are measures of the stiffness of an artery. Compliance is defined as the change in volume per unit change in pressure (dV/dP), while distensibility is adjusted for the arterial diameter and defined to be the “normal” or “specific” compliance. Thus distensibility measures the percentage change in volume per unit change in pressure [(dV/V)/dP]. There are various methods and devices for calculating indices of arterial stiffness, all with different strengths and weaknesses. Many have been widely used in clinical research studies in various applications. The DynaPulse method uses a simple physical model of the brachial artery segment and proprietary curve fitting methods. Further evidence and more details can be found in DeMaria, Am J Cardiol. 1997 Aug. 1; 80(3): 323-30 and O’Connor, Hypertension. 1996 Oct; 28(4):599-603.

Equations used to derive brachial artery compliance (BAC) and distensibility (BAD) are:

\[
Compliance (mL/mmHg) = \frac{dV}{dP} = \frac{\pi^2 \cdot D_e^2 \cdot (D_e + L_e)}{(dP/\Delta t)pp \cdot Tpp}_{SW}
\]

\[
Volume (mL) = \pi \left( \frac{D_e}{2} \right)^2 \cdot L_e
\]

\[
Distensibility (\% / mmHg) = \frac{Compliance}{Volume} = \frac{\frac{dV}{dP}}{V} = \frac{\frac{dV}{dP}}{V} = \frac{4 \cdot \pi \cdot (D_e + L_e)}{(dP/\Delta t)pp \cdot Tpp}_{SW} \cdot L_e
\]

\[
\approx \frac{4 \cdot \pi}{(dP/\Delta t)pp \cdot Tpp}_{SW} \cdot 100\% \\
D_e << L_e
\]

Where, only systolic wave (the systolic cycle, SW) parameters, dP/dt and Tpp, were used. \( L_e \) is the effective length of cuff that couples to brachial section, and \( D_e \) is the estimated brachial artery diameter.

Distensibility is a specific BA compliance, normalized to the volume of cuff-artery coupled section. It’s independent to brachial diameter or the size of cuff used.
Brachial artery resistance (BAR) was calculated using following equation:

\[
\text{Peripheral Resistance (}[\text{mm Hg/L}]\text{/min}) = \frac{(\text{MAP} - \text{DBP}) \cdot [(\text{dP/dt})_{pp} \cdot \text{Tpp}]}{\pi^2 \cdot D_o^3 \cdot (\text{dP/dt})_{DW}}
\]

Where, diastolic pressure and diastolic wave (diastolic cycle, \(D W\) \(dP/dt\), MAP and systolic wave \(dP/dt\) and Tpp, estimated brachial diameter were used.

The remaining parameters may be derived from other parameters. Together with following available clinical studies, they may provide a much better comprehensive assessment of the cardiovascular status, and useful clinical utilities for physicians, as well as researchers and teachers who are interested in using Pulse Dynamics. Refer to the “Sample Report” on the DynaPulse web site, www.dynapulse.com, for definitions of these parameters.

=================================================================================================

**************************************************************************
Summary of Clinical Studies and Applications using DynaPulse Blood Pressure and Hemodynamic Monitoring:

In this booklet, we further summarize and organize the results, abstracts and key findings, of over 100 clinical studies, case studies, etc., conducted by researchers in the US and worldwide that used Pulse Dynamics for measuring hemodynamic parameters and their clinical applications.

The booklet is organized with seven areas of hemodynamics in clinical research applications, plus one in techniques and validations (Studies cover multi-areas of interests may appear more than once):

1. Hypertension management – Studies on drug and non-drug therapies
2. Hypertension and cardiovascular risk studies – Epidemiology, risk factors, Genetic and environmental risks, obesity, diets, new markers, and preventions
3. Hypertension and heart diseases – Studies on hemodynamics and cardiac problems and functions
4. Hypertension and renal diseases – Studies on hemodynamics and kidney problems and functions
5. Hypertension and stroke/vascular diseases – Studies on hemodynamics and cerebrovascular/vascular problems and functions
6. White-coat and essential hypertensions – 24-hour ambulatory blood pressure monitoring (ABPM) and circadian rhythm studies
7. Hypertension and women’s cardiovascular health – Studies on hemodynamics and pregnancy
8. Pulse Dynamics R&D – The development of DynaPulse blood pressure and hemodynamic monitoring technique and clinical validation studies

We sincerely thank those researchers for their contribution to the development of Pulse Dynamics and its clinical applications.
(1) Hypertension management – Studies on drug and non-drug therapies

2006-Book

In this article, Pulse Dynamic waveform and central or end-systolic and end-diastolic blood pressures derived by DynaPulse blood pressure monitor (DP-200M) were illustrated to reflect arterial stiffness.

(Book 2006: Chapter 35)

2006
Health benefits of Tai Chi Chuan training: improved arterial distensibility and compliance in aged subjects*

Chun-Hsiung Wang, M.D., M.H.A., Sir-Chen Lin, M.D., and Wan-An Lu, M.D., Ph.D.

Abstract: This study evaluated the effect of three-month Tai Chi Chuan (TCC) training on the brachial artery distensibility and compliance in the elder adults. Seventeen TCC practitioners and twenty TCC trainees were recruited in this study. The BrachD and hemodynamics were measured by pulse waveform analysis (DynaPulse 2000A, Pulse Metric, Inc.) between TCC practitioners and TCC trainees before TCC training. The changes in BrachD measures and hemodynamics after 3-month TCC training were compared. The TCC trainees participated in the training program with classical Yang's Tai Chi Chuan (40 minutes/time, 7 times/week). We found that after three-month TCC training in the trainees group, systolic blood pressure and pulse pressure were all decreased significantly from 126.9 ± 10.7 mmHg to 118.8 ± 17.3 mmHg, and from 58.5 ± 9.6 mmHg to 51.3 ± 13.3 mmHg respectively. Brachial artery distensibility and brachial artery compliance were all increased significantly from 5.28 ± 1.69 %/mmHg before TCC training to 6.35 ± 2.54 %/mmHg after three-month TCC training (p = 0.008), and from 0.05 ± 0.01 ml/mmHg before TCC training to 0.06 ± 0.02 ml/mmHg after three-month TCC training (p = 0.008) respectively. Besides, the brachial artery distensibility and compliance in the TCC practitioners group were all significantly higher than those of TCC trainees before TCC training. We concluded that the long-term effect of TCC was to improve arterial stiffness of the elder adults. The TCC might be a good health promotion calisthenics that can be recommended to the elder adults.

(*To be published, private comm. 2006)

2004
Effect of Antihypertensive Monotherapy and Combination Therapy on Arterial Distensibility and Left Ventricular Mass

Joel M. Neutel, David H.G. Smith, and Michael A. Weber

Background: Angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers (CCBs) increase arterial compliance and decrease left ventricular mass in hypertensive patients. This study examined whether combined therapy has greater arterial and cardiac effects than doubled doses of the individual drugs.

Methods: This prospective, randomized, open-label study enrolled 106 patients aged >=18 years with mild-to moderate hypertension. Patients were randomized to 5 mg of amlodipine or 20 mg of benazepril for 2 weeks; then, depending on randomization assignment, they were forccetitred to 10 mg of amlodipine or 40 mg of benazepril monotherapy, or to combination amlodipine (5 mg) and benazepril (20 mg) treatment
for 22 weeks. Arterial distensibility was assessed using the DynaPulse ambulatory system, and left
ventricular mass was assessed by echocardiography.

**Results:** Combination therapy (0.71% +/- 0.51% mL/mm Hg) increased arterial distensibility more than
amlodipine (0.28% +/- 0.69% mL/mm Hg; P = .008) or benazepril (0.39% +/- 0.62% mL/mm Hg; P = .03)
monotherapies. Left ventricular mass decreased more with combination treatment (65 +/- 56 g) than with
amlodipine (28 +/- 4 g; P < .02); the difference from benazepril (42 +/- 50 g) was not significant.

**Conclusions:** Combined ACE inhibitor and CCB treatment was more efficacious than high doses of the
individual agents in increasing arterial compliance and reducing left ventricular mass. These findings
indicate that appropriately selected combinations of antihypertensive drugs might have enhanced
cardioprotective effects.

Am J Hypertens 2004;17:37–42

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2003

**The Effect of Angiotensin Converting Enzyme Inhibitor on Vascular Distensibility**

Chen Qiling, Sun Ningling, Liu Jing, et al.
(Department of Hypertension, The People’s Hospital of Beijing University, Beijing, China)

**Abstract**

**Objective:** To evaluate the curative effect of angiotensin converting enzyme inhibitor (ACEI) on the
vascular protection of hypertensive patients.

**Methods:** 25 primary Hypertensive patients were studied. The DP200M noninvasive blood pressure
monitor was used to measure brachial artery pressure of patients before therapy. The arterial pressure
waveform, arterial compliance, resistance and elasticity parameters were recorded. The patients began to
take ACEI. After a course of treatment, the parameters were measured again after therapy. The parameters
were compared before and after therapy.

**Results:** After the therapy, systemic vascular compliance (SVC) and brachial artery compliance (BAC)
increased significantly. SVC increased from 1.086 ± 0.31 ml/mmHg to 1.11 ± 0.26 ml/mmHg (P < 0.001), BAC increased from 0.637 ± 0.368 ml/mmHg to 0.694 ± 0.289 ml/mmHg (P < 0.05). BAD improved from 5.21 ± 1.95 %/mmHg to 5.39 ± 1.43 %/mmHg. PP decreased from 67.25 ± 16.58 mmHg
to 64.38 ± 18.14 mmHg (P < 0.001), SVR decreased from 1739.10 ± 346.89 dynes/ cm^5 to 1682.94 ± 394.75 dynes/ cm^5 (P < 0.001), BAR decreased from 286.44 ± 187.19 dynes/ cm^5 to 216.38 ± 151.22 dynes/ cm^5 (P < 0.001). Ang decreased significantly. Binary logistic regression analysis showed that PP, BAC, SVR and BAD were all related with SVC.

**Conclusion:** The patients with the hypertension for years will turn up the abnormal of artery distensibility.
ACEI can improve the artery distensibility and decrease pulse pressure. Therefore, ACEI may delay and
decrease the occurrence of the complication of cardio2cerebral vascular disease.

**Key Words** Noninvasive blood pressure monitor Hypertension Arterial compliance Arterial
distensibility ACEI

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2002/05

**Cardiovascular Reactivity and Diurnal Arterial Compliance during Nebivolol Treatment of Young Obese Essential Hypertensives**

Golubev SA, Tsai J, Mily MN, Afanassiev VV, Vitebsk State Medical University, Vitebsk, Belarus; Pulse
Metric, Inc., San Diego, CA, USA.

**Objective:** To evaluate changes in systemic and peripheral hemodynamics in resting, under stress tests and
daily life conditions during short-term treatment with nebivolol in a special high-risk population.
**Design and Methods:** Twelve randomly selected verified never treated essential hypertensives (aged 38.6±8.4 years, body mass index 31.2±5.2 kg/m²) underwent ambulatory blood pressure monitoring (DynaPulse 5000A; Pulse Metric, Inc., USA), standard mental arithmetic (MT) and cold pressor (CT) tests before and 4 weeks after treatment with nebivolol (5 mg once daily). Systemic and local (brachial artery) vascular hemodynamics parameters were derived blindly from each measurement by previously validated web-based pulse dynamics analysis technology.

**Results:** Ambulatory BP and HR were significantly reduced by nebivolol without excessive nighttime falls and variability affecting. 24-hour, but not resting systemic vascular compliance was significantly improved (1.19±0.11 vs. 1.36±0.16 mL/mm Hg; p<0.05) without changes in brachial artery compliance. Nebivolol reduced diastolic BP response to MT (17.0±8.5 vs. 14.0±11.2 mm Hg; p<0.05), and enhanced the rise in systemic vascular resistance during CT (1.5±1.6 vs. 4.7±3.3 mm Hg; p<0.05).

**Conclusions:** In the studied overweight young essential hypertensives, under significant short-term antihypertensive effects of nebivolol during daily life and MT, favorable changes in systemic but not in brachial artery compliance are registered, probably due to main peripheral points of nitric oxide modulating. The last might result in some discrepancies registered in hemodynamics and compliance changes between different stress tests, resting and 24-hour conditions. Daily arterial compliance evaluation is useful for comprehensive judgment about vascular effects of antihypertensive agents.

*Presented at the American Society of Hypertension 17th Annual Scientific Meetings, New York, New York, 2002

**2001/08**

**Non-Invasive Hemodynamics in Hypertension: Preliminary Results with Angiotensin II Receptor Blocker and Epithelial Sodium Channel Blocker**

1Antonio J. Delgado, 2Carlos L. Delgado León, 1Antonio Delgado-Almeida, 2Elymir Galvis

1Hypertension Research Unit, University of Carabobo, Valencia, Venezuela
2Cardiology Unit, M Perez Carreño Hospital, Venezuela Central University, Caracas

Recording of Blood Pressure (BP) remains as the basic clinical approach in evaluating the clinical course of hypertension. However, we now are able to obtain non-invasive recording of Left Ventricle (LV) & Systemic Vascular (SV) functions and, thus, evaluate how these hemodynamics are modified by drugs. There were 33 HT (20 M, 13 F, aged 54.3 ±12, HR 76 ±18) included in a prospective study with Telmisartan (19 cases, T =40 mg) or Amiloride (14 cases, A= 5 mg). Although all pts had computerized recordings BP, HR, PP, LV, SV (DynaPulse 200C) before/after isometric handgrip test; this study only present the resting parameters before (0 day) and after (4 weeks) treatment. **RESULTS: With T, BP were reduced (163 ±13/ 94 ±5 to 141 ±5/ 85 ±5 mm Hg, p 0.003) with LV after-load (1.8±0.3 vs 1.5±0.4 mm Hg/ml, p<0.001), dP/dTmax (1449 ±345 vs 1128±247 mm Hg/s, p<0.001) & cardiac work (73.8±13 a 59±9 J/min, p<0.001). SVR and SVC also improved: SVR (1826± 275 a 1478 ±252 dyn.cm-5, p<0.001), SV Compliance arterial (1.06 ±0.28 a 1.42 ±0.4 mmHg/ml, p <0.001). With A, BP decreased (161±7/ 96 ±4 to 138 ±7/ 86 ±6 mm Hg, p 0.004) while dP/dTmax (1358±223 a 1110± 246, p <0.001) & cardiac work (70±14 a 61 ±17, p 0.03) but unchanged LV afterload. SVR and SVC also improved: SVR (1756± 349 a 1611 ±460, p 0.06) & SVCompliance (1.08 ±0.3 a 1.4 ±0.4, p>0.001. Finally, SV/CO were unchanged wit either drug. Conclusions: Despite better LV hemodynamic with T, both drugs showed important hemodynamic effects on LV and SV function in addition of the reduction on BP.

*Presented at the 34th Venezuelan Congress of Cardiology, Maracaibo, Venezuela, August 2001 Advances Cardiologicos, Vol 21, suppl 1, S47, 2001 (article in Spanish)

**2001/5**

**Improved LV Function, Systemic Vascular and Brachial Artery Parameters in Hypertension: The Venezuelan Telmisartan Study**

Delgado AJ, Delgado-Almeida AR, Celis SI, and Delgado-Leon CL

Hypertension Research Unit, University of Carabobo, Valencia, Carabobo, 2002, Venezuela
Despite numerous advances in pharmacology of HT, few therapeutic approach has been designed to assess drug effects on complex CV functions during measurement of BP. To assess such parameters, non-invasive Arterial Waveform Analysis (DynaPulse 200M) at rest, isometric hand grip and 15 min later, was recorded in 31 HT subjects (Female n=18, Male n=13, age 54.1±9) on Telmisartan. LVET, dP/dT, LV contractility, LV Stroke Volume (LVSV), LV Stroke Work (LVSW), CO, Cardiac Work, SV Resistance and Compliance, Brachial Artery (BA) Compliance, BP, Pulse Pressure (PP), and HR were obtained basal and after 1 month of Telmisartan 40mg. Paired T-test was performed, with statistical significance p=0.05.

RESULTS: With Telmisartan: SBP (165±22 vs 132±15, p=0.00), DBP (90±14 vs 77±12, p=0.00) and PP (75±18 vs 55±12, p=0.00) were reduced, HR unchanged. dP/dT max (1393±332 vs 1134±263, p=0.00), dP/dT40 (35±8 vs 28±7, p=0.00), LVSW (90±19 vs 71±16, p=0.00) and Cardiac Work (78±16 vs 63±13, p=0.00) were also reduced; while LVET, LVSV, and CO remained unchanged. SVR (1783±277 vs 1524±275, p=0.00) was decreased; SV Compliance (1.16±0.3 vs 1.45±0.49, p=0.00) and BA Compliance (0.073±0.022 vs 0.097±0.032, p=0.00) increased at 1 month. CONCLUSION: This study provided the first integral evaluation of cardiac and vascular functions and BP on hypertensives receiving Telmisartan.

*Presented at the American Society of Hypertension 16th Scientific Meeting, San Francisco, CA, 2001

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2000/11

Observation of Long-term Effects of Hypertension Medication on Hemodynamic Changes - A New Home Monitoring Method

Xie Q, Lin-Liu S, Ng AS, Tsai JJ, Tang BL, and Chio S-S

Pulse Metric, Inc., San Diego, California USA

Brief background: Long-term trending information of medication effects on hemodynamic rarely reported largely due to lack of appropriate tool and methodology. Monitoring the perpetuate changes of Systemic Vascular Resistance(SVR) and Systemic Vascular Compliance(SVC) among chronic Cardiovascular Disease(CVD)patient over treatment course is essential for adjustment of prescription. Methods: Total 372 DynaPulse measurements including Blood Pressure(BP), SVR, and SVC readings from a 72 years old CAD and hypertensive male patient had been analyzed. Results were compared to a normal population (N=877,Male) in the US. Patient’s SVR and SVC trends were plotted against the medication history. Results: Normal age grouped SVR and SVC profiles (19,1.4) were compared to the patient’s reading. Lowered abnormality only found in SVC(1.1) at initial period. Dramatic improvements on both parameters were observed in corresponding to medications adjustment. Angiotensin II (Diovan®, Novartis 160mg/day) alone did not show significant change on these two parameters in early treatment stage. Angiotensin II plus diuretic (Aldactone® spironolactone 50mg/day) gives both clear reduction on SVR and elevation on SVC. Adding beta blockade (Toprol-XL®, Zeneca) into the regime, perseverance of improvement on SVR and SVC was demonstrated.

Conclusions: Significant SVC and SVR improvement during the course of treatment were clearly observed. It indicates the essential clinical value in achieving better adjustment of medication regime by periodical home monitoring of BP and hemodynamic changes. This is the first time we observed and reported the trending of hemodynamic change, specifically on SVR and SVC with over 27 months. These measurements were taken and recorded by a patient at home indicated the potential application for hypertensive and CVD patient’s case management. Further investigation is undergoing.
**2000-a**

**Hemodynamics, Quality of Life and Metabolic Changes during Nebivolol Treatment of Young Overweight Hypertensives**

V.V. Afnasiev, M.N. Miliy, S.A. Golubev
Vitebsk Regional Cardiology Center, Vitebsk State Medical University, Vitebsk, Belarus

**Objective:** To evaluate hemodynamics, metabolic and the quality of life (QL) changes during short-term treatment of young overweight essential hypertensives (EH) with nebivolol (N), a new highly selective, - blocker with nitric oxide modulating properties.

**Design and Methods:** Twelve patients (aged 36.1 ±7.2 years, BMI 32.0 ±5.3 kg/m²) were randomly selected from a group of newly verified never treated EH. Ambulatory BP monitoring (DynaPulse 5000A; Pulse Metric, Inc., USA), conventional echocardiography, QL evaluation (General Well-Being Adjustment Scale) and metabolic tests (serum insulin before and 2 h after standard oral TTG, lipids, uric acid, fibrinogen) were performed before and 4 weeks after treatment with 5 mg N once daily.

**Results:** BP and HR were significantly reduced (daytime DBP 90.3 ±4.6 vs. 79.5 ±5.8; nighttime DBP 76.3 ±6.0 vs. 69.0 ±7.5 mm Hg; daytime HR 79.0 ±12.2 vs. 62.0 ±6.7; nighttime HR 63.8 ±6.6 vs. 54.8 ±4.5 bpm; p < 0.01), with normalization DBP (daytime DBP < 90, nighttime DBP < 80 mm Hg) in ten patients (83%). No significant changes were observed in nighttime falls and BP variability (SD). LV eject fraction was not changed, and LV compliance (E to A peaks of diastolic filling ratio) tended to increase (1.2 ±0.36 vs. 1.53 ±0.62; p = 0.17). The total QL score tended to improve (82.6 ±22.6 vs 100.5 ±14.0 points, p = 0.09) without any correlation with ambulatory BP parameters. No significant changes were revealed in the metabolic tests monitored with tendency to a decrease of fasting insulin (136.3 ±92.5 vs. 81.8 ±18.5 pmol/l; p = 0.18).

**Conclusions:** In the investigated young overweight EH N has demonstrated favorable short-term effects on ambulatory BP. **Keywords:** Hemodynamics, Quality of Life, Nebivolol

(Journal of Hypertension 2000; 18 (Suppl. 2): S164)

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**2000-b**

**Insulin-Resistant Hypertensives: Hemodynamics, Quality of Life and Metabolic Changes during Nebivolol Treatment**
V.V. Afanasiev, M.N. Miliy, S.A. Golubev, Vitebsk State Medical University, Vitebsk, Belarus; Vitebsk Cardiology Center, Vitebsk, Belarus

Objective: To evaluate haemodynamics, metabolic and quality of life (QL) changes during short-term treatment of insulin resistant (IR) essential hypertensives (EH) with nebivolol (N), a new highly selective β-blocker with nitric oxide modulating properties.

Design and Methods: Ten patients (aged 46.7±7.7 yrs, BMI 32.0±5.7) with conventional IR features were randomly selected from a group of newly verified never treated EH. Ambulatory BP (DP 5000A; Pulse Metric, Inc., USA), echocardiography, QL evaluation (General Well-Being Adjustment Scale) and metabolic tests (1 before and 2 h after routine TTG, lipids, uric acid, fibrinogen) were performed before and 4 weeks after 5 mg N o.d.

Results: BP and HR were significantly reduced (daytime DBP 91.0±4.5 vs. 79.0±6.0; nighttime DBP 76.1±6.4 vs. 69.1±8.1 mmHg; daytime HR 78.7±13.0 vs. 62.0±7.2; nighttime HR 62.6±6.1 vs. 54.4±4.8 bpm; p<0.01) without excessive nighttime falls and BP variability (SD) affecting. LV eject fraction was not changed, and LV compliance (E/A peaks ratio) tended to increase. The total QL score was improved (78.9±21.6 vs. 100.7±15.1 points, p<0.01) without any correlations with ambulatory BP parameters. No significant changes were revealed in the metabolic tests monitored.

Conclusions: N has demonstrated favorable short-term haemodynamics and cardiac effects without metabolic deterioration in IR EH, the positive QL changes making a basis for long-term evaluation, which should be performed further.

*Presented at the International Society of Hypertension 18th Scientific Meeting, 2000 (see Hypertension 2000 Vol 18, Suppl 4, pg. S167)

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1997/06

Angiotensin Converting Enzyme Inhibitor Increases Vascular Compliance More than Adrenergic β-Blockade Despite Similar Blood Pressure Reduction

CP Liu, TJ Brinton, CJ Tseng, CW Chiou, SL Lin, SS Chio, HT Chiang, Veterans General Hospital-Kaohsiung, Taiwan, ROC, Pulse Metric, Inc., CA, USA.

Objective: To compare the effect of ACEI and adrenergic β-blockade on vascular compliance in hypertensives.

Design and Methods: Fourteen patients were treated with either peridonpril or lisinopril (group A) and 16 patients were treated with acebutolol (group B). Mean arterial pressure (mAP), double products (HRxMAP), dp/dtmax, and vascular compliance (Vc) were measured by using a cuff sphygomonometer waveform analysis.

Results: Following 4 to 6 months of treatment, the reduction of mAP, double products and dp/dtmax were similar in two groups (15 vs 12% for mAP, 26 vs 27% for double products, and 20 vs 15% for dp/dt max, respectively). However, Vc was significantly increased only in the ACEI group (20±10% vs 5±11%, p<.01, see TABLE *). Furthermore, the blood pressure reduction was observed much earlier than the improvement of Vc (2 vs 8 weeks). These results suggest that only ACEI could significantly improve vascular compliance and this advantage is not dependent on systolic or rate changes.

<table>
<thead>
<tr>
<th></th>
<th>MAP</th>
<th>HRxMAP</th>
<th>dp/dtmax</th>
<th>Vc</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pre</td>
<td>121±3</td>
<td>9933±847</td>
<td>1416±93</td>
<td>.09±.007</td>
</tr>
<tr>
<td>post</td>
<td>104±2</td>
<td>7385±332</td>
<td>1128±81</td>
<td>.11±.009</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pre</td>
<td>121±10</td>
<td>9138±464</td>
<td>1385±123</td>
<td>.086±.003</td>
</tr>
<tr>
<td>post</td>
<td>104±9</td>
<td>6672±746</td>
<td>1177±139</td>
<td>.090±.005</td>
</tr>
</tbody>
</table>

Conclusions: We conclude that ACEI can improve vascular compliance more than adrenergic β-blockades despite similar antihypertensive effect.

* Presented at the 8th European Meeting on Hypertension, European Society of Hypertension, Milan, Italy, June 1997

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Adrenergic ®-Blockade with Intrinsic Sympathomimetric Activity May Attenuate Improvement in Vascular Compliance During Exercise

CP Liu, TJ Brinton*, ED Walls*, SL Lin, SS Chio, HT Chiang. Veterans General Hospital-Kaohshiung, Taiwan, ROC and Pulse Metric, Inc., San Diego, CA, USA.

Intrinsic sympathomimetic activity (ISA) may balance the negative inotropic and chronotropic effects of ®-blocker therapy theoretically. However, the effect of adrenergic ®-blockade with ISA on vascular compliance C is still not thoroughly known. We measured mean arterial pressure (MAP), HR, maximum left ventricle dP/dt (dP/dt\_LV\_max), and C utilizing cuff sphygmomanometer waveform analysis in 28 hypertensive patients who received either propranol (group A, n = 16) or acebutolol (group B, n = 12). C was assessed during rest and submaximal exercise. Results mean ± SD (*p<0.05)

<table>
<thead>
<tr>
<th>Wk</th>
<th>MAP (mmHg)</th>
<th>HR (bpm)</th>
<th>dP/dt_LV_max (mmHg/sec)</th>
<th>C (ml/mmHg)</th>
<th>Exercise %</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0</td>
<td>116.9± 11</td>
<td>74.4± 13</td>
<td>1369± 221</td>
<td>0.087± 0.026</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>103.1± 12*</td>
<td>61.1± 7*</td>
<td>1189± 251*</td>
<td>0.092± 0.023</td>
</tr>
<tr>
<td>B</td>
<td>0</td>
<td>126.9± 12</td>
<td>75.4± 13</td>
<td>1399± 171</td>
<td>0.084± 0.013</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>111.8± 11*</td>
<td>64.9± 7*</td>
<td>1205± 226*</td>
<td>0.088± 0.025</td>
</tr>
</tbody>
</table>

Following 8 weeks therapy, the improvement in blood pressure and C was similar in both groups. However, the reduction in HR in group B was less than group A. Although the response of C to exercise in both groups was not different, the net increase in C after therapy is significantly larger in group A than in group B (21.3± 7.6% vs. 11.7± 8.9%, p<0.05). These results suggest that acebutolol, a ®-blocker with ISA, may attenuate propranolol induced improvement in vascular compliance during exercise in hypertensive patients.

* Presented at 12th Annual Scientific Meeting of The American Society of Hypertension, San Francisco, April, 1997

Arterial Compliance by Cuff Sphygmomanometer: Application to Hypertension and Early Changes in Subjects at Genetic Risk

Brinton TJ, Kailasam MT, Wu RA, Cervenka JH, Chio S-S, Parmer RJ, DeMaria AN, O’Connor DT; UCSD and VAMC, La Jolla, CA, and Pulse Metric, Inc., San Diego, CA.

Abnormalities of the arterial pulse waveform reflect changes in cardiovascular structure and function. These abnormalities may occur early in the course of essential hypertension, even before the onset of blood pressure elevation. Previous studies of cardiovascular structure and function have relied on invasive intrarterial cannulation to obtain the arterial pulse wave. We evaluated arterial structure and function using a noninvasive cuff sphygmomanometer in hypertensive (n=5) and normotensive (n=36) subjects, stratified by genetic risk (family history) for hypertension. Using a simple physical model in which the aorta was assumed to be a T tube and the brachial artery a straight tube, we determined vascular compliance and peripheral resistance by analyzing the brachial artery pulsation signal from a cuff sphygmomanometer. Essential hypertensive subjects tended to have higher peripheral resistance (P=.06) and significantly lower vascular compliance (P=.001) than normotensive subjects. Vascular compliance correlated with simultaneously determined pulse pressure in both groups (n=51, r=.74, P<.0001). Higher peripheral resistance (P=.07) and lower vascular compliance (P=.04) were already found in still-normotensive offspring of hypertensive parents (ie, normotensive subjects with a positive family history of hypertension) than in normotensive subjects with a negative family history of hypertension. Multivariate analysis demonstrated that both genetic risk for hypertension (P=.030) and blood pressure status (P=.041), although
not age (P=.207) were significant predictors of vascular compliance (multiple R=.47, P=.011). However, by two-way ANOVA, genetic risk for hypertension was an even more significant determinant (F=7.84, P=.007) of compliance than blood pressure status (F=2.69, P=.089). Antihypertensive therapy with angiotensin-converting enzyme inhibitors (10 days, n=10) improved vascular compliance (P=.02) and reduced resistance (P=.003) significantly; treatment with calcium channel antagonists (4 weeks, n=8) tended to improve vascular compliance (P=.07) and significantly reduced peripheral resistance (P=.006). We conclude that arterial vascular compliance abnormalities detected by a noninvasive cuff sphygmomanometer reflect treatment-reversible changes in vascular structure and function. Early changes in vascular compliance in still-normotensive individuals at genetic risk for hypertension may be a heritable pathogenetic feature of this disorder.

(Hypertension, 1996 Vol 28, No.4, pp. 599-603.)

1996/04

**Angiotensin Converting Enzyme Inhibitors Improve Vascular Compliance and Pump Performance in Hypertensive Patients**

Brinton TJ, Walls ED, Hsu T-L, Chio S-S, Chang M-S, Liu C-P, Pulse Metric, Inc., San Diego, CA, Chung Yuan University, Taiwan, R.O.C. and Veterans General Hospital, Taipei, Taiwan, R.O.C.

i) **Objectives**: To evaluate the effects of angiotensin converting enzyme inhibitors (ACEI) on vascular compliance (Cm) and the efficiency of the pump system in hypertensive patients.

ii) **Design and Methods**: 14 hypertensive patients were treated with ACEI (either Lisinopril or Perindotril) for 4 to 6 months. We measured the mean arterial blood pressure (MAP), double product (MAP*HR, an index of energy consumption), Cm and dP/dtmax by using a cuff sphygmomanometer waveform analysis. Submaximal exercise (10 mets) was used to evaluate cardiovascular reserve function.

iii) **Results**: Following 4 to 6 months of treatment, the MAP and dP/dtmax decreased significantly, while the Cm showed a significant increase (p<0.05) (TABLE). However, the time course of blood pressure reduction was much earlier than the improvement of Cm (2 vs 8 weeks). Data are expressed as mean± sem.

<table>
<thead>
<tr>
<th>Mean ± sem</th>
<th>MAP</th>
<th>MAP*HR Rest</th>
<th>MAP*HR Exercise</th>
<th>dP/dtmax</th>
<th>Cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>121.4± 2.8</td>
<td>9933.4± 647</td>
<td>12081.4± 993</td>
<td>1416.3± 93</td>
<td>0.0944± 0.0069</td>
</tr>
<tr>
<td>Post</td>
<td>103.6± 2.2</td>
<td>7385.5± 332</td>
<td>8213.4± 359</td>
<td>1127.6± 81</td>
<td>0.115± 0.0086</td>
</tr>
</tbody>
</table>

The change in double product required to reach the submaximal exercise level was significantly reduced after treatment (20.8% vs 11.2%; p<0.05). These results suggest that pump efficiency was promoted after chronic ACEI therapy, and that advantage was not due to systolic enhancement.

iv) **Conclusion**: We conclude that ACEI therapy can improve vascular compliance, and this structural benefit is not directly dependent on its antihypertensive effect. Furthermore, this vascular remodeling may lead to a more efficient pump system during exercise.

*Presented at the International Society of Hypertension 16th Scientific Meetings, 1996.

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(2) Hypertension and cardiovascular risk studies – Epidemiology, risk factors, genetic and environmental risks, obesity, diets, new markers and preventions

2007

Overweight and hyperinsulinemia provide individual contributions to compromises in brachial artery distensibility in healthy adolescents and young adults

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aThe Divisions of Preventive Cardiology; bBiostatistics; and cEndocrinology, Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, USA; the dDepartment of Pediatrics and eDepartment of Internal Medicine, Division of Endocrinology, College of Medicine, University of Cincinnati, Cincinnati, Ohio, USA; and the fDepartment of Pediatrics, University of Colorado School of Medicine, Denver, Colorado, USA

Abstract: Brachial artery distensibility (BrachD) was measured in healthy children to identify associations with atherosclerotic risk factors. Nine hundred sixty-nine black and white subjects, 13–22 years of age, were classified as lean (L) or overweight (O) and as hyperinsulinemic (H-I) or normoinsulinemic (N-I). Blood pressure (BP) and BrachD were obtained with a DynaPulse Pathway instrument. Analysis of variance was performed, looking for group mean differences. Correlations between BrachD and risk variables were examined. Determinates of BrachD were determined by backward elimination regression, stratified by body mass index (BMI)-insulin group. Decreased BrachD correlated with male gender, O, higher BP, heart rate, fasting glucose, and log of fasting insulin after adjusting for pulse pressure (PP). BrachD was greatest in L N-I, with progressive decreases seen in L H-I, O N-I, and O H-I subjects. Regression modeling found that PP and HR were major determinates of BrachD. Glucose was significant for subjects with N-I, regardless of adiposity. Excluding BP, glucose remained important in N-I subjects. Gender was significant for all. HR retained significance only in O subjects, regardless of insulin level. In healthy adolescents, hyperinsulinemia and obesity adversely affect brachial artery function, with overweight contributing to a greater degree. In normoinsulinemic subjects, fasting glucose was inversely related to BrachD. Metabolic factors may play a role in vascular function in youth.


2006/05

Rho Kinase Polymorphism Influences Blood Pressure and Systemic Vascular Resistance in Human Twins Role of Heredity


Abstract: The Rho/Rho kinase (ROCK) pathway is implicated in experimental hypertension. We, therefore, explored the role of ROCK2 genetic variation in human blood pressure (BP) regulation, exploiting the advantages of a human twin sample to probe heritability. The focus of this work is the common nonsynonymous variant at ROCK2: Thr431Asn. Cardiovascular and autonomic traits displayed substantial heritability (from ~33% to 71%; P<0.05). The Asn/Asn genotype (compared with Asn/Thr or Thr/Thr) was associated with greater resting systolic (P<0.001), diastolic (P<0.0001), and mean BP (P<0.0001); allelic variation at ROCK2 accounted for up to ~5% of BP variation (P<0.0001). Systemic vascular resistance was higher in Asn/Asn individuals (P=0.049), whereas cardiac output, large artery compliance, and vasoactive hormone secretion were not different. Coupling of the renin-angiotensin system to systemic resistance and BP was diminished in Asn/Asn homozygotes, suggesting genetic pleiotropy of Thr431Asn, confirmed by bivariate genetic analyses. The Asn/Asn genotype also predicted higher BP after
environmental (cold) stress. The rise in heart rate after cold was less pronounced in Asn/Asn individuals, consistent with intact baroreceptor function, and baroreceptor slope was not influenced by genotype. Common genetic variation (Thr431Asn) at ROCK2 predicts increased BP, systemic vascular resistance (although not large artery compliance), and resistance in response to the endogenous renin-angiotensin system, indicating a resistance vessel-based effect on elevated BP. The results suggest that common variation in ROCK2 exerts systemic resistance-mediated changes in BP, documenting a novel mechanism for human circulatory control, and suggesting new possibilities for diagnostic profiling and treatment of subjects at risk of developing hypertension.

Hypertension. 2006;47:1-11

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2006/02

**Homocysteine, circulating vascular cell adhesion molecule and carotid atherosclerosis in postmenopausal vegetarian women and omnivores**

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**Abstract:** Since the adoption of vegetarian diets as a healthy lifestyle has become popular, the cardiovascular effects of long-term vegetarianism need to be explored. The present study aimed to compare the presence and severity of c(CA), and the blood levels of Vitamin B12, homocysteine (Hcy) arotid atherosclerosis and soluble vascular cell adhesion molecule-1 (sVCAM-1) between 57 healthy postmenopausal vegetarians and 61 age-matched omnivores. Carotid atherosclerosis, as measured by ultrasound, was found to be of no significant difference between the two groups. Yet, fasting blood glucose, low-density lipoprotein cholesterol, and Vitamin B12 were significantly lower, while Hcy and sVCAM-1 were higher in the vegetarians as comparing with the omnivores. Multivariate regression analysis showed that the level of Vitamin B12 was negatively associated with the level of Hcy. Vegetarianism itself and Hcy level were significantly associated with sVCAM-1 level in univariate analysis; however, after adjustment for covariates, we identified age but not vegetarianism as the determinant of sVCAM-1 level. Multiple linear regression analysis identified age and systolic blood pressure, but not vegetarianism, as determinants of common carotid artery IMT. In conclusion, there was no significant difference in CA between apparently healthy postmenopausal vegetarians and omnivores. The findings of elevated Hcy in vegetarians indicate the importance of prevention of Vitamin B12 deficiency.

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2005

**Impact of Multiple Cardiovascular Risk Factors on Brachial Artery Distensibility in Young Adults - The Bogalusa Heart Study**

Elaine M. Urbina, Lyn Kieltkya, Jeffrey Tsai, Sathanur R. Srinivasan, and Gerald S. Berenson

**Background:** Cardiovascular (CV) risk factors are associated with abnormalities in vascular function and structure. Arterial distensibility decreases with age and extent of atherosclerosis. Mediators of atherosclerosis may affect segments of the vascular tree differently, and information is limited on vascular changes of the brachial artery. Therefore, we explored the effect of multiple CV risk factors on brachial artery distensibility (BrachD).
Methods: A cross-sectional study of CV risk factors and BrachD was performed in an ongoing epidemiologic study (the Bogalusa Heart Study). Data were collected on 803 young adults (42% male, 72% white, aged 19 to 37 years) including BrachD measured by pulse waveform analysis (DynaPulse 2000A, Pulse Metric, Inc.) CV risk factors (anthropometric, hemodynamic, and metabolic variables) were considered abnormal if ranked in the highest age-, ethnicity-, and sex-specific quartile for this population (lowest quartile for HDL).

Results: BrachD was significantly lower in African American than in white subjects (6.33% v 6.76% Δ/mm Hg, P < .005). An inverse linear relationship was noted between BrachD and number of CV risk factors clustering in an individual (P < .0001 trend analysis).

Conclusions: In young adults, increasing numbers of adverse CV risk factors is associated with decreased brachial artery distensibility. Noninvasive brachial artery function measures are useful in measuring subclinical arteriosclerotic vascular changes.


2005/11

Associations Between Submicrometer Particles Exposures and Blood Pressure and Heart Rate in Patients With Lung Function Impairments

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From the Institute of Occupational Medicine and Industrial Hygiene, College of Public Health (Mr Chuang, Dr Chan, Dr Su) and Department of Internal Medicine, Cardiology Section, National Taiwan University Hospital (Dr Su), College of Public Health, National Taiwan University, Taipei, Taiwan; and the Chest Department (Dr Shiao), Taipei Veterans General Hospital, Taipei, Taiwan. This study was supported by a grant from the National Science Council of Taiwan (NSC90-2320-B-002-126).

Abstract
Objective: The objective of this study was to evaluate whether submicrometer particle is associated with elevated blood pressure (BP) and heart rate (HR).

Methods: We measured ambulatory systolic BP (SBP), diastolic BP (DBP), and HR using a portable BP monitoring system and number concentrations of submicrometer particle with a size range of 0.02 to 1 m (NC0.02–1) by a P-TRAK Ultrafine Particle Counter for 10 patients with lung function impairments.

Results: We found NC0.02–1 exposures at 1- to 3-hour moving averages were associated with the elevation of SBP, DBP, and HR. There were 1.4 to 3.4-mm-Hg increases in SBP, 1.4 to 2.2-mm-Hg increases in DBP, and 0.3 to 3.5-beats/min increases in HR for 10,000 particles/cm³ increases in NC0.02–1 at 1- to 3-hour moving averages. Conclusions: Exposures to submicrometer particles were associated with short-term increases in BP and HR in patients with lung function impairments. (J Occup Environ Med. 2005;47:1093–1098)

JOEM • Volume 47, Number 11, November 2005 1093

2005/02

Brachial Artery Distensibility as A Cardiovascular Risk Marker in Asymptomatic Individuals

Meng-Cheng Chiang, Wei-Hsian Yin, Yeu-Tyng Lin2, Hsu-Lung Jen, Jiann-Jong Wang, Wen-Pin Huang, An-Ning Feng, Yung-Nien Yang, and Mason Shing Young

Abstract: Previous studies have shown that brachial arterial distensibility (BD) is a measure of arterial stiffness and may be used in risk assessment for cardiovascular disease (CVD). The aim of this study was to explore the predictive value of BD for CVD risk levels and to seek cardiovascular risk factors influencing BD. In this study, BD data were obtained using the DynaPulse 2000A instrument (Pulse Metric, Inc, USA) in 300 asymptomatic, apparently healthy subjects (M/F=152/148; aged 52 13 years) who
were admitted for routine physical check-up. Family history, serum lipids and lipoproteins, glucose levels and mercury sphygmanomanometer blood pressure measurements were obtained. The risk for CVD in each individual was assessed using the **Framingham Risk Score** system. Significant correlations were found between unadjusted BD and age, measures of blood pressure, height, body mass index, total cholesterol levels, LDL-cholesterol levels, and glucose levels. Multivariate regression analyses showed that age, systolic and diastolic blood pressures and glucose levels independently predicted changes in BD. There was a significantly negative correlation between BD and the Framingham risk scores ($r = -0.45, P <0.0001$). Subjects with a 10-year risk for a future coronary heart disease events of 10% had significantly higher BD than those whose risk for coronary heart disease was 10% (6.12 ± 1.25 %/mmHg vs. 4.94 ± 1.2 %/mmHg, $P=0.0001$). These findings indicate that non-invasive measures of BD are effective in assessing CVD risk.


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**2004/11**

**The effect of Tai Chi Chuan on The Vascular Compliance and Resistance in Adults**

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**Objective:** To evaluate the effects of Tai Chi Chuan (TCC) on the vascular compliance and resistance in adults.

**Design:** Cheng’s TCC was practiced 3 times a week, one hour on each time for the study group. Intervention length was 3 months, with biochemistry and hemodynamics measured before and after intervention.

**Participants:** A total of 70 participants, 26 were TCC beginner, mean age was 58.2. 28 were control group, mean age was 59.5. 16 were TCC senior (practice for more than 2 years), mean age was 57.8. Measurement: Biochemistry (AC glucose, cholesterol, triglyceride, HDL, LDL, Uric acid), and hemodynamics (Blood Pressure, pulse pressure, vascular compliance, resistance, distensibility) were obtained using DynaPulse 200M monitor

**Results:** Cholesterol and uric acid were declined after TCC practice. (Cholesterol from 212.4 +/- 40.0 to 193.1 +/- 31, $p<0.001$, and uric acid from 6.1 +/- 2.0 to 5.6 +/- 1.7, $p<0.064$). HDL was increased from 53.2 +/- 12.4 to 55.2 +/- 13.5 ($p=0.055$). Systemic vascular compliance was from 1.138 +/- 0.186 to 1.218 +/- 0.227 ($p<0.05$).

**Conclusion:** A moderate TCC intervention can impact favorable on some biochemistry indices of cardiovascular risk. This intervention can also favorable effects upon the hemodynamic parameters (systemic vascular compliance and brachial artery resistance). These finds indicate that moderate TCC intervention might have enhanced cardio-protective effects.

(Presented at The 3rd Int. Cong. on CVD, 2004, Taipei, Taiwan)

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**2004/7-a**

**Brachial artery distensibility and relation to cardiovascular risk factors and events in the community, specified by hypertension status - the Chin-Shan Community Cardiovascular Cohort (CCCC) Study**

National Taiwan University Hospital

This study used DynaPulse-2000A and Pulse Dynamic online hemodynamic analysis to obtain brachial artery distensibility. A sample of 990 subjects (25% hypertensive) was studied. It concluded: “Brachial artery distensibility was a subclinical disease marker and associated with atherosclerotic risk factor. Its role in predicting cardiovascular diseases was different between hypertensive and normotensive adults in the community.”
Brachial Arterial Resistance and Relation to cardiovascular risk factors in population at risk of Atherosclerosis: The Chin-Shan Community Cardiovascular Cohort (CCCC) Study

National Taiwan University Hospital

This study used DynaPulse-2000A and Pulse Dynamic online hemodynamic analysis to obtain brachial artery (BA) resistance. A sample of 990 subjects (25% hypertensive) was studied. It concluded: “Hypertension contributes to Atherosclerosis and remodeling of cardiovascular system, with altered arterial structure, function and dynamics. BA resistance is an independent risk of cardiovascular events (CE) specifically in hypertensive individuals, but not in normotensive ones. Peripheral artery resistance reflects Atherosclerosis, and hypertension may account for greater irreversibility, which leads to the important predictive role of BA resistance in hypertension status.

Both papers above were presented at 1) the Annual Meeting of Taiwan Society of Cardiology, July 24, 2004, Taipei, Taiwan, and 2) the ESC Congress 2004, 28 August to 1 September 2004 in Munich, Germany, and 3) the 27th World Congress of Internal Medicine, Granada Spain, September 26th to October 1st

Effects of Occupational Noise Exposure on Blood Pressure

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We measured 24-hour ambulatory blood pressure and 16-hour noise exposure continuously for 20 automobile workers, and used linear mixed-effects regression models to estimate transient and sustained effects of noise exposure on blood pressure. The occupational noise levels of the high-exposure workers with 85 +/- 8 dBA were significantly higher than those of the low-exposure workers with 59 +/- 4 dBA (p<0.05). We found a significant difference of 16 +/- 6 mmHg in sleep-time systolic blood pressure (SBP) existed between 2 exposure groups, and a marginal increase of 1 mmHg SBP per 1-dBA increase in occupational noise exposure at 60-minute lag time during work (p = 0.07). Occupational noise exposure had both transient and sustained effects on workers’ SBP. (DynaPulse 5000A ABPM was used in this study.)

Insertion/Deletion Polymorphism of the Angiotensin Converting Enzyme Gene and Arterial Elasticity at High Altitude

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Abstract
Objective: To investigate the relationship among Insertion/Deletion polymorphism of the angiotensin converting enzyme (ACE) gene, arterial elasticity (AE) in healthy men at high altitude and acute mountain sickness (AMS).
Methods: 30 subjects who had lived in sea-level were included in our research. All subjects underwent non-invasive office BP measurement (DynaPulse 200M, Pulse Metric, Inc. USA) in sea-level or in high altitude (4000m) to obtain data of the AE of healthy men at high altitude at the same time. ACE genotypes
were determined by PCR, and prevalence of AMS was determined also. Finally, relationship among them was analyzed.

**Results:** SVR, SVC BAD, BAR and SaO2 between II genotype and ID+DD genotype at sea-level healthy men did not differ significantly (p>0.05); but on acute exposure to high altitude in the sea-level natives, the SVR and SaO2 differ significantly between II genotype and ID+DD genotype (p<0.05); Logistic regression showed that significantly variety of SVR was an importantly dangerous factor for AMS (F = 16.04, p = 0.000), and II genotype is a protecting factor for AMS on acute exposure to high altitude (F = 13.63, p = 0.001).

**Conclusions:** Our results demonstrate the Insertion/Deletion polymorphism of the angiotensin converting enzyme (ACE) gene did not affect arterial elasticity (AE) in healthy men at sea-level; Significantly variety of SVR was an importantly dangerous factor for AMS, and II genotype is a protecting factor for AMS on acute exposure to high altitude.


2002/04

**Brachial Artery Distensibility and Relationship to Cardiovascular Risk Factors in Healthy Young Adults: The Bogalusa Heart Study**

Urbina EM, MD, Brinton TJ, MD, Elkasabany A, MD, PhD and Berenson GS, MD

**Background:** Arterial distensibility decreases with age and atherosclerosis leading to increased pulse pressure and increased left ventricular work resulting in left ventricular hypertrophy, a risk factor for cardiovascular morbidity and mortality.

**Methods and Results:** In the current study, a reproducible, non-invasive technology was employed to compare brachial artery compliance and distensibility measured on 920 healthy young adults (40% male, 70% white, 18-38 years) to levels of cardiovascular risk factors. Laboratory, anthropometric, blood pressure and heart rate measurements were obtained. Brachial artery pulse curve data were collected using the DynaPulse 2000A instrument (Pulsemetric, Inc.). Brachial artery compliance decreased with age in females (p<0.05) with males higher than females (p=0.0001) even when adjusted for pulse pressure. Whites had greater distensibility than blacks with females greater than males (p<.0001) even after adjustment for age. Distensibility decreased with age only in females (p<.05). Distensibility adjusted for pulse pressure was negatively correlated with measures of body size, blood pressure, glucose, insulin, LDL-C, VLDL-C and age (p<.05). When distensibility was plotted as a function of pulse pressure to control for distending pressure, the lowest quintiles of SBP, DBP and MAP tended to have greater distensibility. No differences were seen by quintiles of lipids. In multivariate analyses, BP, age, measures of body size, gender and VLDL entered the model (r^2=0.56; p<.02).

**Conclusions:** Race and gender differences in brachial artery compliance do not persist after adjustment for weight and controlling for pulse pressure. However, distensibility, which includes a normalization factor to control for body size, did show race and gender differences (w>b, f>m) even after adjustment for age. For the entire population, stiffer vessels with decreased distensibility were seen in subjects with higher levels of cardiovascular risk factors across the range of normal pulse pressure. These findings indicate that non-invasive measures of distensibility are useful in measuring sub-clinical vascular changes related to arteriosclerosis.

*American Journal of Cardiology 2002; 89:946-951

2002-a

**Changes on Brachial Artery Distensibility (BAD) and Systemic Vascular Resistance (SVR) Over Aging of Normal Population**

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Evaluation of population based trends in Brachial Artery Distensibility (BAD) and Systemic Vascular Resistance (SVR) over aging was conducted. The BAD and SVR changes are genetic, lifestyle, and diet dependent. Abnormality of these hemodynamic parameters is one of the primary indicators of cardiovascular disease and could be used for the clinical assessment of cardiac and arterial physiological conditions. Pulse Dynamics is a clinically validated non-invasive method to obtain hemodynamic measurements such as SBP, DBP, MAP, Pulse Pressure (PP), Heart Rate (HR), Cardiac Output (CO), BAD, and SVR by analysis of the oscillometric waveform of a cuff sphygmomanometer Global data of above from normal population has been pooled together for BAD and SVR trending analysis. The trended association information between BAD and SVR among normotensive (NT) vs. age and gender had not been previously described on the population bases. Accumulative 8578 normal subjects were checked by Pulse Dynamics method in order to find the blood pressure status and the association along with aging by gender. Among all, there are 5410 Females and 3168 Males, age from 18 to 92, and 22.7% are hypertensive. NT was defined as SBP<140 and DBP<90. BAD declines along with SVR increases observed among 6628 NT (F=4374, M=2254) represent the aging process. But higher declining rate is found in female compare to male. BAD decreases as SVR increases along with aging in both gender. Female has overall faster rate change. Mid 40s of both groups showed the turning points and leveled after

![Graph showing trends in BAD and SVR over age]

*Presented at the American Society of Hypertension 17th Annual Scientific Meetings, New York, 2002

2002-b

**Diurnal Patterns of Vascular Resistance and Compliance may Impact on Blood Pressure Night Fall**

Golubev SA, Mily MN, Tsai J, Vitebsk State Medical University, Vitebsk, Belarus and Pulse Metric, Inc., San Diego, CA, USA.

**Objective:** Underlying mechanisms of non-dipping phenomenon are under discussions in aspects of demographic and metabolic factors, daily activities, autonomic cardiovascular regulation. We aimed to investigate by means of 24-hour noninvasive pulse wave analyses possible differences in daytime and nighttime vascular hemodynamics between essential hypertensives (EH) with and without sufficient nighttime BP fall.

**Design and Methods:** Nineteen randomly selected untreated verified EH (11 males; aged (mean±SD) 37.9±9.4 years; daytime SBP 156.1±15.3, daytime DBP 90.3±9.9 mmHg) underwent 24 hour ambulatory oscillometric BP and HR measurements (DynaPulse 5000A; Pulse Metric, Inc., USA) with systemic vascular (SV) and brachial artery compliance and resistance evaluation at each measurement by the previously validated pulse dynamics analysis technology [1]. The vascular hemodynamics variables were compared between dippers (10 subjects) and non-dippers (9 subjects).

**Results:** In the sample investigated non-dippers were significantly older then dippers (44.4±5.8 vs. 32.0±8.2 years; p<0.01), but didn’t differ in hypertension duration, BMI, 24-hour and daytime SBP and DBP. Non-dippers had significantly higher nighttime SV resistance (22.3±2.9 vs. 19.0±1.9 mmHg/L/min; p<0.01) but not systemic compliance or brachial artery parameters compared with dippers. After adjustment for age the difference in nighttime SV resistance disappeared.

**Conclusions:** In the studied EH non-dippers differ from dippers by nighttime but not by daytime vascular hemodynamics with higher SV resistance during sleep, and were older. Relationships between aging and
non-dipping status, reported also by others, seems to be associated with enhanced resistive vessels remodeling rather than with less daytime activity. [1] T. J. Brinton et al. 1997, Am J Cardiol, 80:323-330.

*Presented at the American Society of Hypertension 17th Annual Scientific Meetings, New York, 2002

2001/08

**Cell K Transport and Arterial Pulse Waveform Analysis: New Studies in Arterial Hypertension**

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Assessment of a possible genetic defect in cell K transport (CKT) and the arterial pulse waveform (APW) comprehend new and important parameters in essential hypertension. In 75 HT (45 males, 30 females, aged 54±13; BP 170±20/94±17 mm Hg, PP 76±18) and 45 NT (25 males, 20 females aged 48±14, BP 128±12/74±9 mm Hg, PP 53±8) the RBC K (Ki)/ Na (Nai) content, TTKG (Transstubular K Gradient) and BKC (Body K Content, Bio-Impedance) were measured to assess CKT while Arterial Pulse Waveform (DynaPulse 200M) recorded for non-invasive hemodynamic of LV (dP/dT, LVET, contractility, SV/CO), Aortic (augmentation index, reflectance waves), Systemic (Sr resistance, S compliance) and brachial artery (Brachial resistance/ B compliance). 

**RESULTS:** All HT had -Ki (84.9 ± 5 mmol/lc vs 96.6± 4 in NT, p<.001) with +Nai in 34% (7.9 ±1.1 mmol/lc vs 6.2±1.3 in NT, p .02) and significant -TTKG (2.61 ± 0.3, p .02) and -BKC (2.757 ± 583 mmol, p .005) vs NT (TTKG 4.7 ±1.5, BKC 3.478 ± 690 mmol). HT with -Ki had inverse correlation with +FP glucose (r=-.63) and +plasma tryglicerides (r = -.47). Non invasive hemodynamic in HT showed +dP/dT (1518 ± 367 mm Hg/s vs 1215± 263 in NT, p.002), + SVR 1997 ± 245 dy.s.cm5 vs 1349± 242 in NT, p < .001 and lower SVC (1.13 ±0.08 ml/mm Hg vs 1.57 ±0.03, p .003) & -BC 0.052 ± 0.023 ml/mm Hg vs 0.089 ± 0.012, p 0.004). In 37 % of HT +aortic augmentation (42 ± 12 mm Hg) & early reflectance waves were recorded, thus suggesting +afterload for LV. 

**In Summary,** this study strongly suggests that both CKT and Arterial Pulse Waveform analysis provide very important information for the evaluation and management of HT.

*Presented at the 34th Venezuelan Congress of Cardiology, Maracaibo, Venezuela, August 2001 Advances Cardiologicos, Vol 21, suppl 1, S31, 2001 (article in Spanish)

2001/07

**Brachial Artery Distensibility and Relationship with Cardiovascular Risk Factors**

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The study of cardiovascular risk factors and their relationship to the development of atherosclerotic diseases such as hypertension has been a major focus of research for over 25 years in the Bogalusa Heart Study. This population study is a mixed, cross-sectional and longitudinal epidemiologic study of cardiovascular risk factors in subjects residing in Bogalusa, Louisiana with ages ranging from birth to early adulthood. This community of approximately 22,000 people is two-thirds white and one-third black. Seven major surveys were conducted since 1973, each consisting of 3-4,000 subjects. More than 14,000 subjects have been examined from birth through age 41 years with many subjects participating in multiple screenings. From these data, much can be learned about the early natural history of atherosclerotic diseases and hypertension. Arterial distensibility decreases with age and atherosclerosis leading to increased pulse pressure and increased left ventricular work resulting in left ventricular hypertrophy, a risk factor for cardiovascular morbidity and mortality. In the current study, a reproducible, non-invasive technology was employed to compare brachial artery compliance and distensibility measured on 920 healthy young adults.
(40% male, 70% white, 18-38 years) to levels of cardiovascular risk factors. Laboratory, anthropometric, blood pressure and heart rate measurements were collected. Brachial artery pulse curve data were collected using the DynaPulse 2000A instrument (Pulse Metric, Inc.). Brachial artery compliance decreased with age in females ($p<0.05$ with males higher than females $p<0.0001$) even when adjusted for pulse pressure. Whites had greater distensibility than blacks with females greater than males ($p<0.05$) even after adjustment for age. Distensibility decreased with age only in females ($p<0.05$). Distensibility adjusted for pulse pressure was negatively correlated with measures of body size, blood pressure, glucose, insulin, LDL-C, VLDL-C and age ($p<0.05$). When distensibility was plotted as a function of pulse pressure to control for distending pressure, the lowest quintiles of SBP, DBP, and MAP tended to have greater distensibility. No differences were seen by quintiles of lipids. In multivariate analyses, BP, age, measures of body size, gender and VLDL entered the model ($r=0.56; p<0.02$). Conclusions: Race and gender differences in brachial artery compliance do not persist after adjustment for weight and controlling for pulse pressure. However, distensibility, which includes a normalization factor to control for body size, did show race and gender differences ($w>b, f>m$) even after adjustment for age. For the entire population, stiffer vessels with decreased distensibility were seen in subjects with higher levels of cardiovascular risk factors across the range of normal pulse pressure. These findings indicate that non-invasive measures of distensibility are useful in measuring sub-clinical vascular changes related to arteriosclerosis.

*Presented at the First International Conference on Non-invasive Hemodynamic Monitoring for Cardiovascular Disease and Management, Taipei, Taiwan, 2001

2001/07

**Study of Hours Blood Pressure Changes in Nurse with Day and Night Shift**

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Thirteen normotensive female nurses aged between 21y/o and 25y/o (mean 23.2 +/-1.48y/o) worked in cardiac intensive care unit comprised the subjects of this study to determine the relationship between shift schedule working and 24-hour blood pressure rhythm. 24-hour ambulatory blood pressure data obtained using a DynaPulse 5000A when they worked in morning schedule for more than 2 months, the second data of the same subjects obtained after they shift to night schedule working for 7-14 days.  The results shown less day-night difference of systolic blood pressure noted after night shift (from morning shift = 7.1923 mmHg (6.3%) to night shift = -0.9615 mmHg (-0.8%)); significant higher 24-hour mean systolic blood pressure (morning shift = 112.15 mmHg to night shift = 116.20 mmHg); significant difference after schedule shift working noted in SBP, MBP, PP, HT and systemic vascular compliance by repeated measures variance assessment.  This study shown sift schedule work of intensive care giver was associated with flattened circadian change of blood pressure and higher mean 24-hour blood pressure.

*Presented at the First International Conference on Non-Invasive Hemodynamic Monitoring for Cardiovascular Disease and Management, Taipei, Taiwan, 2001

2001/05-a

**Biophysical, Biochemical, Non-invasive Hemodynamic Studies for New Routine Evaluation in Hypertension**

Delgado-Almeida AR, Delgado AJ, Celis SI, Delgado-Leon CL, and Delgado MC

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Since Blood Pressure regulation involves cardiovascular, renal, neural, and endocrine systems, the evaluation of hypertension (HT) seems to be far from minimal standard. We propose 4 aspects for routine evaluation: (A). **Biophysical**: RBC Na/K content, plasma/urine Na, K, Cl, Mg, ionic Ca++, Creatinine Clearance, plasma/urine osmolality; (B). **Biochemical**: FPG and Lipid Profile; (C). **Non-invasive**
**Hemodynamic** (DynaPulse-200M): LVET, dP/dT, LVSV, CO, LVSW, Systemic Vascular Resistance and Compliance, Brachial Artery Resistance and Compliance, BP, Pulse Pressure (PP), HR; (D). Resting ECG. We evaluated 145 untreated HT (Female n=75, Male n=70, aged 54±13 yr., BP 170±20/94±17 mmHg; PP 76±18 mmHg) vs 75 NT (Female n=39, Male n=36, aged 48±14., BP 128±12/74±9; PP 52±8). **RESULTS:**

(A). Low RBC K (78.9±5 mmol/l cell in HT vs 96.6±4 mmol/l cell in NT, p<0.0001). High RBC Na (7.9±1.1 mmol/l, 34% of HT vs 6.1±1.1 mmol/l in NT p<0.002); low plasma Ca++ in 21% of HT (1.96±0.2 vs 2.3±0.2 in NT, p<0.05); urine Na/K excretion unrelated to Na/K intake; (B). Lipid profile as normal in non-obese HT as in NT; (C). HT had higher SV Resistance (1977±245 dy.s.cm5 vs 1549±242 in NT, p=0.00), Lower SV Compliance (1.10±0.22 ml/mmHg vs 1.32±0.11 in NT, p=0.00), Lower BA Compliance (0.052±0.023 ml/mmHg vs 0.089±0.012 in NT, p=0.00); (D). ST-T changes was noted in 42% of HT vs 5% NT. **CONCLUSION:** This study presents new evidences in support of more complete systems evaluation in clinical HT.

*Presented at the American Society of Hypertension 16th Scientific Meeting, San Francisco, CA, 2001

2001/05-b

**Hemodynamic Characterization of Systolic Hypertension: New Findings on CV Parameters**

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Despite important advances in clinical HT, hemodynamics in Systolic HT (SHT) are not fully defined. To assess such changes in SHT we included non-invasive Arterial Waveform Analysis (DynaPulse 200M) in all HT subjects. In one year study, 19 (Female n=16, Male n=3, aged 68±11 yr.) out of 235 Hypertensives had SHT (8%). Non-Invasive Hemodynamic: LVET, dP/dT max, LV stroke volume (LVSV), CO, Cardiac Work, LV Stroke Work (LVSW), SV Resistance and Compliance, Brachial Artery (BA) Resistance and Compliance, BP, Pulse Pressure (PP) and HR was recorded at rest, isometric hand grip and 15 min after.

**RESULTS:**

a) BP was 192.6±20/79.5±7 mmHg; PP 119±14 and HR 55±12 bpm;

b) marked increased LV dP/dT max 1.655±441 mmHg/s, LVET 463.6±34 msc, Contractility index 19.2±5 1/s, Cardiac Work 92.4±18 J/min, and increased aortic stiff index (2.28±0.7 unit) resulted in 2 peak aortic waveform and increased augmentation index (41±9 mmHg); c) increased SV Resistance index 3.208±274 dy.s.cm5, decreased SV compliance (0.81±0.2 ml/mmHg) and brachial artery compliance (0.026±0.026 ml/mmHg) with brachial distensibility 5.2±0.4%. Conclusion: The results of this study indicates that SHT represents a severe form of HT, with disturbed arterial structure and vascular resistance, occurring more frequent in women.

*Presented at the American Society of Hypertension 16th Scientific Meeting, San Francisco, CA, 2001

2000/07

**Comparison of Normal Ranges for Pulse Dynamic Hemodynamic Parameters Between U.S. and Chinese Population**

Q Xie, JJ Tsai, AS Ng, BL Tang, TJ Brinton, and SS Chio. Pulse Metric, Inc., San Diego, CA.

Cardiovascular aging and abnormalities are genetic, lifestyle, diet dependent. Abnormal hemodynamic parameters are one of the primary indicators of cardiovascular disease and can be used for the clinical assessment of cardiac and arterial physiological conditions. Observation of changes to these indicators would provide an essential tool in cardiovascular risk assessment and disease management. Establishment of reference levels based on large scale studies of different ethnic groups would offer crucial baseline values for disease evaluation and management. Pulse Dynamics is a clinically validated non-invasive method to obtain hemodynamic measurements such as SBP, DBP, MAP, Pulse Pressure (PP), Heart Rate (HR), Cardiac Output (CO), and compliance by analysis of the oscillometric waveform of a cuff sphymomanometer. Comparisons of normal ranges were made between a U.S. population sample (n =
2,464) of varying race and a Chinese population sample (n = 1,379). Both had age ranges from 18 to 80 years. Three successive measurements were recorded using DynaPulse monitors (Pulse Metric, Inc., San Diego) and averaged for each patient. Statistical analyses were made to the samples respectively based on genders and blood pressure status. Normotensive (NT) was defined as SBP<140 and DBP<90 (1,976 U.S., 994 Chinese). Differences and similarities of the measurement readings between the two population samples were compared and examined by Student’s t-test on means adjusted by age. Normal ranges of the parameters (mean ± 2 SD) for U.S. and Chinese populations are:

<table>
<thead>
<tr>
<th></th>
<th>US (n = 1,976)</th>
<th>ASIA (n = 994)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female (1,277)</td>
<td>Male (699)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>Mean 118.0, SD 10.86</td>
<td>96-140</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>Mean 66.1, SD 6.98</td>
<td>52-80</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>Mean 82.6, SD 7.69</td>
<td>67-98</td>
</tr>
<tr>
<td>PP (mmHg)</td>
<td>Mean 52.0, SD 8.53</td>
<td>35-69</td>
</tr>
<tr>
<td>HR (BPM)</td>
<td>Mean 71.0, SD 11.41</td>
<td>48-93</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>Mean 4.4, SD 0.40</td>
<td>3.5-5.18</td>
</tr>
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Results show that for normotensive population samples, Chinese male have significant elevation in means of SBP, DBP, MAP and HR against US population, while Chinese female showed significant lower in mean CO at the early age (<40). From middle age (40) to young elderly (65), such trends both for male and female continued except that the lowered mean of CO is observed among Chinese male. Finally, elderly (> 65) Chinese population remained lower mean of CO in both gender but significant higher in mean of SBP, DBP, MAP, and PP, in comparison with US population. Keywords: hemodynamic, population norm

* Presented at the Tenth Conference on Health Problems Related to the Chinese in North America, San Francisco, July 2000

1999

**Relationship between Brachial Artery Distensibility and Levels of Cardiovascular Risk Factors in Healthy Young Adults: The Bogalusa Heart Study**

Elaine M Urbina, Elkasabany Abdalla, Todd J Brinton, Gerald S Berenson, Tulane Ctr for CV Health, New Orleans, LA

Measures of vascular distensibility reflect changes in arterial function due to arteriosclerosis. Both atherosclerosis & hypertension cause structural changes (increased wall thickness) in vessels resulting in alterations of vascular physical properties. Previous studies have shown decreased arterial distensibility (D) with age & elevated levels of BP. In the current study, a non-invasive method to measure brachial artery D was used to explore relationships between D & levels of cardiovascular risk factors in a random sample of 920 healthy young adults in the Bogalusa Heart Study (40% male, 70% white, 18-38 years). Following rigid protocols, serum lipids & lipoproteins, anthropometric & mercury sphygmomanometer BP measurements were obtained. Brachial artery pulse curve data were obtained using the DynaPulse 2000 instrument (PulseMetric, Inc, San Diego, CA). Whites had greater D than blacks with females greater than males (p<.05). These trends remained after adjustment for age. D decreased with age only in females (p<.05). Unadjusted D was positively correlated with HDL & negatively correlated with measures of body size, BP, glucose, insulin & age. After adjustment for pulse pressure, all relationships remained but D was not correlated with HDL & was negatively correlated with LDL & VLDL (all p<.05). When D was plotted as a function of PP to control for distending pressure, the lowest quintiles of SBP, DBP & MAD tended to have greater distensibility. No differences were seen by quintiles of lipids. In multivariate analyses, BP, age, measures of body size, gender & VLDL entered the model (r² = 0.56; p<.02). These findings indicate that non-invasive measures of D are useful in measuring sub-clinical vascular changes related to arteriosclerosis.

(Circulation 1999; Vol.100, No.18:1-676)
Race (Black-White) and Gender Differences in Brachial Artery Compliance and Cardiac Contractility in Healthy Young Adults: The Bogalusa Heart Study


Arterial compliance (Cp) decreases with age and HTN. Reduced Cp leads to increased SBP, pulse pressure (PP) and greater LV work resulting in LVH, a risk factor for cardiovascular (CV) morbidity and mortality. It is not known if race and gender differences in Cp exist which may influence the distribution of CV diseases. The current study examined race and gender differences in brachial artery Cp in a random sample of 775 healthy young adults with previous CV risk factor data collected for the Bogalusa Heart Study (40% male, 70% white, 18-38 years). BP, HR and brachial artery pulse curve data were obtained using the DynaPulse 2000 instrument (Pulse Metric, Inc., San Diego, CA). Waveforms of actual arterial pressure throughout the cardiac cycle are recorded using an oscillo-metric technique. The calibrated arterial pulse wave is incorporated into a physical model of the CV system to calculate brachial artery Cp (ml/mmHg) and peripheral resistance (BAPR, mmHg/L/min), and dP/dt L vmax (mmHg/sec), a non-invasive estimate of cardiac contractility validated with cardiac catheterization data. Across all age ranges, blacks had higher SBP and DBP than whites when analyzed by gender. Females had higher HR than males. In this age range, Cp decreased in females only (p <= 0.05). White males had the highest Cp values with males significantly higher than females (p <= 0.0001). These trends remained when adjusted for MAP or PP or when Cp was plotted as a function of PP. BAPR increased with age (p <= 0.02). Females had higher BAPR (p δ 0.006) with blacks greater than whites when analyzed by gender (p <= 0.05). Black males had the highest dP/dt L vmax with blacks significantly higher than whites (p <= 0.001). When adjusted for afterload (SBP), females had higher dP/dt L vmax than males (p <= 0.0001) and contractility decreased with age (p < 0.05). It is concluded that race and gender differences in Cp and cardiac function exist which may influence the prevalence and expression of diseases related to atherosclerosis.

(American Journal of Hypertension 1997 Vol 10, No. 4, Part 2, pg. 207A)

Use of patient education and monitoring software in community pharmacies

Miller LG
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OBJECTIVE: To determine the level of use of health education and monitoring software programs in independent community pharmacies in rural locales.

DESIGN: The use of seven software programs that deliver patient education and provide blood pressure monitoring was assessed at five sites of the Nebraska Drug Information Network (NDIN) for one month. Direct Access, a Windows-based software program, documented which programs were accessed and for what time period.

RESULTS: During a one-month period, 326 accesses were logged representing 44 hours of computer time. Extrapolated to all 30 sites of NDIN, this represents 264 hours and 1,956 accesses monthly. On average, each pharmacy logged 8.8 hours within 65 accesses each month. Each access averaged 8 minutes. DynaPulse (167 accesses; 16.4 hours) was the most frequently used product, followed by Home Medical Advisor Pro (54 accesses; 8.9 hours) and Mayo Clinic The Family Pharmacist (35 accesses; 8.3 hours). The least amount of time was spent with BodyWorks (0.6 hours) but Wellness Checkpoint had fewest accesses (7 accesses).

CONCLUSION: Applied medical informatics is assuming a larger role in daily clinical practice as pharmacy practitioners strive to better inform their patients. This is congruent with the finding that a better informed public can be a healthier public. This study demonstrates that computer systems are readily used by patients and pharmacists in rural communities.
Arterial Compliance by Cuff Sphygmomanometer: Application to Hypertension and Early Changes in Subjects at Genetic Risk

Brinton TJ, Kailasam MT, Wu RA, Cervenka JH, Chio S-S, Parmer RJ, DeMaria AN, O’Connor DT; UCSD and VAMC, La Jolla, CA, and Pulse Metric, Inc., San Diego, CA.

Abnormalities of the arterial pulse waveform reflect changes in cardiovascular structure and function. These abnormalities may occur early in the course of essential hypertension, even before the onset of blood pressure elevation. Previous studies of cardiovascular structure and function have relied on invasive intra-arterial cannulation to obtain the arterial pulse wave. We evaluated arterial structure and function using a noninvasive cuff sphygmomanometer in hypertensive (n=5) and normotensive (n=36) subjects, stratified by genetic risk (family history) for hypertension. Using a simple physical model in which the aorta was assumed to be a T tube and the brachial artery a straight tube, we determined vascular compliance and peripheral resistance by analyzing the brachial artery pulsation signal from a cuff sphygmomanometer. Essential hypertensive subjects tended to have higher peripheral resistance (P=.06) and significantly lower vascular compliance (P=.001) than normotensive subjects. Vascular compliance correlated with simultaneously determined pulse pressure in both groups (n=51, r=.74, P<.0001). Higher peripheral resistance (P=.07) and lower vascular compliance (P=.04) were already found in still-normotensive offspring of hypertensive parents (ie, normotensive subjects with a positive family history of hypertension) than in normotensive subjects with a negative family history of hypertension. Multivariate analysis demonstrated that both genetic risk for hypertension (P=.030) and blood pressure status (P=.041), although not age (P=.207) were significant predictors of vascular compliance (multiple R=.47, P=.011). However, by two-way ANOVA, genetic risk for hypertension was an even more significant determinant (F=7.84, P=.007) of compliance than blood pressure status (F=2.69, P=.089). Antihypertensive therapy with angiotensin-converting enzyme inhibitors (10 days, n=10) improved vascular compliance (P=.02) and reduced resistance (P=.003) significantly; treatment with calcium channel antagonists (4 weeks, n=8) tended to improve vascular compliance (P=.07) and significantly reduced peripheral resistance (P=.006).

We conclude that arterial vascular compliance abnormalities detected by a noninvasive cuff sphygmomanometer reflect treatment-reversible changes in vascular structure and function. Early changes in vascular compliance in still-normotensive individuals at genetic risk for hypertension may be a heritable pathogenetic feature of this disorder.

(Hypertension, 1996 Vol 28, No.4, pp. 599-603.)

Pharmaceutical Care in Rural Community Pharmacy Clerkships: Emphasis on Developing Computer Skills to Enhance Patient Education

Miller LG, Jungnickel PW and Scott DM.
College of Pharmacy, University of Nebraska Medical Center College of Pharmacy

Two pharmacy computer training laboratories were developed at opposite ends of Nebraska to facilitate student acquisition of computer skills focusing on patient education prior to rural clerkships at Nebraska Drug Information Network sites. The labs were equipped with IBM-compatible multimedia computers housing 20 patient education and nine professional software programs. Students (n=28) completed a two-day laboratory evaluating these products. Integration of these tools with pharmaceutical care activities was discussed. Student experiences with software databases were assessed prior to the laboratory and their use of the computer in delivering education was evaluated during the following one-month clerkship at Network sites. Most (96 percent) of students (n=25) had experience with IBM compatible computers predominantly in word processing (88 percent), graphics (62 percent) and spreadsheets (54 percent). The
The majority had previously used Identidex (88 percent), Poisindex (85 percent) and Drugdex (81 percent), however few were familiar with patient education programs (After case: 31 percent, Home Medical Advisor Pro: 16 percent and DynaPulse: 15 percent). Of the 5,109 student-patient interactions during the ensuing month, drug and health information were provided in 2,752 (54 percent) of the interactions. Computer-assisted education occurred in 464 (17 percent) of these encounters. In nearly half of the cases (n=2,357; 46 percent) the student was involved only in the dispensing of the product. Given how critical patient education and pharmaceutical care are to the future of pharmacy, it is important that students have exposure to these products that should be the mainstay of their future practice. This validates the need for the computer training laboratories. Additionally, patient counseling in their clerkship experience is in need of enhancement and should occupy a greater percentage of student clerkship activities.

(Am. J. Pharmaceutical Education 1996; 60: 249-255)

1994/05
Non-Invasive Arterial Pulse Waveform Analysis in Hypertension: Development of the Method, and Early Compliance Changes in Subjects at Genetic Risk of Hypertension


Abnormalities of arterial pulse wave and arterial compliance may occur early in the course of essential hypertension. Such observations have resulted from invasive waveform studies. We measured brachial arterial compliance and peripheral vascular resistance in essential hypertensives and their normotensive counterparts with and without family history for hypertension, using a non-invasive method to obtain large arterial pulse waveform from a simple blood pressure cuff. With the DynaPulse we obtained data on 15 unmedicated essential hypertensives and 36 normotensives. Using a simple mechanical model wherein the aorta was assumed to be a “T” tube and the brachial artery a straight tube, we derived peripheral resistance and compliance of the brachial artery from arterial cuff waveforms. A significant correlation occurred between distal compliance from DynaPulse waveform and systemic compliance calculated by impedance cardiography (r=0.62, p<0.001, n=38). In hypertensives, mean arterial pressure was 28 mmHg higher than in normotensives (p<0.001); hypertensives had higher peripheral resistance (p<0.05) and lower compliance (p<0.001) than normotensives. In hypertensives, peripheral resistance declined and arterial compliance improved (increase) significantly following chronic therapy with antihypertensive drugs such as ACE inhibitors (n=10) or calcium channel blockers (n=8). Higher peripheral resistance (p<0.1) and lower arterial compliance (p<0.05) were also found in still-normotensive offspring of hypertensive parents (i.e., normotensives with a positive family history for hypertension) compared to family history negative normotensives. We conclude that arterial compliance can be accurately assessed by non-invasive brachial artery waveform analysis, and that compliance abnormalities may reflect early structural changes in large arteries in subjects at genetic risk of hypertension.

Hypertension and heart diseases – Studies on hemodynamics and cardiac problems and functions

2007/05

Amiloride and Red Blood Cell Potassium Transport in Coronary Artery Disease: Reversion of the Clinical and ECG Alterations

Delgado-Almeida Antonio, Delgado-Leon Carlos, Delgado-Leon A.

**Background:** A novel therapeutic approach for coronary artery disease (CAD) using amiloride (Ami) have been developed. This model based on the critical role of RBC in vascular rheology, endothelial function, platelet aggregation, as well as in our findings of a defective RBC K transport in hypertensives and in half of their offspring, has been recently supported for our findings that Ami reversed ST-T alterations in hypertensives with CAD or LVH (Am J Hypertension.2004: 17(5):S189). Subjects: 75 subjects with proved CAD (previous myocardial infraction, 2-3 vessels disease by coronary angiography, or combined ECG-ECHO ischemic changes), either hypertensives (n=40; 167 ±13/103 ±5 mmHg, HR 69±8 l/min), or normotensives (n=35; 132±6/ 75±4 mmHg, HR 61± 7 l/min), both sexes, aged 63 ±9. All had evidence of CAD by angina (II-IV), heart failure (NYHA II-III), ventricular extrasystoles, and ST-T alterations, despite nitrates, aspirin, calcium-antagonists or/and anti-aggregants, and control of BP in hypertensives (IECA, spironolactone, thiazide, AT1 receptor blocker). Drug design: Open prospective trial of Ami (5 mg/day, when RBC K≤96.4 mal/lc) + calcium gluconolactate (1 g/day, when ionized Ca++≤1.1 mal/l). Control were as our previous trial at 1, 3 and 6 months and 1 year, but most patients continued up to 2nd year. Methods: All has serial ECG, non-invasive hemodynamic (DP 200M) for cardiac (LVET, LV dP/dT, C0, SV), Aortic BP, Systemic Vascular Resistance Compliance (SVR/SVC), and Brachial Artery Distensibility/Compliance (BAD/BAC), ECHO, along with measurement of RBC (K, Na), plasma (K, Na, Cl, Ionized Ca++, Mg++), 12-hours night urinary volume (K, Na, Cl, pH) and Bio-Impedance Analysis (BIA, Quantum X, RJL) for Total body K, Total body water/ extracellular fraction, Fat Mass and Fat-Free Mass.

**Results:** Within 1 month, all patients were free of angina and symptoms of heart failure, requiring no SL nitrates, calcium-antagonists or β blocker. RBC K↑(84.5±4 vs 93.5±4 mmol/lc, p<.001) and Ca++ ≥1.05 mmol/l, while urinary Na/K was decreased and BIA showed ↑total body water and FFM. In hypertensives, LV dP/dT↑(1757±313 vs1302±276 mmHg/s, p<.001), SVR↑(2114±348 vs 1668±432 dynes/s/cm5, p.001), while SVC↑ and BAC↑(0.92±0.16 vs 1.22± 0.21 ml/mmHg, p .003, and 0.57 ± 0.021 vs 0.069± 0.02 ml/mmHg, p.005; but improvement was unrelated to BP levels. At 3rd month, ST-T alterations were improved in most patients (74%) with CAD despite no nitrates, anti-aggregants or aspirin, although in hypertensives LVH voltage was significantly decreased (p< 0.001). At 6th month, ECG were normal in 1 out 4 normotensives with CAD (DI, AVLV4-V6) and 1 out of 3 hypertensives subjects. Only (15%) ECG with previous inferior infraction remained unresolved, but without angina. No patient had cardiovascular events or death (0%) in 2 years of follow-up.

*Presented at Inter-American Society of Hypertension (IASH) Meeting, 2007/05

2003

**Measures of Brachial Artery Distensibility in Relation to Coronary Calcification**

MJ Budoff, F Flores, J Tsai, T Frandsen, H Yamamoto and J Takasu
Harbor-UCLA Research and Education Institute, USA

**Background:** Brachial artery measures of arterial distensibility have been demonstrated to be independent risk factor for development of heart diseases. These measures have been suggested as reflecting the endothelial function or atherosclerotic burden; however, they have not been compared with levels of
subclinical Atherosclerosis. This study sought to compare measures of brachial artery distensibility to subclinical Atherosclerosis as measured by electron beam tomography (EBT).

**Methods:** Brachial artery pulse waveform data were collected using the DynaPulse 2000A (Pulse Metric, Inc., San Diego, CA). Distensibility measurements were taken on 201 healthy adults and compared with levels of coronary artery calcification (CAC) as measured by EBT. Laboratory values, risk factors, blood pressure (BP), and heart rate measurements were also obtained. We then compared the results of the brachial artery measurements to measures of standard risk factors and CAC.

**Results:** Multivariate analysis was performed, revealing that brachial artery measures were the strongest predictor of CAC. For women, brachial artery (BA) resistance was the strongest independent predictor of log CAC score (r = 0.373, P = .004). For men, BA distensibility was the only independent predictor of calcium scores (P = .012). We then divided the patients into quintiles of calcium score. Patients in the top quintile had a mean BA distensibility that was significantly higher than those of the lowest quintile (P = .02).

**Conclusions:** Stiffer vessels with decreased distensibility were seen in subjects with higher levels of coronary artery calcium. Therefore, noninvasive measures of distensibility are useful in measuring subclinical vascular changes related to arteriosclerosis. This noninvasive measure might provide a simple and inexpensive method to identify patients with significant atherosclerotic burden.

*Am J Hypertens 2003; 16:350–355*

2001/11

**Measures of Noninvasive Brachial Artery-Derived Estimates of Brachial Reactivity and Systemic Compliance in Relation to Plaque Burden**

Matthew Budoff, Junichiro Takasu, Harbor-UCLA Med Ctr, Torrance, CA; Jeffrey Tsai, Timothy Frandsen, Pulse Metric, Inc., San Diego, CA

A new technology has recently been developed which records a brachial artery pressure waveform from a cuff sphygmomanometer and estimates brachial artery distensibility (BAD), systemic vascular compliance (SVC) and left ventricular dP/dt using proprietary pulse waveform analysis (PWA) algorithms. The purpose was to correlate these non-invasive measures from this new noninvasive technology with plaque burden estimates of risk obtained using electron beam tomography (EBT). We evaluated 130 patients who underwent EBT measures of coronary artery calcium (CAC) and non-invasive DynaPulse arterial pulse waveform analysis (Pulse Metric, Inc.). This non-invasive device analyzes the brachial artery pulsation signal to derive BAD and SVC from a physical model that is based on the rate of pressure changes (dP/dt) and heart rate. We compared the results to patients with measures of standard risk factors and CAC. We divided the patients into CAC scores > 75th percentile (n=96). The patients with scores >75th percentile had a mean BAD of 5.38 %/mmHg, significantly worse than those patients with scores <75th percentile (6.01 %/mmHg, p = 0.024). Patients with scores >75th percentile had a mean CAC score of 974, significantly higher than those with scores <75th percentile (17, p=0.001). Systemic Vascular Compliance (SVC) also showed a significant difference between groups (1.13 for >75th percentile scores vs 1.26 for <75th percentile, p = 0.037). Left ventricular dP/dt max, demonstrated a higher value for >75th percentile than scores <75th percentile (1243 vs 1156, p = 0.037). Other significant differences between groups included, Age (60 vs 56 years, p = 0.008), systolic blood pressure (146 vs 139, p = 0.012) and pulse pressure (65 vs 58, p = 0.008). Using a BAD threshold of 5.7% (halfway between the means of the 2 risk groups), sensitivity for identifying someone with significant plaque burden (high CAC score) was 78.4% and the specificity was 81.0%. This non-invasive measure might provide a simple and inexpensive method to identify patients with significant atherosclerotic burden.

*Presented at the American Heart Association 74th Scientific Session, Anaheim, CA 2001*

2001/08

**Non-Invasive Hemodynamic Evaluation of LV Function, Systemic Vascular and Brachial Artery Parameters in Hypertension**
Arterial Pulse Waveform (APW) and non-invasive hemodynamic parameters (Dyna Pulse 200, Shiu Shin Chio, Ph D) is a technological advances with new development at several major research center (University of California, Taipei, University of Carabobo). The aim of this work is to present new observations on non-invasive hemodynamic of LV (dP/dT, LVET, SV/ CO and contractility), Aortic (augmentation index, reflectance waves), Systemic Vascular (S resistance, S compliance) and brachial artery (BA resistance/ BA compliance) in 275 untreated hypertensives at basal, isometric handgrip test and 15 minutes later. 

RESULTS: a) LV function was evaluated on terms of Isovolumic Contraction Phase, Ejection Contraction Index and Pressure-volume relation; b) Aortic compliance assessed by augmentation index, level on reflection wave and estimates of velocity in backward waves; c) Recording of abnormal reflection in aorta in HT with normal BP during drug therapy; d) Systolic Time Intervals by APW and simultaneous resting Phono-ECG recordings; d) Correlation of SV/CO by APW with that obtained by Echocardiograms.

Conclusions: Computerized analysis of APW with its non-invasive hemodynamics may rapidly change some concepts and current management of arterial HT.

*Presented at the 34th Venezuelan Congress of Cardiology, Maracaibo, Venezuela, August 2001
Advances Cardiologicos, Vol 21, suppl 1, S32, 2001 (article in Spanish)

2001/05

Non-invasive Hemodynamic Evaluation of Left Ventricular Function by Arterial Waveform Analysis in Hypertension

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Since arterial blood pressure waveform results from the complex interaction between heart hemodynamic and the physical properties of arterial tree, it has considerable importance in the routine evaluation of such
factors in HT. In a one year study, we included routine **Non-Invasive Hemodynamic:** LVET, Arterial end-systolic elastance (Ea), LV Isovolumetric Phase indices (dp/dT max, dp/dT40 and Contractility), Ejection Phase Indices (SV, SV index, CO, CI) and Pressure Volume relation (LVSW, LVSW index, Cardiac Work and Cardiac Work Index), derivated from Arterial Waveform Analysis (DynaPulse 200M). This study, at rest, isometric hand grip & 15 min later, was recorded in 287 untreated HT subjects (Female n=150, Male n=137, age 53±14; BP 144.6±28/79.5±13 mmHg; PP 66±117 and HR 70±12 b/m).

**RESULTS:** LVET 323±47 msc; Ea 1.78±0.72 mmHg/ml; dP/dT max 1.218±367 mmHg/s, dP/dT40 30.45±9 s-1; Contractility 15.5±4.5 1/s; SV 75±20 ml/b, SV index 42±11 ml/b/m2; CO 6.1±1 l/min, CI 2.8±0.5 l/min/m2; LVSW 74±22 mmHg.ml/b, LVSW index 41±12 mmHg.ml/b/m2; Cardiac Work 67±18 J/min and Cardiac Work Index 37±9 J/min/m2. **Linear correlation:** SBP was significantly correlated with dP/dT max (r=-0.67, p <0.001) dP/dT 40 (r=-0.67, p 0.000) and Ea (r=-0.40, p 0.000). DBP and MBP showed good correlation with LVSW (0.47, p 0.000), Cardiac work (r=0.60, p 0.000), CW index (r=0.61, p 0.000).

**CONCLUSION:** This study document that HT imposes harder hemodynamics to heart function and that these parameters should be routinely evaluated.

*Presented at the American Society of Hypertension 16th Scientific Meeting, San Francisco, CA, 2001

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2001/03

**Blood Pressure and Left Ventricular Myocardial Function: Its Relation in Hypertensive Patients**

Antonio J. Delgado, Carlos L. Delgado León, Susana I. Celis
Unidad de Investigaciones Clínicas, Universidad de Carabobo, Valencia, Venezuela

The assessment of left ventricular (LV) myocardial function through pulse wave form analysis (non invasive hemodynamics), enable us to study and evaluate LV performance in cardiovascular diseases. **Aim:** To determine the relationship between SBP, DBP and MBP, and LV performance parameters: LV ejection time (LVET), Afterload (elastance Ea), Iso-volumetric phase indices (dp/dT max, dp/dT DP=40 mmHg [dp/dt40], Ejection phase indices (Stroke volume [SV], SV index [SV-I], Cardiac Output [CO], Cardiac Index [CI]) and LV pressure-volume relations (Stroke work [SW], Stroke work index [SW-I], Cardiac work [CW] and Cardiac work index [CW-I]).

**Methods:** 243 subjects hypertensive (BP = 140/90 mm Hg) enter in the study (males n=128, females n=115), age 55.77 ±14.59. BP measurements and hemodynamic recordings were obtained for each subject with a DynaPulse 200M (Pulse Metric, Inc.). Linear correlation was performed: statistical significance p <0.05.

**Results:** (1) **SBP** Good correlation (r=0.50-0.75, p <0.001) with dp/dT max and dp/dt40. Considerable correlation (r=0.25-0.50, p <0.001) with Ea, SW, SW-I, CW and CW-I. (2) **DBP** : Good correlation (r=0.50-0.75, p<0.001) with CW, and CW-I. Considerable correlation (r=0.25-0.50, p<0.001) with Ea, dp/dT max dp/dt40, SW and SW-I. (3) **MBP** : Good correlation (r=0.50-0.75, p<0.001) with dp/dT max, dp/dT40, CW and CW-I. Considerable correlation (r=0.25-0.50, p<0.001) Ea, SW and SWI.

**Conclusion:** These findings will help us know which of the LV myocardial function could be more susceptible to be modified by the use of antihypertensive drugs.

*Presented at the 14th Scientific Meeting of the InterAmerican Society of Hypertension, Santiago de Chile, Chile, March 2001 Hypertension, Vol 37, No. 3, 1001, March 2001

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1998

**The (dp/dt)max derived from arterial pulse waveforms during 24 hr blood pressure oscillometric recording**

Giuseppe Germanò, Stefania Angotti, Miryam Muscolo, Francesco D’Auria and Marcello Giordano

**Background** The modern developments in engineering allow one to record the speed at which the blood pressure rises on the advancing pulse wave front. It was possible to obtain this through the conversion of a
conventional pulse from a single suprasystolic oscillation to the oscillometric envelope into its first
derivative with respect to time.

**Objective** The aim of this study was to report a preliminary comparison between healthy subjects and
patients with heart failure as a first step towards the clinical use of this first derivative of a time-dependent
function (dP/dt).

**Methods** For 10 normal healthy subjects (aged 37 ± 5 years) and five subjects with ischaemic
cardiomyopathy (aged 41 ± 7 years), whose ejection fractions (invasively assessed) were <40%, we
evaluated six sequential oscillometric measurements of blood pressure obtained by using a DynaPulse 5000
(Pulse Metric, San Diego, California, USA) device, which simultaneously records blood pressure and
analyses every arterial waveform. The mean and SD of (dP/dt)max for each subject were calculated,
together with the relative mean distribution and the significance of the differences.

**Results** The data show that (dP/dt)max of subjects with an impairment of cardiac function is less than
normal. The mean (dP/dt)max of normal subjects was significantly different (P< 0.05) from that of patients
with ischaemic cardiomyopathy and lower than normal ejection fractions.

**Conclusions** These preliminary results allowed us to raise the hypothesis that this parameter, being
representative of the cardiac function, because many data are obtained, is extremely useful for monitoring
changes during daily activities or to outline the nycthoemeral rhythm. We have to test the hypotheses that
the analyses of the correlations between (dP/dt)max and other haemodynamic parameters may be used in
the pathophysiological study of cardiomyopathies and that the comparison of differences in (dP/dt)max can
be used in the evaluation of the effects of the treatment.

(Blood Pressure Monitoring 1998; 3:213-216)

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1997/05

**Suprasystolic dP/dt max Obtained by Cuff Sphygmomanometer Traces**

**Discriminates Subjects with Impaired Contractile Cardiac Function**

M Muscolo, G Germano, S Angotti, V Pecchioli, A scuteri, U Germano, M Giordano - Universita “La
Sapienza” Policlinico Umberto I, Rome (Italy)

Technological evolution allowed to record high fidelity traces that - when analyzed by complex
mathematical systems – may provide extremely detailed and new information about all the factors involved
in the determinism of pulse wave. Suprasystolic waves, i.e. those recorded immediately before systolic
pressure, may be regarded as similar to aortic pressure waves evaluated during cardiac catheterization.
Suprasystolic dP/dt max was calculated from the profile of pulse wave recorded by the DynaPulse (an
automatic non-invasive oscillometric method to simultaneously measure BP and analyze arterial
waveforms) in 10 normal healthy subjects and 5 subjects with dilative cardiomyopathy whose ejection
fraction - invasively assessed was < 40%. The mean suprasystolic dP/dt max was 405 ± 120 in normal
subjects and 267 ± 135 mmHg/sec (p<0.05) in patients with cardiomyopathy and reduced ejection fraction.
In conclusion, we found a significant difference in the suprasystolic dP/dt max values between healthy
subjects and patients with impaired cardiac function.

(Am. J. Hypertension 1997: 10: 71A)

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1996/03

**The Assessment of Systemic Vascular Compliance During Cardiac Output**

**Measurement to Evaluate Cardiovascular Loading Status**

Hospital- Taipei, Taiwan, R.O.C.

Systemic vascular compliance (SVC), dV/dP, is an important index of cardiovascular loading status.
SVC was determined using cardiac output (CO) derived by thermo-dilution and non-invasive pulse pressure (PP) and heart rate measurement obtained by a new oscillometric technology, \( \text{SVC} = \frac{\text{CO}}{\text{PP} \times \text{HR}} \). SVC measurement obtained by this method were compared to the effective arterial elastance (Ea) obtained by micromanometer tipped catheter in 30 myocardial infarction (MI) and 20 control patients. By definition, SVC corresponds inversely to Ea which was determined by the ratio of left ventricle developed pressure to stroke volume. A good correlation \((r=0.85)\) was observed between SVC and \( \frac{1}{\text{Ea}} \) (top figure). In order to evaluate the relationship between blood pressure load and cardiovascular loading status, SVC was compared to mean arterial pressure (MAP) in both MI and control patients. The relation between SVC and MAP is best fitted with a second order polynomial \((r=0.77)\) and the data of both groups follows the same fitting function (lower figure). The results suggest that SVC can be accurately assessed during cardiac output measurement utilizing a new noninvasive blood pressure and heart rate technology and results are not significantly affected by disease state.

Reliability of a noninvasive device to measure systemic hemodynamics in hemodialysis patients

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Objective: To evaluate the reliability of a noninvasive hemodynamic monitor in hemodialysis patients.

Methods: We enrolled 15 male patients (mean age 63 +/- 12 years) on stable chronic hemodialysis. Blood pressure and hemodynamic readings were obtained with the DynaPulse 500 Guardian device (Pulse Metric, Inc., San Diego California, USA), which measures systemic hemodynamics on the basis of oscillometric waveforms obtained through a cuff placed over the brachial artery. Measurements were taken sequentially, in duplicate, before, during and after hemodialysis, in the supine, seated and standing positions on four separated midweek dialysis sessions over 2-week period.

Results: The repeatability of the method was tested using 200 pairs of valid measurements. The average values (+/-SD) were 137 +/- 22 mmHg for systolic blood pressure, 80 +/- 13 mmHg for diastolic blood pressure, 1320 +/- 268 mmHg/s for dp/dtmax, 2.8 +/- 0.5 l/min/m2 for cardiac index, and 1455 +/- 359 dyn/s/cm5 for systemic vascular resistance. The mean differences (+/- SD of the difference) between readings were 0.1 +/- 10.4 mmHg for systolic blood pressure, 0.3 +/- 6.0 mmHg for diastolic blood pressure, -0.2 +/- 8.0 bpm for heart rate, 0.2 +/- 234 mmHg/s for dp/dtmax, 0.03 +/- 0.26 l/min/m2 for cardiac index and -10 +/- 177 for systemic vascular resistance, yielding limits of agreement (95%) of –20 to 20 mmHg for systolic blood pressure, -11 to 12 mmHg for diastolic blood pressure, -16 to 17 bpm for heart rate, -458 to 458 mmHg/s for dp/dtmax, -0.5 to 0.5 l/min/m2 for cardiac index and –338 to 357 dyn/s/cm5 for systemic vascular resistance. Other hemodynamic parameters fared similarly, and coefficients of variation were all between 7 and 18%.

Conclusion: We conclude that the DynaPulse 500 Guardian has adequate reliability indices in hemodialysis patients.


A Study on Adrenomedullin Level in Patients with Chronic Renal Failure and Its Changes during Dialysis

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[Abstract]
Objective: To investigate properties of adrenomedullin (ADM) in chronic renal failure patients at different disease stages and their relationship with systemic vascular compliance (SVC).

Methods: ADM levels in 19 hemodialysis (HD) patients with end2stage renal disease (ESRD), and 15 patients with chronic renal failure (CRF) but not receiving dialysis therapy were detected by radio immunoassay (RIA). SVC of all patients and 15 normal people (as control) were detected by Dynapulse 200M. ADM levels at pre2, post2 and 5 hours after2HD of 13 chronic HD patients were measured and compared.

Results: Compared with normal, ADM level increased in CRF and HD patients (P <0. 01), ADM level of HD patients were higher than that of CRF patients (P < 0.01). Significant SVC decrease and ADM increase occurred right after the dialysis (P < 0. 01, P < 0.05). However, in 5 hours after HD, SVC and
ADM changed back to the level before HD ($P > 0.05$). No significant correlation was found between SVC and ADM ($P > 0.05$).

**Conclusion s:** ADM of chronic renal failure patients increases significantly. The changes of ADM caused by HD are reversible; SVC and ADM had no significant relationship.

**Key words** kidney failure, chronic; adrenomedullin; nephrosis; renal dialysis; compliance; blood vessels

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### 2005/08

**Arterial Compliance in Elderly Men with Chronic Kidney Disease**

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**Abstract**

**Background/Aim:** Chronic kidney disease (CKD) is associated with decreased arterial compliance (AC). The stage of development of impaired arterial function in CKD in relation to loss of glomerular filtration rate (GFR) is not known. This study’s aim was to evaluate the relationship between GFR and AC in patients with CKD. **Methods:** We recruited 91 men aged 6–60 years with GFR 15–89 ml/min (mean 47 ± 21) to evaluate the relationship between GFR and AC in a cross-sectional study. We measured AC at the brachial artery with an oscillometric device (brachial artery distensibility; BAD). **Results:** There was no correlation between GFR and BAD ($r = 0.08, p = 0.44$). When stratified according to CKD stages, all groups showed decreased BAD compared with reference values, and there were no differences among them (one way ANOVA). Bivariate analyses showed statistically significant correlations between BAD and age ($r = –0.23, p = 0.03$), antihypertensive drug number ($r = 0.27, p = 0.009$) and serum hemoglobin ($r = 0.24, p = 0.02$), but only age and antihypertensive drug number remained significant markers of BAD in a multiple regression model. **Conclusion:** Older men with CKD have impaired arterial function, but GFR and CKD stage have no relationship to the degree of decrease in brachial artery distensibility.


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### 2004/06

**Properties of Brachial Arterial Elasticity in Patients With Chronic Renal Failure**

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2. Department of Nephrology, People’s Hospital of Peking University, Beijing, China

**Abstract:**

**Objective:** To investigate properties of brachial arterial elasticity of renal failure patients in different stages.

**Methods:** Brachial arterial elastic function of 19 hemodialysis (HD) patients with end stage renal disease (ESRD) and 15 patients with chronic renal failure (CRF) was detected with Dynapulse 200M before

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dialysis. The data were assessed and compared with those of 15 normotensive controls who had normal renal function.

**Results:** In CRF and HD patients, brachial arterial compliance (BAC), brachial arterial distensibility (BAD) were significantly lower (P < 0.01), and systolic pressure (SBP) and pulse pressure (PP) were significantly higher (P < 0.01) than those of controls. Simple correlation and multi-regression indicated that BAC and BAD had a significant inverse relationship with PP (r = -0.15, P < 0.01). Inpatients with CRF, a significant independent relationship was found between creatinine clearance (ccl) and BAD (r = 0.176, P < 0.01).

**Conclusions:** BAC and BAD in HD and CRF patients reduce significantly; PP is the major influence factor to brachial arterial elasticity. In CRF patients, BAD correlates significantly with ccl.

**Key words** brachial arterial; elasticity; renal dialysis; kidney failure, chronic; kidney failure

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2003/09

**The study of arterial elastic function in hemodialysis patients with end-stage renal disease**

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**Abstract**

- **Objective:** To investigate arterial elastic function of hemodialysis patients with end-stage renal disease (ESRD).
- **Methods:** One hundred and seventy-two chronic hemodialysis patients with ESRD were detected before dialysis by Dynapulse 200M.
- **Results:** Systemic vascular compliance (SVC), brachial artery compliance (BAC) and brachial artery distensibility (BAD) of hemodialysis patients were significantly reduced in comparison to the normal standard (P < 0.01). SVC, BAC and BAD of patients with pulse pressure at the level of 60~100 mmHg were higher than those of patients with pulse pressure at the level of 40~60 mmHg (P < 0.01). Between the two groups (age ≥ 65 years and age < 65 years), the former had lower SVC and BAC than the latter (P < 0.01). There was no significant difference of BAD (P > 0.05). There was no significant change among different causes of disease and different years of hemodialysis (P > 0.05). A significant correlation was found between SVC and BAD (r = 0.718, P < 0.01), SVC, BAC and BAD all had inverse relationship with pulse pressure, the correlation coefficient between pulse pressure and BAD was the strongest (r = 0.865, P < 0.01).
- **Conclusions:** Arterial elastic function of hemodialysis patients with ESRD reduces prevalently, moreover, it has close relation with pulse pressure.

**Key words** Arterial elastic function; Hemodialysis; Hypertension

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2001-Letter

**The (dP/dt)max derived from arterial pulse waveforms: prospective applications in the haemodialysis setting**

John Kyriazis, John Glotsos, Leonidas Bilirakis and Nikos Smirnoudis

Quote: “A new non-invasive, pulse-dynamic technology [1] can provide not only automated systolic and diastolic pressures, but also measurements of the rate of pressure change during the cardiac cycle.
Measurements of the maximum rate of BP increase in systole are derived from the brachial pulsation signal, obtained with the use of an inflated cuff, after converting it into its first derivative \((dP/dt)_{\text{max}}\) with respect to time. These peripheral \((dP/dt)_{\text{max}}\) calculations are in good agreement \((r=0.87)\) with invasive measurements of left ventricular \((dP/dt)_{\text{max}}\) \([1]\). Recently, Germano et al. \([2]\) reported that the \((dP/dt)_{\text{max}}\) of normal subjects was significantly greater \((P<0.05)\) than that of cardiac patients with ejection fraction <40%. In the present study, we (i) further investigated the associations between brachial pulse \((dP/dt)_{\text{max}}\) and other haemodynamic parameters in a chronic haemodialysis population and (ii) examined the potential role of \((dP/dt)_{\text{max}}\) as a tool to track effectively haemodynamic changes during HD.

These findings raise the hypothesis that brachial pulse's derivative can be adopted as an additional representative of cardiac function. Given that each arterial pulse waveform obtained during a 24 h BP oscillometric recording can be converted to its first derivative \((dP/dt)_{\text{max}}\), the latter would be extremely useful to monitor cardiac performance during daily activities, or to outline the nycthoemeral rhythm \([3]\). Furthermore, owing to its satisfactory reproducibility in the HD setting, \((dP/dt)_{\text{max}}\) may be adopted in the evaluation of the effects of therapeutic interventions on cardiac function.

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*Nephrol Dial Transplant (2001) 16: 1087-1088*

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**2000**

**Intradialytic and Interdialytic Effects of Treatment With 1.25 and 1.75 mmol/L of Calcium Dialysate on Arterial Compliance in Patients on Hemodialysis**

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Arterial compliance (AC) is an important determinant of vascular structure, and abnormalities of AC can greatly affect the cardiovascular system. Given the vasoconstrictive properties of increased levels of serum ionized calcium (iCa), we investigated the way that dialysate calcium level can influence AC in the hemodialysis (HD) population. In a crossover randomized design, 19 dialysis patients undergoing regular bicarbonate HD (three times weekly) underwent two cycles of four successive HD sessions each with a low (LdCa; 1.25 mmol/L) and high dialysate calcium concentration (HdCa; 1.75 mmol/L). At the fourth session of each cycle, iCa level and hemodynamic parameters (systolic blood pressure [SBP], diastolic blood pressure, mean arterial pressure [MAP], pulse pressure [PP], heart rate, and AC) were measured pre-HD and post-HD. AC was measured noninvasively at the brachial artery by arterial pulse waveform analysis. The dialysate calcium level was a significant determinant of both pre-HD \((r = 0.335; \ P < 0.05)\) and post-HD iCa level \((r = 0.767; \ P < 0.001)\). Pre-HD AC increased significantly \((P < 0.05)\) by 0.01± 0.02 mL/mm Hg \((7\% \pm 19\%)\) on switching from HdCa to LdCa treatment. Multiple regression analysis showed that both pre-HD PP and iCa level were major inverse determinants of pre-HD AC in both the LdCa \((R^2 = 0.65; \ P < 0.001)\) and HdCa \((R^2 = 0.51; \ P < 0.01)\) treatment groups. AC increased by 32% \((P < 0.01)\) and 37% \((P < 0.05)\) during LdCa and HdCa dialysis, respectively. Intradialytic changes in AC were inversely correlated with changes in SBP and PP. In the HdCa group, changes in iCa level related significantly to MAP \((r = 0.464; \ P < 0.05)\). The results show that changes in AC during HD are mainly mediated through concurrent changes of systemic hemodynamics, which are largely affected by dialysate calcium level through parallel changes in iCa level. Interdialytically, a significant, blood pressure–independent, inverse relationship between AC and iCa level exists. Therefore, HD with LdCa, by reducing the incidence of HD-induced hypercalcemia, may have a beneficial role in preventing the ongoing reductions of AC in HD patients and thus improving cardiovascular prognosis. Keywords: Arterial compliance, blood pressure, calcium, dialysis solutions, hemodialysis, hemodynamics


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Hypertension and stroke/vascular diseases – Studies on hemodynamics and cerebrovascular/vascular problems and functions

2006/01

Twenty-four-hour ambulatory blood pressure and duration of hypertension as major determinants for intima-media thickness and Atherosclerosis of carotid arteries

Ta-Chen Su, Yuan-The Lee, Suzzana Chou, Wen-Tsan Hwang, Chen-Fong Chen and Jung-Der Wang

Abstract: The relationship between time factors of elevated blood pressure (BP) and carotid Atherosclerosis (CA) is still unclear. The associations between time-weighted average 24h ambulatory systolic BP (TWA-SBP), duration of hypertension in years (hypertension-year), and CA were investigated in a petrochemical company sample of 95 executive and 91 gender- and age-matched non-executives employees. Intima-media thickness (IMT) and plaque scores of extracranial carotid artery (ECCA) were determined bilaterally by high-resolution B-mode ultrasound. The determinants of segment-specific carotid IMT and odds ratios for CA, in terms of thicker IMT (IMT>=75th percentile) and ECCA score>=3, were evaluated by multivariate regression analysis. Results revealed TWA-SBP and hypertension-year were two major determinants of IMT at common carotid artery (CCA) and carotid bulb by using mixed regression models. However, TWA-DBP was a negative determinant of IMT at CCA and carotid bulb. Meanwhile, the executives were found to be a negative association with IMT at carotid bulb. Measurements at both internal carotid and bulb identified duration of diabetes mellitus as significant determinant of IMT. After controlling covariates, multivariate logistic regression analysis identified TWA-SBP and hypertension-year as the important determinants for thicker IMT and ECCA>=3. And, TWA-DBP was found as a negative determinant for CA. In conclusion, both TWA-SBP and hypertension-year were two major determinants for carotid IMT and CA, which seem to imply that both short-term and long-term durations of elevated BP are probably crucial in pathogenesis of CA.

(Atherosclerosis, 184 (1) 2005: 151-156)

2001/07-a

Clinical Observations on Hemodynamic Changes and Angiographs of a Patient with Vertebral and Subclavian Artery Stenosis and Steal Phenomenon, Pre and Post Stent Operation


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Assessment of arterial blood pressures, flow, pulse waveform, and other hemodynamic parameters are useful for diagnosing arterial complications (1-3). Arterial pressure waveform was recorded from cuff sphygmomanometer of an oscillometric blood pressure device using a DynaPulse 2000A. (Pulse Metric, Inc. San Diego, CA, USA) This method has been validated against invasive (4) and non-invasive measurements (5-7). Clinical observations and evaluations with this non-invasive pulse waveform analysis and ultrasonography for screening and diagnosing a patient with severe vertebral and subclavian artery stenosis, together with angiographs, pre and post to stent operation, was found interesting and may provide essential information on the changes of hemodynamics and reactions of the body to the patient’s circulation system. This study reports in detail the observations of hemodynamic parameters, blood pressures, heart rates, arterial compliances and distensibility, vascular resistances, etc. by the Pulse-Dynamic pulse waveform analysis, blood flows with an ultrasonographic method, and angiogram of a 55-year-old female patient, pre and post to her stent operation. The observations included five stages of hemodynamic monitoring and angiography, pre and post of the stent operation: 1) Prestent, 1-2 years prior to the stent operation, blood pressure and ultrasound assessments indicated that the patient’s left arm SBP was 30-40
mmHg lower than the right’s with reversed blood flow at left vertebral artery and decreased blood flow at left subclavian observed by the ultrasonography; Pulse waveform analysis showed lower than normal Systemic Vascular Compliance (SVC) and Brachial Arterial Compliance (BAC) and Distensibility (BAD), and higher than normal Systemic Vascular Resistance (SVR) and Brachial Arterial Resistance (BAR). 2) Pre-stent, angiogram prior to the stent operation indicated Stenosis: 85% at ostium of left VA, and 80% at proximal of left subclavian with steal phenomenon when using contract enhancement. 3) Post-stent, angiogram after the stents were placed in both left VA and subclavian, subclavian steal disappeared. 4) Post-stent day one, left arm systolic BP became closer to the right’s within 10 mmHg; higher heart rate (HR), 109 vs. 80, and lower diastolic BP, 68 vs. 80, together with significant increases of BAC and BAD, but decrease of SVC, and decrease of both BAR and SVR were observed; Ultrasonography showed blood flows at both left vertebral and subclavian arteries became normal. 5) Post-stent, 3 months after, the left arm BP stabilized at a lower level than the right’s (SBP ~14 mmHg and DBP ~9 mmHg lower); HR diastolic BP and all cardiac parameters returned to the ranges of pre-stent values; SVC and SVR were slightly improved; significant improvements were observed on BAC/BAD and BAR. This study demonstrates the feasibility and the potential clinical values of simple-to-use non-invasive hemodynamic monitoring, such as the DynaPulse, in screening and assisting the diagnosis with ultrasonography and the treatment of an angiogram stent procedure for patients with vertebral and subclavian arterial Stenosis.

*Presented at the First International Conference on Non-invasive Hemodynamic Monitoring for Cardiovascular Disease and Management, Taipei, Taiwan, 2001

2001/07-b

**DynaPulse Blood Pressure Monitoring in Stroke**

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The recent advances in engineering allow one to record the speed at which the blood pressure rises on the propagating pulse wave front. It was possible to obtain this through the conversion of a conventional pulse from a single suprasystolic oscillation to the oscillation to the oscillometric envelope into its first derivative with respect to time. In the past time, high-tech manpower was needed in the laboratory to handle the tedious post-processing analysis of the recorded data. However, through the recent development of the e-technology, the massive data analysis could be handled efficiently and rapidly through the internet transmission. People could get the automatic technology support from the remote server. Previous animal studies have shown that stroke in the right hemisphere produces more significant sympathetic effect than leftsided stroke. Tokgozoglu et al. has also shown in human that right-sided stroke produced more decrease in HRV than that in leftsided stroke. It was found that stroke in the right hemisphere has a greater role in influencing the autonomic function and a poorer recovery in arterial compliance. In conclusion, these preliminary results have shown that with the use of recent advanced e-technology, it became possible to study or get the more powerful prognostic hemodynamic factors in the patients with stroke.

*Presented at the First International Conference on Non-invasive Hemodynamic Monitoring for Cardiovascular Disease and Management, Taipei, Taiwan, 2001

2001/07-c

**Subclinical Atherosclerosis and Measures of Vascular Stiffness**

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The process of vascular aging involves both the development of atheroma and structural changes to the arteries including thickening of the arterial walls, dilation of the arterial lumen, degradation of elastin and increases in collagen. Numerous technologies are available that allow the non-invasive evaluation of these processes. Ultrasound allows the precise measure of carotid artery wall thickness and lumen diameter and
can also be used to quantify extent of focal plaque. Measures of wall thickness have been shown to be associated with incident cardiovascular events in population studies and have been used to evaluate progression of disease over time. The newer technology of Electron Beam Tomography (EBT) allows the evaluation of the coronary arteries directly. Calcified areas of plaque can be used to quantify the overall plaque burden in the coronary arteries and the aorta. Age-related structural changes of the arteries result in increased vascular stiffness which in turn is associated with increased cardiac after load and less efficient filling of the coronary arteries during diastole. Our laboratory uses three different measures of arterial stiffness. Aortic pulse wave velocity, the pressure strain modulus and the distensibility coefficient from the Pulse Metric DynaPulse system. We have found these measures to be modestly correlated with one another. Thus, each is likely measuring vascular stiffness from a slightly different perspective. As one would expect, these measures are most strongly associated with age and blood pressure. After controlling for these variables, measures of body fat such as weight and waist circumference also appear to be independently predictive of vascular stiffness. Measures of glucose metabolism also figure prominently, suggesting that components related to the insulin resistance syndrome may play a role in vascular aging. The consequences of vascular stiffness may be best represented by the long term outcome of subjects with isolated systolic hypertension, where the underlying etiology is a stiffening of the central arteries. In comparison to normotensive controls, these individuals have much higher rates of subclinical atherosclerosis as identified by carotid ultrasound and electron beam tomography. The long-term outcome with respect to cardiovascular events and total mortality is dramatically higher for those with systolic hypertension in comparison to controls. Thus, atheroma formation and vascular stiffening are separate but interrelated processes, each contributing to the vascular aging process.

*Presented at the First International Conference on Non-invasive Hemodynamic Monitoring for Cardiovascular Disease and Management, Taipei, Taiwan, 2001

2001/05

Assessment of Systemic Vascular Parameter and Brachial Artery Function in Hypertension

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Although HT is currently identified by measurement of BP, there is growing medical consensus that endothelial function and vascular compliance are on the basis of its pathogenesis. To assess the significance of vascular parameters, non-invasive Arterial Waveform Analysis (DynaPulse 200M) at rest, isometric hand grip & 15 min later, was recorded in 287 untreated HT subjects (Female n=150, Male n=137, age 53±14 yrs). SV Resistance (SVR), SV Compliance (SVC), Brachial Artery (BA) Resistance and Compliance, BA Distensibility, BP, Pulse Pressure (PP) and HR were obtained basal and after 1 month follow-up. Correlations between BP levels and vascular parameters were evaluated. RESULTS: a) Hypertensives had basal BP of 144.6±28/79.5±13 mmHg; PP: 66±17 and 70±12 b/m; b) Vascular parameters were: SVR 1606±431 dy.s.cm5 and SVR index 2864±685 dy.s.cm5/m2; SVC 0.87±0.15 ml/mmHg and SVC index 0.51±0.08 ml/mmHg/m2; BAC 0.088±0.033 ml/mmHg and BA distensibility 4.21±0.89% mmHg. c) Linear Correlation: SBP was significantly correlated to SVC (r=-0.56, p=0.000), SVC index (r=-0.60, p=0.000), BAC (r=-0.61, p=0.000) and BAC index (r=-0.67, p=0.000), SVR (r=0.48, p=0.000), SVR index (r=0.50, p=0.000); white DBP and MBP showed good correlation with SVR (r=0.33, 0.000), SVR index (r=0.47, p=0.000). CONCLUSION: Pathogenesis of HT involves significant alterations in SV and brachial artery function which have not been apparent from traditional BP evaluation.

*Presented at the American Society of Hypertension 16th Scientific Meeting, San Francisco, CA, 2001

2001/03

Systemic Vascular and Brachial Artery Parameters: Its Relationship With Blood Pressure in Hypertensive Patients
Blood pressure (BP) measurements and the assessment vascular parameters (VP), through pulse wave form analysis let us to study these characteristics in hypertensive diseases and to evaluate how they are modified with drugs interventions. **Aim:** To determinate the relationship between SBP, DBP and MBP, and VP: (1) Systemic vascular parameters: Vascular Compliance (VC), Vascular Compliance Index (VCI), Vascular Resistance (VR), Resistance Index (VRI); (2) Brachial artery parameters: Brachial artery compliance (BAC) and Brachial artery compliance index (BAC-I). **Methods:** 243 subjects hypertensive (BP = 140/90 mm Hg) enter in the study (males n=128, females n=115), age 55.77 ±14.59. BP measurements and hemodynamic recordings were obtained for each subject with a DynaPulse 200M (Pulse Metric, Inc.). Linear correlation was performed: statistical significance <0.05. **Results:** (1) SBP: Good correlation (r=0.50-0.75, p <0.001) with VC, VCI, BAC, BAC-I. Considerable correlation (r=0.25-0.50, p <0.001) with VR and VRI. (2) DBP: Considerable correlation (r=0.25-0.50, P<0.001) with VC and VRI. Null correlation (r<0.25) with VC, VCI, BAC and BAC-I. (3) MBP: Good correlation (r=0.50-0.75, p<0.001) with VRI, while considerable correlation (r=0.25-0.50, p<0.001) VC, VCI, BAC and BACI. **Conclusions:** SBP and MBP have good relation with Systemic vascular and Brachial artery parameters while DBP has with VR.

*Presented at the 14th Scientific Meeting of the InterAmerican Society of Hypertension, Santiago de Chile, Chile, March 2001; Hypertension, Vol. 37, No. 3, 1001, March 2001*
(6) White-coat and essential hypertensions – 24-hour ambulatory blood pressure monitoring (ABPM) and circadian rhythm studies

Introduction to Monitoring of White Coat Hypertension with ABPM:

Ambulatory Blood Pressure Monitoring (ABPM) is a simple procedure that takes multiple blood pressure readings over a 24-hour period. A small lightweight device, such as the DynaPulse 5000A ABP monitor, is worn by the patient throughout the day and automatically records measurements of blood pressure at preset intervals. Usually the start and end of the procedure is done in a doctor’s clinic to perform the initial setup and save the recorded data. Many studies have shown ABPM to be particularly useful in patients with “white coat” hypertension, where blood pressure readings may be normal during home blood pressure monitoring, but elevated while taken in the doctor’s clinic. Other studies have been performed using ABPM examining blood pressure patterns and circadian rhythms, relationships with target organ damage and hypertension, prognosis of cardiovascular events, and the effects of hypertensive drugs (NIH Working Group Report on ABPM, 1992). Following studies demonstrate the evaluation of “white coat” hypertensives and specific cardiovascular diseases by ABPM using the DynaPulse 5000A. In combination with the ability to measure 24-hour hemodynamic parameters, the DynaPulse technology allows physicians to have a better understanding of the patterns in hemodynamic performance.

2006/01

Twenty-four-hour ambulatory blood pressure and duration of hypertension as major determinants for intima-media thickness and Atherosclerosis of carotid arteries

Ta-Chen Su, Yuan-The Lee, Suzanna Chou, Wen-Tsan Hwang, Chen-Fong Chen and Jung-Der Wang

Abstract: The relationship between time factors of elevated blood pressure (BP) and carotid Atherosclerosis (CA) is still unclear. The associations between time-weighted average 24h ambulatory systolic BP (TWA-SBP), duration of hypertension in years (hypertension-year), and CA were investigated in a petrochemical company sample of 95 executive and 91 gender- and age-matched non-executives employees. Intima-media thickness (IMT) and plaque scores of extracranial carotid artery (ECCA) were determined bilaterally by high-resolution B-mode ultrasound. The determinants of segmen-specific carotid IMT and odds ratios for CA, in terms of thicker IMT (IMT>=75th percentile) and ECCA score>=3, were evaluated by multivariate regression analysis. Results revealed TWA-SBP and hypertension-year were two major determinants of IMT at common carotid artery (CCA) and carotid bulb by using mixed regression models. However, TWA-DBP was a negative determinant of IMT at CCA and carotid bulb. Meanwhile, the executives were found to be a negative association with IMT at carotid bulb. Measurements at both internal carotid and bulb identified duration of diabetes mellitus as significant determinant of IMT. After controlling covariates, multivariate logistic regression analysis identified TWA-SBP and hypertension-year as the important determinants for thicker IMT and ECCA>=3. And, TWA-DBP was found as a negative determinant for CA. In conclusion, both TWA-SBP and hypertension-year were two major determinants for carotid IMT and CA, which seem to imply that both short-term and long-term durations of elevated BP are probably crucial in pathogenesis of CA.

(Atherosclerosis, 184 (1) 2005: 151-156)
2004

Effect of Antihypertensive Monotherapy and Combination Therapy on Arterial Distensibility and Left Ventricular Mass

Joel M. Neutel, David H.G. Smith, and Michael A. Weber

**Background:** Angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers (CCBs) increase arterial compliance and decrease left ventricular mass in hypertensive patients. This study examined whether combined therapy has greater arterial and cardiac effects than doubled doses of the individual drugs.

**Methods:** This prospective, randomized, open-label study enrolled 106 patients aged >=18 years with mild-to moderate hypertension. Patients were randomized to 5 mg of amlodipine or 20 mg of benazepril for 2 weeks; then, depending on randomization assignment, they were force-titrated to 10 mg of amlodipine or 40 mg of benazepril monotherapy, or to combination amlodipine (5 mg) and benazepril (20 mg) treatment for 22 weeks. Arterial distensibility was assessed using the DynaPulse ambulatory system, and left ventricular mass was assessed by echocardiography.

**Results:** Combination therapy (0.71% +/- 0.51% mL/mm Hg) increased arterial distensibility more than amlodipine (0.28% +/- 0.69% mL/mm Hg; P = .008) or benazepril (0.39% +/- 0.62% mL/mm Hg; P = .03) monotherapies. Left ventricular mass decreased more with combination treatment (65 +/- 56 g) than with amlodipine (28 +/- 4 g; P < .02); the difference from benazepril (42 +/- 50 g) was not significant.

**Conclusions:** Combined ACE inhibitor and CCB treatment was more efficacious than high doses of the individual agents in increasing arterial compliance and reducing left ventricular mass. These findings indicate that appropriately selected combinations of antihypertensive drugs might have enhanced cardioprotective effects.

Am J Hypertens 2004;17:37–42

2003/12

Effects of Occupational Noise Exposure on Blood Pressure

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We measured 24-hour ambulatory blood pressure and 16-hour noise exposure continuously for 20 automobile workers, and used linear mixed-effects regression models to estimate transient and sustained effects of noise exposure on blood pressure. The occupational noise levels of the high-exposure workers with 85 +/- 8 dBA were significantly higher than those of the low-exposure workers with 59 +/- 4 dBA (p<0.05). We found a significant difference of 16 +/- 6 mmHg in sleep-time systolic blood pressure (SBP) existed between 2 exposure groups, and a marginal increase of 1 mmHg SBP per 1-dBA increase in occupational noise exposure at 60-minute lag time during work (p = 0.07). Occupational noise exposure had both transient and sustained effects on workers’ SBP. (DynaPulse 5000A ABPM was used in this study.)


2001/07

Circadian Blood Pressure and Arterial Compliance in White Coat Hypertension

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Increased blood pressure is one of the most powerful predictor of cardiovascular morbidity. It is the average level of blood pressure to which the circulation is exposed over prolonged periods of time that causes the adverse effects of hypertension rather than the pressure at any one moment, such as during a
From the ambulatory blood pressure monitoring data and non-invasive hemodynamic data. We conclude that there were no significant difference between white coat hypertension and normotension by the present study, ie, white coat hypertension is a rather benign condition, but long term follow-up and reinforce lifestyle modifications is necessary.

*Presented at the First International Conference on Non-invasive Hemodynamic Monitoring for Cardiovascular Disease and Management, Taipei, Taiwan, 2001
Mental Stress-Induced Hypertension and White-Coat Effect are not Identical Phenomena: Arterial Compliance Impact Differences

M.N. Mily, J.Tsai, S.A. Golubev.

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Objective: Underlying pathophysiological mechanisms of white-coat effect (WCE) and mental stress-induced hypertension (MSH) remains controversial. The aim of this study was to evaluate the impact of 24h hemodynamics and arterial compliance in WCE and MSH in essential hypertensives (EH).

Design and Methods: Twenty-three untreated verified mild-to-moderate EH (15 males; aged 41.3± 11.1 years, BMI 31.2±4.9 kg/m²) underwent oscillometric BP and HR measurements (DynaPulse 5000A; Pulse Metric, Inc., USA) during clinic, ambulatory and standard 5 min arithmetic test conditions with systemic and brachial artery (BA) hemodynamics and compliance evaluation at each measurement by the previously validated pulse dynamics analysis technology [1]. WCE was assessed as differences between office BPs and day-time ambulatory BPs, and MSH as percentage of maximal changes in BP.

Results: WCE for DBP and HR were significantly and negatively correlated with mean daytime HR (Spearman rank coefficient r= -0.56 for both; p<0.05). MSH for SBP and DBP were correlated negatively with 24h mean BA compliance (r= -0.56 and -0.57, respectively; p<0.05). MSH for SBP was positively related to 24-h BA resistance (r = 0.51; p<0.05) and MSH for DBP to the daytime BA resistance (r = 0.53; p<0.05). No significant relationships were observed between WCE and systemic or BA compliance and resistance, as well as between MSH and 24h, daytime or nighttime HR.

Conclusions: In the studied EH mental stress BP response but not WCE seems to be determined by increased arterial stiffness and may be a marker of enhanced vascular remodeling. WCE might be presumably related to sympathetic nervous tone, lower clinic-ambulatory BP difference being revealed in patients with preexisting sympathetic overactivity. [1] T.J.Brinton et al. 1997, Am J Cardiol, 80:323-330.

* Presented at the Eleventh European Meeting on Hypertension, Milan, Italy, 2001

Monitoring of White Coat Hypertension with ABPM

Assessment of the Homogeneity of the Blood Pressure Reduction: Influence of White-Coat Effect and Anxiety Level

M.N. Mily, V.V. Afanassiev, S.A. Golubev.

Vitebsk Emergency Hospital, Vitebsk State Medical University, Vitebsk, Belarus.

Objective: Priority of different approaches of assessment of antihypertensive effect smoothness is much discussed. The aim of this study was to examine possible relation between white-coat effect (WCE) and the level of anxiety with smoothness of antihypertensive effect assessed by previously suggested smoothness index (SI) and trough: peak ratio (T/P) in essential hypertensives (EH).

Design and Methods: Fourteen patients with verified mild-to-moderate EH (8 males; aged 39.4±8.3 years, BMI 31.3±5.0 kg/m²) underwent office BP measurement, ambulatory BP monitoring (DynaPulse 5000A; Pulse Metric, Inc., USA), and anxiety level (A) evaluation (Sheehan’s Anxiety Self-Assessment Scale) before and 4 weeks after treatment with 5 mg nebivolol o.d. Individual SI and T/P-ratio for SBP and DBP were calculated. WCE was computed as difference between clinic and average daytime ambulatory BP and HR (WCE1) and as difference between average (WCE2) or peak (WCE3) value of the first hour of ambulatory BP monitoring and the remaining average daytime ambulatory BP and HR.

Results: T/P for SBP, but not SI was significantly and negatively correlated with pretreatment WCE2 for HR (r = - 0.61; p<0.05). SI for SBP and DBP were positively correlated with baseline A (r = 0.61 and 0.6,
respectively; p<0.05), in patients with A above median SI for DBP being revealed as 1.38±0.5 vs. 0.39±0.53 in ones with A below median (p<0.05). Moreover, A was related to the SD of hourly BP reductions (r = -0.65 and -0.6 for SBP and DBP, respectively; p<0.05) but not to the average values of hourly BP reductions. No significant relationships were revealed between A and T/P.

**Conclusions:** In the investigated EH the extent of pretreatment WCE might influence on values of smoothness of antihypertensive effect assessed by T/P-ratio, but not by SI. Anxiety seems to be a predictor of smooth antihypertensive action of a lipophilic prolonged b-blocker nebivolol, what may explain the direct relationship between SI and pretreatment A score.

* Presented at the Eleventh European Meeting on Hypertension, Milan, Italy, 2001

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2001-c

**Evaluation of A 24-hour Ambulatory Blood Pressure Monitoring Device**

Lin CW, Luo TC, Chiu SR, and Tseng YZ  
*Institute of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University*

**Abstract** -- This report focuses on the comparisons between two currently available standards (AAMI vs BHS) for the validation of 24-hour ambulatory blood pressure monitoring devices. Part of the validation procedures was then applied to the evaluation of a commercial unit (DynaPulse 5000A, Pulse Metric, Inc.). Result supports the clinical accuracy and usefulness of DynaPulse 5000A ABPM, and met the current standards, and its derived hemodynamic parameters were also been evaluated, and concluded of additional clinical values to better diagnosis and treatments of hypertension.

(Article in Chinese, published at Taiwan Univ. Collage of Medicine and Engineering J., 2001)

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2001-d

**Resynchronization of Blood Pressure Circadian Rhythm After Westward Trans-7-Meridian Flight with and without Melatonin Treatment**

Barattini P, Doci C, Montaruli A, Roveda, E, and Carandente F

Blood pressure (BP) of a healthy 37-yr-old male traveling from Milan to Houston was monitored for 36 hr before the flight and continued for 5 days after the arrival. The rhythmometric analysis of BP data was made to investigate the rate of adaptation to a rapid rest-activity cycle shift. Since two trips were evaluated, during the second one the subject took melatonin (3 mg) before the nocturnal rest. In the first trip the BP circadian rhythm synchronization occurred on the 5th day. In the second trip melatonin promoted an immediate but unstable adaptation to the new rest-activity cycle. (DynaPulse-5000A ABPM was used in this study.)

*Published in Aviation, Space, and Environmental Medicine, March, 2001 Vol 72, No. 3, pp 221-224

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2000-a

**Ambulatory Blood Pressure Monitoring Variables as Predictors of the Quality of Life in Essential Hypertensives**

M.N. Miliy, V.V. Afanasiev, S.A. Golubev  
*Vitebsk State Medical University, Vitebsk Regional Cardiology Center, Vitebsk, Belarus*

**Objectives:** To estimate whether ambulatory blood pressure monitoring (ABPM) variables predict the quality of life (QL) parameters in essential hypertensive subjects (EH).
**Design and Methods:** A noninvasive twenty-four hours ABPM (DynaPulse 5000A; Pulse Metric, Inc., USA) was carried out in 33 untreated verified mild-to-moderate EH (19 males, 14 females; mean age 43.8 ±11.0 years; BMI 30.3 ±5.0 kg/m²; duration of hypertension 9.0 ±8.7 years). At each monitoring session conventional ABPM variables were calculated, including daytime and nighttime means and SD, time indexes (TI, %) of BP load. The QL assessment was performed using the well-validated measures: the General Well-Being Adjustment Scale (GWBAS) and Giessen Somatic Complaints Questionnaire. The Total Well-Being Index (TWBI), the Total Complaints Index (TCI) and indexes on the questionnaires subscales were calculated, a higher score indicating greater well-being or complaints expressions.

**Results:** TWBI and TCI were observed to correlate negatively with Spearman rank coefficient r = -0.51 (p = 0.02). TCI was inversely related to both daytime DBP (93.1 ±7.5 mmHg) and TI of DBP (60.7 ±21.1) (r = 0.54, p = 0.01 and r = 0.52, p = 0.02, respectively); and directly-to daytime SD of SBP (14.4 ±3.4; r = 0.49, p = 0.02). The associations between TWBI and nighttime SD of SBP (13.0 ±3.9) and DBP (9.8 ±2.8) were revealed (r = 0.43, p = 0.04; and r = 0.44, p = 0.04, respectively). Nighttime SD of SBP and DBP most closely and negatively correlated with GWBAS “anxiety” (r = -0.58, p = 0.008; r = -0.54, p = 0.013, respectively).

**Conclusions:** In mild-to moderate EH stable BP elevation is accompanied with safe feeling, what may cause the difficulties in hypertension management via a lower patients’ compliance. Low nighttime BP variability associates with a higher level of anxiety and worse well-being, probably due to deterioration of REM/NREM sleep stages proportion in EH with anxious disorders. Keywords: Ambulatory Blood Pressure, Quality of Life

(Journal of Hypertension 2000; 18 (Suppl 2): S55)

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2000-b

**Hemodynamics, Quality of Life and Metabolic Changes during Nebivolol Treatment of Young Overweight Hypertensives**

V.V. Afanasiev, M.N. Miliy, S.A. Golubev

*Vitebsk Regional Cardiology Center, Vitebsk State Medical University, Vitebsk, Belarus*

**Objective:** To evaluate hemodynamics, metabolic and the quality of life (QL) changes during short-term treatment of young overweight essential hypertensives (EH) with nebivolol (N), a new highly selective, - blocker with nitric oxide modulating properties.

**Design and Methods:** Twelve patients (aged 36.1 ±7.2 years, BMI 32.0 ±5.3 kg/m²) were randomly selected from a group of newly verified never treated EH. Ambulatory BP monitoring (DynaPulse 5000A; Pulse Metric, Inc., USA), conventional echocardiography, QL evaluation (General Well-Being Adjustment Scale) and metabolic tests (serum insulin before and 2 h after standard oral TTG, lipids, uric acid, fibrinogen) were performed before and 4 weeks after treatment with 5 mg N once daily.

**Results:** BP and HR were significantly reduced (daytime DBP 90.3 ±4.6 vs. 79.5 ±5.8; nighttime DBP 76.3 ±6.0 vs. 69.0 ±7.5 mm Hg; daytime HR 79.0 ±12.2 vs. 62.0 ±6.7; nighttime HR 63.8 ±6.6 vs. 54.8 ±4.5 bpm; p < 0.01), with normalization DBP (daytime DBP < 90, nighttime DBP < 80 mm Hg) in ten patients (83%). No significant changes were observed in nighttime falls and BP variability (SD). LV eject fraction was not changed, and LV compliance (E to A peaks of diastolic filling ratio) tended to increase (1.2 ±0.36 vs. 1.53 ±0.62; p = 0.17). The total QL score tended to improve (82.6 ±22.6 vs 100.5 ±14.0 points, p = 0.09) without any correlation with ambulatory BP parameters. No significant changes were revealed in the metabolic tests monitored with tendency to a decrease of fasting insulin (136.3 ±92.5 vs. 81.8 ±18.5 pmol/l; p = 0.18).

**Conclusions:** In the investigated young overweight EH N has demonstrated favorable short-term effects on ambulatory BP. Keywords: Hemodynamics, Quality of Life, Nebivolol

(Journal of Hypertension 2000; 18 (Suppl. 2): S164)
Insulin-Resistant Hypertensives: Hemodynamics, Quality of Life and Metabolic Changes during Nebivolol Treatment

V.V. Afanasiev, M.N. Miliy, S.A. Golubev, Vitebsk State Medical University, Vitebsk, Belarus; Vitebsk Cardiology Center, Vitebsk, Belarus

**Objective:** To evaluate haemodynamics, metabolic and quality of life (QL) changes during short-term treatment of insulin resistant (IR) essential hypertensives (EH) with nebivolol (N), a new highly selective β-blocker with nitric oxide modulating properties.

**Design and Methods:** Ten patients (aged 46.7±7.7 yrs, BMI 32.0±5.7) with conventional IR features were randomly selected from a group of newly verified never treated EH. Ambulatory BP (DP 5000A; Pulse Metric, Inc., USA), echocardiography, QL evaluation (General Well-Being Adjustment Scale) and metabolic tests (1 before and 2 h after routine TTG, lipids, uric acid, fibrinogen) were performed before and 4 weeks after 5 mg N o.d.

**Results:** BP and HR were significantly reduced (daytime DBP 91.0±4.5 vs. 79.0±6.0; nighttime DBP 76.1±6.4 vs. 69.1±8.1 mmHg; daytime HR 78.7±13.0 vs. 62.0±7.2; nighttime HR 62.6±6.1 vs. 54.4±4.8 bpm; p<0.01) without excessive nighttime falls and BP variability (SD) affecting. LV eject fraction was not changed, and LV compliance (E/A peaks ratio) tended to increase. The total QL score was improved (78.9±21.6 vs. 100.7±15.1 points, p<0.01) without any correlations with ambulatory BP parameters. No significant changes were revealed in the metabolic tests monitored.

**Conclusions:** N has demonstrated favorable short-term haemodynamics and cardiac effects without metabolic deterioration in IR EH, the positive QL changes making a basis for long-term evaluation, which should be performed further.

*Presented at the International Society of Hypertension 18th Scientific Meeting, 2000 (see Hypertension 2000 Vol 18, Suppl 4, pg. S167)

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2000-d

Fasting or Postload Insulin in Overweight Hypertensives: Which is Related to Ambulatory Blood Pressure and Myocardial Remodeling?

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**Objectives:** To assess whether and how hyperinsulinemia relate to ambulatory BP profile and left ventricular (LV) remodeling in essential hypertensives (EH).

**Design and Methods:** Twenty-four verified untreated overweight mild-to-moderate EH (13 males, 11 females; mean age 45.6 ±11.7 years; BMI 30.5 ±5.0 kg/m²; duration of hypertension 9.1 ±9.2 years) were undergone standard oral glucose tolerance test with fasting (FI) and two-hours postload (PI) serum insulin RIA measuring. Twenty-four hours ambulatory BP monitoring (Dynapulse 5000 A; Pulse Metric, Inc., USA) as well as conventional M- and B-mode echocardiography were performed.

**Results:** Patients from the top quartile of PI were more obese than the bottom quartile ones (BMI 35.5 ±3.1 vs. 28.4 ±2.4 kg/m²; p = 0.004) and had higher LV mass index (64.1 ±13.55 vs. 46.47 ±10.0 g/m²; p < 0.05). Significantly higher PI levels were observed in EH with LV concentric hypertrophy (n = 11) compared with normal LV geometry ones (n = 5) (579.3 ±309.3 vs. 236.5 ±190.1 pmol/l; p = 0.01) without any relationships between FI and LV remodeling type. No significant differences were revealed between the analyzed PI quartiles in daytime and nighttime SBP and DBP means, their SD, and BP loads. However, patients defined as non-dippers in accordance with DBP nightfall (n = 6) had higher PI level than dippers (n = 8) (598.1 ±280.3 vs. 317.5 ±125.7 pmol/l; p = 0.04). There was a tendency to higher daytime and nighttime HR in the top PI quartile compared with the bottom one (72.0 ±13.9 vs.62.5 ±7.7 and 63.8 ±12.6 vs. 55.5 ±6.6 bpm, NS, respectively).

**Conclusions:** In the investigated mild-to-moderate overweight EH high PI, but not FI levels are found in patients with LV concentric hypertrophy.

(Journal of Hypertension 2000; 18 (Suppl. 2): S126)
The Correlation of Arterial Blood Pressures and Compliance vs. Left-Ventricular (LV) Hypertrophy in Essential Hypertension

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We used a non-invasive ambulatory blood pressure monitoring (DynaPulse 5000A) and a new arterial pulse waveform analysis technology on 32 hypertensive and 25 normotensive subjects. 24 hour blood pressures, arterial compliance and peripheral resistance were obtained (analyzed by Pulse Metric, Inc. of USA). Their variations were compared with and correlated to the left ventricle (LV) weight index measured by ultrasound imaging technique. Results indicated that at matching age and sex, 24 hour averaged systolic, diastolic, mean arterial pressure and pulse pressure were higher in hypertensive group than in normotensive group and is significant (p<0.001). The hypertensive group has lower arterial compliance (0.110± 0.015 vs. 0.130± 0.014, P<0.01) and higher peripheral resistance (478.61± 76.74 vs. 431.31± 58.53, P<0.05) when compare to the normotensive group. Linear correlation analysis showed that 24 hour pulse pressure and systolic had a significant negative correlation (r1 = -0.7765, P<0.001, r2 = 0.5983, P<0.001). LV weight index had good correlation to the 24 hour pulse pressure and peripheral resistance (P<0.05), and to the arterial compliance (r = -0.3441, P<0.0852). The results of this study indicate that blood pressure increase, the changes of arterial structural and functional properties in hypertensive subjects, and the end-organ damage had direct and significant correlation, and 24 hour pulse pressure is a good indicator for it. Using non-invasive ambulatory blood pressure monitoring and new arterial pulse waveform analysis for arterial blood pressure, compliance and peripheral resistance may provide us early detection and guidance for correct treatment in hypertension management.

* Translation from Chinese abstract presented at the 11th Symposium on Cardiovasology of PLA, April 24-28, 1998, Shanghai, China (article in Chinese)

A New Technology to Determine Circadian Blood Pressure and Arterial Compliance Variations During Ambulatory Monitoring


OBJECTIVE: To derive simultaneous blood pressure (BP) and arterial compliance (C, ml/mmHg) measurements during a 24-hour period and evaluate changing hemodynamics in circadian BP regulation.

METHODS: 18 subjects, age 53± 3 years (9 treated hypertensives, 9 normotensives), underwent 24-hour ambulatory BP and C monitoring using the DynaPulse 5000A. Measurements were performed at 15 minute intervals during both day and night. The new noninvasive device utilizes a cuff sphygmomanometer to determine BP and C from analysis of the oscillometric pulsation signal. C measurements are derived at MAP (near-end systolic) in the cardiac cycle.

RESULTS: Average 24-hour blood pressure was 145/77 mmHg in hypertensives and 136/73 mmHg in normotensives. However, circadian BP variations had an inverse correlation with C in both groups. Interestingly, C had the strongest correlation with pulse pressure (PP) for each monitoring. The non-linear PP vs C relation was best fit by a power function with average correlation r = 0.78.

CONCLUSION: Results suggest that C and PP demonstrate a strong inverse non-linear relation. Therefore, circadian blood pressure regulation may be influenced by vascular function. Since hypertension may affect BP regulation, the ability to evaluate both BP and C should prove useful in both disease diagnosis and treatment.

*Presented at the Italian Society of Chronobiology Scientific Meetings, 1996
(7) Hypertension and women’s cardiovascular health – Studies on hemodynamics and pregnancy

2006/02

Homocysteine, circulating vascular cell adhesion molecule and carotid atherosclerosis in postmenopausal vegetarian women and omnivores

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Abstract: Since the adoption of vegetarian diets as a healthy lifestyle has become popular, the cardiovascular effects of long-term vegetarianism need to be explored. The present study aimed to compare the presence and severity of carotid atherosclerosis and 61 age-matched omnivores. Carotid atherosclerosis, as measured by ultrasound, was found to be of no significant difference between the two groups. Yet, fasting blood glucose, low-density lipoprotein cholesterol, and Vitamin B12 were significantly lower, while Hcy and sVCAM-1 were higher in the vegetarians as comparing with the omnivores. Multivariate regression analysis showed that the level of Vitamin B12 was negatively associated with the level of Hcy. Vegetarianism itself and Hcy level were significantly associated with sVCAM-1 level in univariate analysis; however, after adjustment for covariates, we identified age but not vegetarianism as the determinant of sVCAM-1 level. Multiple linear regression analysis identified age and systolic blood pressure, but not vegetarianism, as determinants of common carotid artery IMT. In conclusion, there was no significant difference in CA between apparently healthy postmenopausal vegetarians and omnivores. The findings of elevated Hcy in vegetarians indicate the importance of prevention of Vitamin B12 deficiency.

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2000/05-a

Relationship between Premenopausal Cardiovascular Risk & Brachial Artery Distensibility in Postmenopausal Women

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Previous studies have demonstrated that premenopausal women are at reduced risk for cardiovascular (CV) disease, in contrast to postmenopausal women. However, limited data is available on the relationship between early carotid atherosclerosis and CV risk factors in premenopausal women, and peripheral artery distensibility (DIST) post menopause. We evaluated 187 postmenopausal women (mean age 59) for brachial artery DIST using pulse dynamic calibrated arterial pressure waveforms obtained by a cuff sphygmomanometer. The method has been previously documented. Risk factors such as blood pressure, fasting insulin, 2-hour glucose tolerance, serum lipids, and alcohol intake were obtained prior to menopause. Presence of early carotid Atherosclerosis was determined using intima-medial thickness (IMT) and plaque index obtained by ultrasound. Univariate analysis demonstrated that higher DIST was associated with lower premenopausal SBP (r=-0.28, p=0.0001), 2-hour glucose tolerance (r=-0.20, p=0.005), fasting insulin (r=-0.16, p=0.03), and triglycerides (r=-0.15, p=0.03). Alcohol consumption demonstrated an interesting trend (r=0.14, p=0.06). Carotid artery IMT (r=-0.20, p<0.005) and plaque index (r=-0.18, p=0.013) also correlated significantly. A log transformation was used to approximate a normal
distribution for DIST. In multivariate linear regression, controlling for age, independent predictors of DIST were lower SBP (p<0.001), lower 2-hour glucose tolerance (p=0.040), and lower alcohol intake (p=0.043). When carotid IMT was added to the model, thicker walls were associated with lower DIST, and this was borderline significant (p=0.075). Thus, we conclude that in healthy middle-aged women, premenopausal values for SBP, 2-hour glucose tolerance, and alcohol consumption are associated with a degree of vascular DIST measured 8 years post menopause. Keywords: cardiovascular risk, menopause, arterial distensibility

* Presented at the American Society of Hypertension 15th Scientific Meeting, New York, May 2000

2001/05-b

**Carotid atherosclerosis and pulse dynamic blood pressure measurement in healthy postmenopausal women: A comparison between vegetarians and omnivores**

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*Departments of Internal Medicine, Neurology, Obstetrics and Gynecology, National Taiwan University, Taipei*

**Backgrounds and Objectives:** It is well known that vegetarians have less risk for atherosclerotic disease. However, few studies have been conducted to evaluate the arterial structure and function between vegetarians and omnivores. This study was designed to estimate whether arterial structure and function variables are better in healthy postmenopausal vegetarians than matched omnivores.

**Design and Methods:** Noninvasive measurements of blood pressure (BP) using pulse dynamics method (DynaPulse 2000), carotid ultrasonography, and cardiovascular (CV) risk factors were carried out in 31 healthy (without any known major CV risks) postmenopausal vegetarians and 31 matched omnivores. Vegetarians are defined as on vegetarian diets that exclude meat, fish, and poultry for at least 5 years. Fasting blood glucose, lipids, lipoprotein (a), CRP, folate and Vitamin B12 were also measured.

**Results:** Levels of fasting blood glucose, low-density lipoprotein cholesterol (LDL), and lipoprotein (a) were found to be significant lower in vegetarians. Compared with omnivores, carotid atherosclerosis indexes were only better in trend in vegetarians. In addition, there were no differences found in the indexes of carotid arterial stiffness. However, indexes of arterial function evaluation by DynaPulse revealed that brachial resistance, compliance, and systemic vascular compliance were better in vegetarians. After adjustment for age, pulse pressure, systolic BP, glucose, LDL, and lipoprotein (a), the differences of indexes of arterial function still exist.

**Conclusions:** Vegetarians had better arterial function assessed by pulse metrics method than matched omnivores. These may suggest noninvasive blood pressure measurement using DynaPulse may be rationally and appropriately used in clinical practice.

*Presented at the Taiwan Heart Association Conference, May 2001

1998/10

**A New Technique to Evaluate Arterial Compliance Changes During Pregnancy**

TJ Brinton, SS Chio, ED Walls, D Cunningham, and EB Grossman.

Pulse Metric, Inc., San Diego, CA USA and University of Rochester, Rochester, NY USA.

**Objective:** The development of a new technique to evaluate arterial compliance (ArtC) changes during the course of pregnancy.

**Methodology:** We previously developed and validated a non-invasive method to evaluate blood pressure (BP) and brachial artery compliance (ArtC) using a cuff sphygmomanometer. (Brinton et al, Amer J Cardiol, 1997). To evaluate potential changes in BP and ArtC during pregnancy, 15 pregnant women underwent study at 14, 24, 28, 32, and 36 weeks using the new method in an ambulatory device. Each 24 hour ambulatory monitoring session consisted of 30-40 determinations of BP and ArtC. Average BP and ArtC were determined for each 24 hour monitoring session.
**Results:** ArtC decreased significantly at 28 weeks and remained low thereafter. SBP was significantly increased at 36 weeks, though a trend toward an increase at 28 weeks appeared to correlate with the decrease in ArtC. DBP did not change.

**Conclusions:** ArtC decreases in the middle of pregnancy, and the changes proceed or possibly coincide with the increase in SBP. The results demonstrate the feasibility of using this non-invasive ambulatory technique for monitoring ArtC during pregnancy and therefore should be useful in studying potential ArtC alterations during preeclampsia.

* 11th World Congress of International Society for Study of Hypertension in Pregnancy, ISSHP, Meeting presentation, Oct. 1998, Kobe, Japan

1998/04

**Brachial Artery Compliance Decreases During Pregnancy**


Arterial compliance (ArtC) may be altered by long-standing hypertension, atherosclerosis, antihypertensive therapy, and genetic predisposition. Pregnancy is a state of great hemodynamic flux, with increased blood volume and changing blood pressure (BP). A recent invasive study (Pappos et al. Circulation, 1997) demonstrated that ArtC is higher during pregnancy than following delivery, but no variation in ArtC was noted during pregnancy possibly because there were only three determinations of ArtC. We utilized a new, non-invasive, oscillometric method which has been validated (Brinton, et al, Amer J Cardiol, 1997) to measure brachial ArtC in 15 pregnant women at 14, 24, 28, 32, and 36 weeks. An ambulatory BP device recorded 30-40 determinations of BP and ArtC during each 24 hour monitoring session. None of the women developed preeclampsia.

<table>
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</tr>
</tbody>
</table>

Values are Mean± SEM, * p < 0.05 vs. 14 wk

ArtC decreased significantly at 28 wk and remained low thereafter. SBP increased significantly at 36 wk, though there appeared to be a trend toward an increase at 28 wk, coinciding with the decrease in ArtC. DBP did not change. We conclude that brachial ArtC decreases in the middle of pregnancy, and these changes precede, or possibly occur contemporaneously with, the increase in SBP. Further, the results demonstrate the feasibility of using this non-invasive method for monitoring ArtC during pregnancy, and should be useful in studying ArtC during preeclampsia.

(Am. J. Hypertension April, 1998; 11: 184A.)

**************************************************

**Brachial Artery Compliance Decreases During Pregnancy**


Arterial compliance (ArtC) may be altered by long-standing hypertension, atherosclerosis, antihypertensive therapy, and genetic predisposition. Pregnancy is a state of great hemodynamic flux, with increased blood volume and changing blood pressure (BP). A recent invasive study (Pappos et al. Circulation, 1997) demonstrated that ArtC is higher during pregnancy than following delivery, but no variation in ArtC was noted during pregnancy possibly because there were only three determinations of ArtC. We utilized a new, non-invasive, oscillometric method which has been validated (Brinton, et al, Amer J Cardiol, 1997) to measure brachial ArtC in 15 pregnant women at 14, 24, 28, 32, and 36 weeks. An ambulatory BP device recorded 30-40 determinations of BP and ArtC during each 24 hour monitoring session. None of the women developed preeclampsia.

<table>
<thead>
<tr>
<th>Week</th>
<th>14</th>
<th>24</th>
<th>28</th>
<th>32</th>
<th>36</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>122±3</td>
<td>122±3</td>
<td>126±3</td>
<td>125±3</td>
<td>130±3*</td>
</tr>
<tr>
<td>DBP</td>
<td>66±2</td>
<td>65±2</td>
<td>66±3</td>
<td>65±1</td>
<td>70±2</td>
</tr>
<tr>
<td>ArtC</td>
<td>0.112±0.005</td>
<td>0.110±0.005</td>
<td>0.099±0.005*</td>
<td>0.102±0.005*</td>
<td>0.099±0.005*</td>
</tr>
</tbody>
</table>

Values are Mean± SEM, * p < 0.05 vs. 14 wk

ArtC decreased significantly at 28 wk and remained low thereafter. SBP increased significantly at 36 wk, though there appeared to be a trend toward an increase at 28 wk, coinciding with the decrease in ArtC. DBP did not change. We conclude that brachial ArtC decreases in the middle of pregnancy, and these changes precede, or possibly occur contemporaneously with, the increase in SBP. Further, the results demonstrate the feasibility of using this non-invasive method for monitoring ArtC during pregnancy, and should be useful in studying ArtC during preeclampsia.

(Am. J. Hypertension April, 1998; 11: 184A.)

**************************************************
(8) Pulse Dynamics R&D – The development of DynaPulse blood pressure and hemodynamic monitoring technique and clinical validation studies

2007*
Development and Validation of a Non-invasive Method to Estimate Cardiac Output Using Cuff Sphygmomanometry

Shiu-Shin Chio, PhD*, Jeffrey J. Tsai, MS, Yen-Ming Hsu, MS, Jeffery C. LaPointe, BS
Pulse Metric, Inc., San Diego, CA
Thao Huynh-Covey, RDAS, Oi Ling B. Kwan, RDAS, Anthony N. DeMaria, MD, FACC
UC San Diego Medical Center Hillcrest, San Diego, CA

ABSTRACT: Hemodynamic based approaches to hypertension management improve blood pressure control over routine care. A new technology was developed which estimates cardiac output using pulse-waveform-analysis (PWA) of a brachial artery cuff sphygmomanometry. This study evaluates the ability of PWA to track changes in CO by Doppler ultrasound during dobutamine-stress-echocardiography. A total of 207 PWA and Doppler measurements were taken during dobutamine stress on 44 patients. Linear regression analysis revealed good intra-patient correlation (r=0.69 to 0.98, p<0.05) with an overall correlation (r=0.82, p<0.001). This approach should be useful for monitoring CO changes in hypertensive and cardiac patients during routine blood pressure measurement.

Background: Obtaining cardiac output (CO) measurements non-invasively during routine blood pressure recording can improve hypertension management. A new method has been developed that estimates cardiac output using pulse-waveform-analysis (PWA) from a brachial cuff sphygmomanometer. This study evaluates the ability of PWA to track changes in CO as derived by Doppler ultrasound during dobutamine stimulation.

Hypothesis: This study aimed to validate the PWA CO estimation over a wide CO range as would be obtained by dobutamine stimulation during Doppler ultrasound evaluation.

Method: 48 patients undergoing standard dobutamine stress echocardiography testing for accepted clinical indications were enrolled. Among them, 44 patients (age 36-83, 18 females, 26 males) with good waveform data for analyses provided estimates of CO in this study. Noninvasive measurements of CO were performed using both Doppler ultrasound recordings and PWA techniques simultaneously at each stage of dobutamine infusion.

Results: A total of 207 simultaneous pulse-waveform-analyses and Doppler measurements were taken during dobutamine stress on 44 cardiac patients. Linear regression analysis revealed good intra-patient correlation between pulse-waveform-analysis and Doppler at different dobutamine induced CO with coefficients from r=0.69 to 0.98 (p<0.05). Analysis of all patients yielded an overall correlation of r=0.82 (p<0.001, bias = 0.4 L/min, standard deviation =1.8 L/min).

Conclusion: CO measured non-invasively from a sphygmomanometer using this PWA method correlate well with those of Doppler through a range of dobutamine-stimulated levels. CO by PWA should be useful for monitoring hemodynamic changes in hypertensive and cardiac patients during routine blood pressure measurement.

(*Accepted by Clinical Cardiology, to be published in 2008)

2007/05-a
Behavior of Brachial Artery Distensibility (BAD) and Resistance (BAR) in Relation to LV dP/dt max

Michael Gutkin, Torres Minerva, Kassalow Nathan, Schultz Delray Medicine, Saint Barnabas Medical Cntr, Livingston, NJ; Mathematics, Millersville University, Millersville, PA

The Chio method (Am J Cardiol 1997;80:323) determines dP/dt max by a method independent of measurement of systolic and diastolic blood pressure (SBP, DBP). Is there information to be gained by
using dp/dt max as a determinant of BAD and BAR?

We examined correlates of BAD and BAR with dp/dt max, SBP, and DBP by Chio’s arterial plethysmography method (PM) in 60 normotensives (NT, 50yr 129/74) and 43 untreated hypertensives (HT, 55yr, 155/87). ("r" = Pearson’s *p < .05 **p < .01 ***p < .001). (Table)

In 6 treated hypertensives, 63±14 yr, BP 145±12/83±9, we measured falls in dp/dt max, BAD, and BAR before, and 2, 4, 8, and 16 min after 0.4 NTG subling, normalizing all values as % δ from baseline. The resulting correlations could not be assigned "p" values because of lack of independence of the 23 observations. % δdp/dt max showed better correlation with % δBAD (-.67) and % δBAR (.82) than did % δSBP with % δBAD (-.52) and % δBAR (.20).

BAD improved as dp/dt max fell, but not more than expected from the regression relation. These observations suggest the following hypotheses:
1) In HT, but not NT, arterioles constrict or dilate in response to changes in dp/dt max to regulate distal tissue flow in the brachial circuit. Changes in BAD in the NT range are due to variations in SBP, but not arteriolar damping.
2) In the HT range, BAD is an expression of both SBP and distal damping.
3) In HT given NTG, falls in dp/dt max appear to predict reductions in BAR better than do falls in SBP.
4) The brachial artery recruits tensile elements as it relaxes after NTG.

Conclusion: dp/dt max can be used to index BAD in HT and NT, and BAR in HT, but appears superior to SBP in estimating BAR after NTG in HT.

<table>
<thead>
<tr>
<th></th>
<th>dp/dt max</th>
<th>SBP</th>
<th>DBP</th>
<th>BAD 60 NT</th>
<th>BAD 43 NT</th>
<th>BAR 60 NT</th>
<th>BAR 43 HT</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAD vs.</td>
<td>-.78***</td>
<td>-75***</td>
<td>-.22*</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>dp/dt max vs.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-.65***</td>
<td>-.83***</td>
<td>.01</td>
<td>.39**</td>
</tr>
<tr>
<td>SBP vs.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-.66***</td>
<td>-.71***</td>
<td>-.04</td>
<td>.37*</td>
</tr>
</tbody>
</table>

2007/05-b

**Does Plethysmographic Measurement (PM) of Cardiac Output (CO) Yield Appropriate Values?**

Michael Gutkin, Torres Minerva, Kassalow Nathan, Schultz Delray Medicine, St. Barnabas Medical Center, Livingston, NJ; Mathematics, Millersville University, Millersville, PA

PM uses body surface area (BSA) as a component of estimating stroke volume (SV). To test whether PM CO is a tautologic expression of BSA and heart rate (HR) in normals (nls) we indexed CO to O2 consumption (VO2), using a metabolic cart, by Chio's PM (Am J Cardiol 1997;80:323) and CO2 re-breathing (CO2 RB); the latter does not employ BSA for its results.

The slopes of regression lines of CO v. VO2 were not different (p = .289) for PM (y = .0161 x + 1.4) r = 0.69+ or CO2 RB (y = 0.0198 x + .99), r = 0.56. For VO2 v BSA, r = 0.69 (PM) and r = 0.71 (CO2 RB). We measured triplicate PM CO before and 16 minutes post 0.4mg NTG subling in treated hypertensives (ARB + other meds), age 63±10, BP 145±12/83,9.

Stroke volume fell from 86±16ml pre to 78±10ml post (p = .04), without a change in heart rate (58±10 pre, 61±8 post, p = 0.292).

Conclusion: In lean normals, BSA does not unduly prejudice PM CO, partly as BSA correlates well with VO2. PM CO, which employs BSA in its formula, correlates as well with VO2 as CO2 RB, which does not employ BSA. PM SV responds approximately to NTG, in the absence of a change in HR.
### 2002/05

**Changes on Brachial Artery Distensibility (BAD) and Systemic Vascular Resistance (SVR) Over Aging of Normal Population**

Qiying Xie, Amparo S. Ng, Sen Lin-Liu, Jeffrey J. Tsai, Shiu-Shin Chio. Pulse Metric, Inc. San Diego

Evaluation of population based trends in Brachial Artery Distensibility (BAD) and Systemic Vascular Resistance (SVR) over aging was conducted. The BAD and SVR changes are genetic, lifestyle, and diet dependent. Abnormality of these hemodynamic parameters is one of the primary indicators of cardiovascular disease and could be used for the clinical assessment of cardiac and arterial physiological conditions. Pulse Dynamics is a clinically validated non-invasive method to obtain hemodynamic measurements such as SBP, DBP, MAP, Pulse Pressure (PP), Heart Rate (HR), Cardiac Output (CO), BAD, and SVR by analysis of the oscillometric waveform of a cuff sphygmomanometer. Global data of above from normal population has been pooled together for BAD and SVR trending analysis. The trended association information between BAD and SVR among normotensive (NT) vs. age and gender had not been previously described on the population bases. Accumulative 8578 normal subjects were checked by Pulse Dynamics method in order to find the blood pressure status and the association along with aging by gender. Among all, there are 5410 Females and 3168 Males, age from 18 to 92, and 22.7% are hypertensive. NT was defined as SBP<140 and DBP<90. BAD declines along with SVR increases observed among 6628 NT (F=4374, M=2254) represent the aging process. But higher declining rate is found in female compare to male. BAD decreases as SVR increases along with aging in both gender. Female has overall faster rate change. Mid 40s of both groups showed the turning points and leveled after

*Presented at the American Society of Hypertension 17th Annual Scientific Meetings, New York, 2002*

### 2002/04

**A New Method of Non-invasive Determination of Cardiac Output by DynaPulse: Comparison with Direct FICK Method and Doppler Echocardiography**

Xi Guorong, Li Tiande, Zhi Guang et al.
General Hospital of PLA, Beijing China

Abstract: DynaPulse, a newly developed non-invasive apparatus, is a valuable in assessing blood pressure, cardiac output and vascular compliance. The purpose of the present study was to evaluate the validity of
cardiac output measurement using DynaPulse (CO_DP) and Doppler echocardiography (CO_DE), (47 subjects, 32 male and 15 female, age 16 to 73), and cardiac output was measured with DynaPulse and FICK method (CO_FM) in additional 26 patients (20 male and 6 female, age 37 to 73). A good correlation was found between CO_DP and CO_DE (r = 0.76 p<0.001). There was an acceptable correlation between CO_DP and CO_FM (r = 0.61, p = 0.001). DynaPulse can provide a noninvasive, clinically useful estimation of cardiac output.

2001/09

**Assessment of Cardiac Output by Brachial Artery Pulse Wave Analysis Cuff Sphygmomanometry: Comparison with Doppler Values During Dobutamine Infusion**

Jeffrey J. Tsai; Tim Frandsen; Mary Ann Kelley; Amparo S. Ng; Yen-ming Hsu; Thao Huynh-Covey; Monet Strachan; Oi Ling B. Kwan; Neil Sawhney; Shiu-Shin Chio; Anthony DeMaria

1 Pulse Metric, Inc., San Diego, CA & 2 UC San Diego Medical Center, San Diego, CA

A new technology has recently been developed which records a brachial artery pressure waveform from a cuff sphygmomanometer and estimates cardiac output using proprietary pulse waveform analysis (PWA) algorithms. The purpose of this study was to evaluate the ability of PWA to track changes in CO as derived by Doppler ultrasound methods during dobutamine stress echocardiography (DSE). The PWA method analyzes the pressure waveform using proprietary curve-fitting algorithms and a model based on the rate of pressure changes (dP/dt), heart rate, and empirically derived scaling factors to obtain CO. An oscillometric NIBP and hemodynamic monitor (DynaPulse 200M, Pulse Metric, Inc., San Diego, CA) was used to acquire the arterial pressure waveform. Doppler measures of CO were derived as the product of the systolic flow velocity integral and the cross-sectional area (as \( \pi \times \text{diameter}^2/4 \)) of the LV outflow tract from apical views. Ninety-four simultaneous PWA and Doppler measurements were taken at each stage of dobutamine stress on 13 cardiac patients (ages 36-82, 6 females, 7 males). Patients were excluded for severe arrhythmias, extreme obesity, or not completing the protocol. Linear regression analysis revealed good intra-patient correlation between PWA and Doppler at different dobutamine induced CO’s, with coefficients from r = 0.69 to 0.98 (p < 0.05). Analysis of all patients yielded an overall correlation of r = 0.87 (p < 0.001) (Figure). Analysis of overall bias was 0.08 L/min with a precision of 1.98 L/min. Thus, CO measures from a sphygmomanometer using this PWA method correlate well with those of Doppler through a range of dobutamine stimulated levels. This approach should be useful for monitoring hemodynamic changes in cardiac patients by home blood pressure measurement.
Evaluation of A 24-hour Ambulatory Blood Pressure Monitoring Device

Lin CW, Luo TC, Chiu SR, and Tseng YZ
Institute of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University

Abstract -- This report focuses on the comparisons between two currently available standards (AAMI vs BHS) for the validation of 24-hour ambulatory blood pressure monitoring devices. Part of the validation procedures was then applied to the evaluation of a commercial unit (DynaPulse 5000A, Pulse Metric, Inc.). Result supports the clinical accuracy and usefulness of DynaPulse 5000A ABPM, and met the current standards, and its derived hemodynamic parameters were also been evaluated, and concluded of potential clinical values to better diagnosis and treatments of hypertension.

(Article in Chinese, published at Taiwan Univ. Collage of Medicine and Engineering J., 2001)

Comparison of Normal Ranges for Pulse Dynamic Hemodynamic Parameters Between U.S. and Chinese Population

Q Xie, JJ Tsai, AS Ng, BL Tang, TJ Brinton, and SS Chio. Pulse Metric, Inc., San Diego, CA.

Cardiovascular aging and abnormalities are genetic, lifestyle, diet dependent. Abnormal hemodynamic parameters are one of the primary indicators of cardiovascular disease and can be used for the clinical assessment of cardiac and arterial physiological conditions. Observation of changes to these indicators would provide an essential tool in cardiovascular risk assessment and disease management. Establishment of reference levels based on large scale studies of different ethnic groups would offer crucial baseline values for disease evaluation and management. Pulse Dynamics is a clinically validated non-invasive method to obtain hemodynamic measurements such as SBP, DBP, MAP, Pulse Pressure (PP), Heart Rate (HR), Cardiac Output (CO), and compliance by analysis of the oscillometric waveform of a cuff sphygmomanometer. Comparisons of normal ranges were made between a U.S. population sample (n = 2,464) of varying race and a Chinese population sample (n = 1,379). Both had age ranges from 18 to 80 years. Three successive measurements were recorded using DynaPulse monitors (Pulse Metric, Inc., San Diego) and averaged for each patient. Statistical analyses were made to the samples respectively based on genders and blood pressure status. Normotensive (NT) was defined as SBP<140 and DBP<90 (1,976 U.S., 994 Chinese). Differences and similarities of the measurement readings between the two population samples were compared and examined by Student’s t-test on means adjusted by age. Normal ranges of the parameters (mean ± 2 SD) for U.S. and Chinese populations are:

| Parameter | US (n = 1,976) | | | ASIA (n = 994) | | |
|-----------|----------------|----------------|----------------|----------------|----------------|
|           | Female (1,277) | Male (699)     | Female (505)   | Male (489)     |                |
|           | Mean | SD | normal range | Mean | SD | normal range | Mean | SD | normal range | Mean | SD | normal range |
| SBP (mmHg) | 118.0 | 10.86 | 96-140 | 123.90 | 9.32 | 105-142 | 120 | 12 | 95.9-139.2 | 123 | 10 | 105.3-142.6 |
| DBP (mmHg) | 66.1 | 6.98 | 52-80 | 68.53 | 7.42 | 53.7-83.4 | 68 | 8 | 52-79.9 | 70 | 8 | 53.7-83.3 |
| MAP (mmHg) | 82.6 | 7.69 | 67-98 | 85.32 | 7.61 | 70-100 | 85 | 9 | 67-97.8 | 87 | 8 | 70-100 |
| PP (mmHg)  | 52.0 | 8.53 | 35-69 | 55.38 | 8.08 | 39-72 | 52 | 8 | 34.7-68.6 | 52 | 8 | 39.1-71.7 |
| HR (BPM)   | 71.0 | 11.41 | 48-93 | 67.08 | 10.09 | 47-87 | 73 | 11 | 49-94.1 | 71 | 11 | 47-88 |
| CO (l/min) | 4.4 | 0.40 | 3.5-5.18 | 5.08 | 0.55 | 3.9-6.18 | 4.05 | 0.27 | 3.5-5.0 | 4.65 | 0.45 | 3.9-6.1 |

Results show that for normotensive population samples, Chinese male have significant elevation in means of SBP, DBP, MAP and HR against US population, while Chinese female showed significant lower in mean CO at the early age (<40). From middle age (40) to young elderly (65), such trends both for male and
female continued except that the lowered mean of CO is observed among Chinese male. Finally, elderly (>65) Chinese population remained lower mean of CO in both gender but significant higher in mean of SBP, DBP, MAP, and PP, in comparison with US population. Keywords: hemodynamic, population norm

* Presented at the Tenth Conference on Health Problems Related to the Chinese in North America, San Francisco, July 2000

2000/05

Establishment of Normal Ranges for Pulse Dynamic Arterial Compliance and Distensibility

JJ Tsai, AS Ng, BL Tang, Q Xie, TJ Brinton, and SS Chio. Pulse Metric, Inc., San Diego, CA.

Pulse Dynamic brachial artery compliance (C) and distensibility (D) are measures of arterial stiffness and may be used in risk assessment for cardiovascular disease. Determination of population norms for C and D from large-scale epidemiological studies are essential to establish reference values for clinical applications. Pulse Dynamics is a non-invasive method to obtain SBP, DBP, MAP, C, and D by analysis of the oscillometric waveform of a cuff sphygmomanometer. This methodology has been previously validated against invasive measurements. A sample size of 2,464 subjects (1,542 females, 922 males) of varying race and age (>18 yrs) was randomly collected from a large U.S. population-based cohort. Three successive measurements were recorded using DynaPulse 2000A monitors (Pulse Metric, Inc., San Diego) and averaged for each patient. D was defined as C divided by arterial volume \((dV/dP)/V\) or the percentage change in volume per mmHg change in pressure. Brachial artery diameter for the reference volume was estimated using an empirically derived model based on gender, height, weight, and MAP, and validated using B-Mode ultrasound \((n = 1,250, r = 0.63, P < 0.05)\). Patient data from the normotensive (NT, SBP<140 and DBP<90) population \((n = 1,976)\) was used to establish measurement norms. Normal ranges (mean ± 2 SD), for females (F) and males (M) are:

<table>
<thead>
<tr>
<th>Female ((n = 1,277))</th>
<th>Male ((n = 699))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C</strong></td>
<td><strong>D</strong></td>
</tr>
<tr>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>0.056</td>
<td>0.012</td>
</tr>
<tr>
<td>6.36</td>
<td>1.38</td>
</tr>
</tbody>
</table>

C differed significantly between F and M \((P < 0.005)\) however D did not \((P = 0.74)\). In F, C decreased from 0.056 to 0.044 and D from 6.36 to 4.28 when compared to HT \((n = 265, P < 0.0001)\). In M, C decreased from 0.089 to 0.078 and D from 6.33 to 4.76 \((n = 223, P < 0.0001)\). These values for C and D establish measurement norms for clinical use as a pre-screening reference for patients at risk of cardiovascular disease. Keywords: arterial compliance, distensibility, population norm

* Presented at the American Society of Hypertension 15th Scientific Meeting, New York, May 2000

1998-a

Validation of pulse dynamic blood pressure measurement by auscultation

Todd J. Brinton, E. Daniel Walls and Shiu-Shin Chio

Background The accurate measurement of arterial blood pressure is essential for the diagnosis and treatment of hypertension. The development of new automated methods of measurement that provide reliable determinations of blood pressure should be valuable in the assessment of hypertension not only in the clinic or hospital but also in the home for self-monitoring.

Design We evaluated a noninvasive method for the measurement of systolic and diastolic blood pressures in 132 subjects.

Methods Measurements obtained using the pulse dynamic method of blood pressure determination were validated with simultaneous manual measurements. Two qualified nurses used Korotkoff sounds to
determine systolic (phase I) and diastolic (phase IV) blood pressures according to the Association for the Advancement of Medical Instrumentation 1987 guidelines.

**Results** Inter-nurse variability was 2.7 ± 4.1 mmHg (mean ± SD) for systolic blood pressure and 4.0 ± 3.7 mmHg for diastolic blood pressure and correlations were r = 0.98 and 0.94, respectively. We observed excellent agreement between auscultatory and pulse dynamic methods for systolic (127 ± 21 versus 132 ± 20 mmHg; r =0.97) and diastolic (72 ± 10 versus 71 ± 10 mmHg; r = 0.89) blood pressures. Bland-Altman analysis demonstrated that there was a mean difference (reference-device) between the two methods of -5 mmHg (pulse dynamic value higher) and SD of 5 mmHg for systolic blood pressure and a mean difference of 1 mmHg (pulse dynamic value lower) and SD of 5 mmHg for diastolic blood pressure.

**Conclusion** The results of this study demonstrate that this noninvasive method of measurement of blood pressure is accurate and reliable and should therefore be appropriate for the evaluation of hypertension both in the home and in clinical settings.


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1998-b

**Age-based differences between mercury sphygmomanometer and pulse dynamic blood pressure measurements**

Todd J. Brinton, E. Daniel Walls, Alay K. Yajnik and Shiu-Shin Chio

**Background** Both the mercury sphygmomanometer and oscillometric measurement methods are widely in use for pediatric, adult, and geriatric patients. However, inherent differences between the methods of measurement may create varying degrees of sensitivity to age and potentially result in differences between measurements for these two techniques.

**Design** Measurements of systolic and diastolic blood pressures in 154 subjects were obtained using the mercury sphygmomanometer and pulse dynamic oscillometric methods in accordance with the 1987 Association for the Advancement of Medical Instrumentation guidelines. Subjects were separated into three age groups and their data analyzed for differences between measurements for these two techniques.

**Methods** Two qualified nurses derived systolic and diastolic blood pressures using phase I and phase IV Korotkoff sounds, respectively, during simultaneous monitoring with the pulse dynamic oscillometric method.

**Results** Inter-nurse variabilities for measurements derived by mercury sphygmomanometer were 1.8 ± 4.1 for systolic and 0.9 ± 3.9 for diastolic blood pressure. Mean differences (reference - device) of -5 ± 5 mmHg (pulse dynamic value higher) for systolic and 1 ± 5 mmHg (pulse dynamic value lower) for diastolic blood pressure between pulse dynamic and mercury sphygmomanometer values were found for all subjects. However, pulse dynamic systolic blood pressure was significantly higher than mercury sphygmomanometer systolic blood pressure for group 1 (n = 51, aged 11-22 years, mean difference -5.6 mmHg, P= 0.03). A similar trend was observed with group 2 (n = 51, aged 23-54 years, mean difference -4.3 mmHg, P=0.06). We observed no significant difference for systolic blood pressure with group 3 (n =52, aged 55-85 years, mean difference -3.8 mmHg, P > 0.1). For all three groups we found no significant difference for diastolic blood pressure.

**Conclusion** The variation in the agreement of systolic blood pressure measurements can be attributed to the differing effects of age-dependent arterial changes on the measurement methods. The findings indicate that, although the pulse dynamic oscillometric method and mercury sphygmomanometer correlate well when agreement between measurements of systolic blood pressure is dependent on age and the method of measurement employed.


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1998

**Suprasystolic dP/dt max an additional parameter of contractile cardiac function obtained by cuff oscillometric tracing**
Technological evolution allowed to record high fidelity traces that—when analyzed by complex mathematical systems—may provide extremely detailed and new information about all the factors involved in the determinism of pulse wave. Suprasystolic waves, i.e. those recorded immediately before systolic pressure, may be regarded as similar to aortic pressure waves evaluated during cardiac catheterization. Suprasystolic dP/dt max was calculated from the profile of pulse wave recorded by the DynaPulse, an automatic portable non-invasive oscillometric method to simultaneously measure BP and analyze arterial waveforms, in 10 normal healthy subjects (age 37 +/- 5) and 5 subjects with ischaemic dilatative cardiomyopathy (age 41 +/- 7) whose ejection fraction—invasively assessed—was < 40%. The 24 h dP/dt max curves were analyzed by parametric and non parametric tests. We found a significant difference (p < 0.001) in the average 24-h dP/dt max between healthy subjects (471 +/- 36.7 mmHg/sec) and patients with impaired cardiac function (271 +/- 54.2 mmHg/sec). The average daytime and nighttime dP/dt max values showed significantly higher values in normal subject in comparison to patients with heart failure (daytime 7.23 h: 529 +/- 74 mmHg/s versus 227 +/- 64 mmHg/s, p < 0.001; nighttime: 572 +/- 82 mmHg/s versus 202 +/- 67 mmHg/s, p < 0.001). We also found a difference in the occurrence of acrophases, at similar blood pressure value, i.e. the highest dP/dt values occurred during the night in normal subject, the opposite in ischaemic patients. Furthermore, the dP/dt max correlates only with systolic blood pressure.

Arch Mal Coeur Vaiss 1998; 91: 947-950

1997/08

**Development and Validation of a Noninvasive Method to Determine Arterial Pressure and Vascular Compliance**

Todd J. Brinton, BS, Bruno Cotter, MD, Mala T. Kailasam, MBBS, David L. Brown, MD, Shiu-Shin Chio, PhD, Daniel T. O’Connor, MD, and Anthony N. DeMaria, MD

The ability not only to record automated systolic and diastolic pressure, but also to derive measurements of the rate of pressure change during the cardiac cycle, would have great potential clinical value. A new method has been developed to obtain pressure measurements at 20-ms intervals by oscillometric cuff signal pattern recognition. Derivation of noninvasive pressure measurements is based on a T tube aorta and straight tube brachial artery, and assumes that the systolic phase of the suprasystolic cuff signal and the diastolic phase of the subdiastolic cuff signal most closely approximate systolic and diastolic aortic pressures, respectively. Arterial pressures obtained by this method were compared with simultaneous invasive measurements from the thoracic aorta in 36 patients. Good agreement was observed between noninvasive and invasive methods for systolic (146 ± 4 vs 145 ± 5 mm Hg), diastolic (80 ± 2 vs 77 ± 2 mmHg), and mean (100 ± 3 vs 100 ± 3 mmHg) arterial pressures, and correlation coefficients were r = 0.94, 0.91, and 0.95, respectively. To assess the validity of measurements of the rate of pressure change, oscillometric cuff signals from a subgroup of 14 patients were analyzed in detail for the peak positive pressure derivative (dP/dtmax), peak negative pressure derivative (dP/dtmin), and time interval between peak positive and peak negative pressure derivatives \(t_{pp}\). Results (mean ± SEM) were:

<table>
<thead>
<tr>
<th>Method</th>
<th>dP/dtmax</th>
<th>dP/dtmin</th>
<th>(t_{pp})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noninvasive</td>
<td>600 ± 41</td>
<td>-466 ± 36</td>
<td>0.25 ± 0.01</td>
</tr>
<tr>
<td>Invasive</td>
<td>508 ± 37</td>
<td>-377 ± 24</td>
<td>0.25 ± 0.01</td>
</tr>
<tr>
<td>r (linear regression)</td>
<td>0.87</td>
<td>0.68</td>
<td>0.85</td>
</tr>
</tbody>
</table>

The incorporation of measurements of the rate of pressure change into a physical model of the brachial artery was used to derive vascular compliance. A significant correlation was observed between vascular compliance derived from the oscillometric signal and determinations by either thermodilution or Fick methods and noninvasive pressures \(n = 20, r = 0.83, p < 0.001\). Day-to-day variability for blood pressure and vascular compliance derived by the noninvasive method did not differ by >4%, representing a reproducible measure of vascular structure and function. We conclude that the measurement of absolute
pressure and rate of pressure change show good correlation with catheter data and that vascular compliance can be reliably assessed by this new method. The technology should provide a valuable noninvasive tool for the assessment of both cardiac function and vascular properties.  

(Am J Cardiol 1997;80:323-330)

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1997/05

The Development and Validation of a New Non-Invasive Method to Evaluate Ventriole Function During Routine Blood Pressure Monitoring

TJ Brinton*, WC Hu, SS Chio, CP Liu. Pulse Metric, Inc. San Diego, CA, USA and Veterans General Hospital-Kaohsiung, Taiwan, ROC

We previously developed and validated a non-invasive (NI) technique to derive the aortic pressure signal using a cuff sphygmomanometer. We have now developed a new method to derive maximum left ventricle dP/dt (dP/dt\text{LV}_{\text{max}}) from the aortic pressure signal assuming gaussian curves for both aortic and left ventricle wave contours. We validated NI end systolic pressure (ESP) and dP/dt\text{LV}_{\text{max}} obtained utilizing this new method with simultaneous measurements from an invasive (INV) micromanometer tipped catheter in twenty-two patients with myocardial infarction (MI) and eleven normal subjects. NI and INV ESP measurements had a good correlation (142±17 vs. 133±16 mmHg, r = 0.91). NI and INV dP/dt\text{LV}_{\text{max}} were also in accordance (1097±232 vs. 1279±241 mmHg/sec, r = 0.75). To test the consistency of the NI measurement, we assessed dP/dt\text{LV}_{\text{max}} at four different heart rate levels in both groups (increment of 15 beats/level from sinus rate). A positive inotropic response was observed in normal subjects and the correlation between the methods was excellent (r = 0.94). Although the positive response of dP/dt\text{LV}_{\text{max}} was significantly blunted in MI patients (p < 0.05), the NI data showed a good correlation with INV data (r = 0.93). These results suggest that ventricle function may be assessed reliably in patients with cardiovascular disease using this new NI method. Due to the excellent correlation between the methods during dynamic conditions, the method should be clinically useful for evaluating changes in cardiac function during routine blood pressure monitoring.  

(Am J. Hypertension 1997; 10: 60A)

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1996/10-a

Arterial Compliance by Cuff Sphygmomanometer: Application to Hypertension and Early Changes in Subjects at Genetic Risk

Brinton TJ, Kailasam MT, Wu RA, Cervenka JH, Chio S-S, Parmer RJ, DeMaria AN, O’Connor DT; UCSD and VAMC, La Jolla, CA, and Pulse Metric, Inc., San Diego, CA.

Abnormalities of the arterial pulse waveform reflect changes in cardiovascular structure and function. These abnormalities may occur early in the course of essential hypertension, even before the onset of blood pressure elevation. Previous studies of cardiovascular structure and function have relied on invasive intra-arterial cannulation to obtain the arterial pulse wave. We evaluated arterial structure and function using a noninvasive cuff sphygmomanometer in hypertensive (n=5) and normotensive (n=36) subjects, stratified by genetic risk (family history) for hypertension. Using a simple physical model in which the aorta was assumed to be a T tube and the brachial artery a straight tube, we determined vascular compliance and peripheral resistance by analyzing the brachial artery pulsation signal from a cuff sphygmomanometer. Essential hypertensive subjects tended to have higher peripheral resistance (P=.06) and significantly lower vascular compliance (P=.001) than normotensive subjects. Vascular compliance correlated with simultaneously determined pulse pressure in both groups (n=51, r=.74, P<.0001). Higher peripheral resistance (P=.07) and lower vascular compliance (P=.04) were already found in still-normotensive offspring of hypertensive parents (ie, normotensive subjects with a positive family history of hypertension) than in normotensive subjects with a negative family history of hypertension. Multivariate analysis demonstrated that both genetic risk for hypertension (P=.030) and blood pressure status (P=.041), although
not age (P=.207) were significant predictors of vascular compliance (multiple R=.47, P=.011). However, by two-way ANOVA, genetic risk for hypertension was an even more significant determinant (F=7.84, P=.007) of compliance than blood pressure status (F=2.69, P=.089). Antihypertensive therapy with angiotensin-converting enzyme inhibitors (10 days, n=10) improved vascular compliance (P=.02) and reduced resistance (P=.003) significantly; treatment with calcium channel antagonists (4 weeks, n=8) tended to improve vascular compliance (P=.07) and significantly reduced peripheral resistance (P=.006). We conclude that arterial vascular compliance abnormalities detected by a noninvasive cuff sphygmomanometer reflect treatment-reversible changes in vascular structure and function. Early changes in vascular compliance in still-normotensive individuals at genetic risk for hypertension may be a heritable pathogenetic feature of this disorder.

(Hypertension, 1996 Vol 28, No.4, pp. 599-603.)

1996/10-b

A New Technology to Determine Circadian Blood Pressure and Arterial Compliance Variations During Ambulatory Monitoring


OBJECTIVE
To derive simultaneous blood pressure (BP) and arterial compliance (C, ml/mmHg) measurements during a 24-hour period and evaluate changing hemodynamics in circadian BP regulation.

METHODS
18 subjects, age 53± 3 years (9 treated hypertensives, 9 normotensives), underwent 24-hour ambulatory BP and C monitoring using the DynaPulse 5000A. Measurements were performed at 15 minute intervals during both day and night. The new noninvasive device utilizes a cuff sphygmomanometer to determine BP and C from analysis of the oscillometric pulsation signal. C measurements are derived at MAP (near-end systolic) in the cardiac cycle.

RESULTS
Average 24-hour blood pressure was 145/77 mmHg in hypertensives and 136/73 mmHg in normotensives. However, circadian BP variations had an inverse correlation with C in both groups. Interestingly, C had the strongest correlation with pulse pressure (PP) for each monitoring. The non-linear PP vs C relation was best fit by a power function with average correlation r = 0.78.

CONCLUSION
Results suggest that C and PP demonstrate a strong inverse non-linear relation. Therefore, circadian blood pressure regulation may be influenced by vascular function. Since hypertension may affect BP regulation, the ability to evaluate both BP and C should prove useful in both disease diagnosis and treatment.

*Presented at the Italian Society of Chronobiology Scientific Meetings, 1996

1996/08

Corresponding Pulse Pressure and Arterial Compliance Variations during Ambulatory Monitoring


Measurements of arterial compliance may provide clinically valuable information about the state of the cardiovascular system. These measurements may be useful in evaluating changes in the structural and functional components of the arterial wall. However, evaluation of arterial compliance measurements may be complicated by the dependent relationship with arterial blood pressure. Therefore, this study evaluates the relation between arterial compliance and blood pressure to better understand the time dependent control of blood pressure and the relation between arterial structure and function.
1996/05-a

**The Compliance Versus Pulse Pressure Relation: A Potential Indicator of Decreased Load Adaptations in Hypertension**


Since blood pressure may be influenced by changing hemodynamics, arterial compliance (C, ml/mmHg) may be a more reliable marker of underlying cardiovascular disease. However, C includes a functional (hemodynamic) component which may complicate measurement interpretation. We have previously reported a strong inverse correlation between C and pulse pressure (PP) during 24-hour ambulatory monitoring with the DynaPulse 5000A. Utilizing the same methodology, we evaluated 18 age and BMI matched patients [9 normotensive (NT) (24-hour, 127± 2/66± 2 mmHg), (mean± sem), 9 medicated hypertensives (HT) (24-hour, 140± 5/73± 2 mmHg)]. In order to evaluate C measurements independent of the functional component, the two groups were matched for hemodynamic measurements (132/70, MAP=88, PP=63). C measurements were significantly higher in the NT group (n = 431, 0.121± 0.002) versus the HT group (n=431, 0.108± 0.001, p<0.001). The C vs. PP correlation was best fit in both NT and HT by a power function (y = 5.69x^{0.940} vs. 1.15x^{0.584}). Although the functions were similar at high PP, the HT function diverged significantly at low PP suggesting a difference in load adaptation. The data suggests that since PP is a hemodynamic functional variant, the structural and functional components of compliance may be evaluated separately using the PP vs. C function derived by ambulatory monitoring. The evaluation of structural compliance independent of functional factors may be a more reliable screening tool for the early detection of hypertension and cardiovascular disease.

![Graph showing compliance vs. pulse pressure for normotensive and hypertensive groups.](image)

* Presented at the American Society of Hypertension 11th Annual Scientific Meetings, 1996.

1996/05-b

**Age Based Differences Between Oscillometric and Auscultatory Measurement Techniques**

Brinton TJ, Walls ED, Chio S-S, Pulse Metric, Inc., San Diego, CA.

Although both Auscultatory (AUSC) and oscillometric (OSC) measurement techniques have been examined extensively, the variability between these two methods with respect to age still needs further investigation. We evaluated 154 (50M/104F) subjects, ranging in age from 11 to 85 years (mean± SEM = 45± 1.6 years), for systolic (SBP, mmHg) and diastolic (DBP, mmHg) blood pressures using both
techniques. Two qualified nurses used Korotkoff sounds to determine SBP (phase 1) and DBP (phase IV) during simultaneous monitoring by a Pulse Dynamic OSC technology. This previously reported OSC technology utilizes phasic changes in the cuff pulsation signal to determine SBP and DBP. Values for each subject reflect the average of three recordings. Subjects were placed into one of three age groups: Group 1 (ages 11 to 32, n = 51), Group 2 (ages 33 to 54, n=51), Group 3 (ages 55 to 85, n=52) (TABLE). SBP was significantly lower in Group 1 using the AUSC method (p = 0.03).

<table>
<thead>
<tr>
<th>Age Group</th>
<th>AUSC</th>
<th>OSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (23 ± 0.7)</td>
<td>114± 1.8</td>
<td>119± 1.8</td>
</tr>
<tr>
<td>Group 2 (42 ± 0.8)</td>
<td>120± 1.6</td>
<td>124± 1.6</td>
</tr>
<tr>
<td>Group 3 (70 ± 1.1)</td>
<td>145± 2.7</td>
<td>148± 2.6</td>
</tr>
</tbody>
</table>

A similar trend was observed in group 2 (p = 0.06). However, there was no significant difference in BP between the two methods in group 3 (p>0.1). Interestingly, DBP showed no significant variation for any group (p>0.1). The difference in SBP may be attributed to the difficulty in identifying phase I Korotkoff sounds for younger subjects. These subjects generally have more elastic arteries that may dampen phase I sounds, and thus make AUSC determination of SBP quite difficult. This phenomenon may not be a factor at DBP due to differing hemodynamic conditions.


1996/04

**Corresponding Arterial Compliance and Pulse Pressure Measurements During 24-Hour Ambulatory Monitoring**


Monitoring simultaneous arterial compliance (C, ml/mmHg) and blood pressure (BP) measurements during a twenty-four hour period would be quite useful in understanding BP regulation and vascular function. However, due to the co-dependent nature of the C and BP relationship, understanding the results of monitoring sessions is complicated, especially in patients with underlying cardiovascular disease. In order to evaluate this relationship, 14 patients ranging from 30 to 80 (mean± SEM, 53± 4 years) underwent 24-hour ambulatory C and BP monitoring with the DynaPulse 5000A. This new non-invasive technology provides simultaneous measurements of C and BP by analysis of the oscillometric waveform. Natural circadian BP variations provided the opportunity to evaluate C without pharmacological intervention. C measurements were derived at mean arterial (MAP) (near end-systolic) during the cardiac cycle.

<table>
<thead>
<tr>
<th>Independent Factors</th>
<th>PP</th>
<th>MAP</th>
<th>DBP</th>
<th>BSA</th>
<th>AGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>STD COEF</td>
<td>-0.710</td>
<td>-0.362</td>
<td>0.288</td>
<td>0.501</td>
<td>0.153</td>
</tr>
<tr>
<td>p value (2 tail)</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

Multivariate stepwise regression analysis was performed to evaluate the effect of several independent factors on C in 798 total individual measurements (TABLE). In addition, each patient demonstrated a significant linear correlation for the C vs. pulse pressure (PP) relationship during ambulatory monitoring, average r = -0.79. Results suggest that besides MAP, pulse pressure is a strong inverse determinant of C. Due to the relationship between C and PP, differences in C in patients with matched PP may be a valuable measure of possible underlying cardiovascular disease.

Presented at the American Society of Hypertension 11th Annual Scientific Meetings, 1996 (see American Journal of Hypertension, 1996 Vol 9, No.4, Part 2, pg. 56A).
A New Non-Invasive Method for Detection and Assessment of Aortic Regurgitation During Routine Blood Pressure Recordings

Brinton TJ, Hsu T-L, Kwan O-L, Liu C-P, Chio S-S, Demaria AN; Veterans General Hospital - Taipei, Taiwan, R.O.C., and UCSD, La Jolla, CA.

Recently, we developed an oscillometric cuff technique (CUFF) to non-invasively derive arterial pressures and waveforms. Using this method we observed a unique pattern of pressure oscillations (PO) in a pt with severe aortic regurgitation (AR). To further define the potential mechanism of this phenomenon, and its value in the detection and assessment of AR, we performed clinical and modeling studies. CUFF was performed in 10 normal (N) and 15 pts in whom AR was documented and semi-quantitated by echo. In 10 N, and all 5 mild AR pts, a bell shaped distribution of PO was observed from supra-systolic to sub-diastolic cuff pressure. However, all 10 pts with grade III (severe) AR exhibited a phasic alteration of PO conforming to a resonance pattern. To test the hypothesis that this phenomenon represented a ventricular-vascular fluid mechanics interaction produced by AR, we utilized a simple amplitude modulation model (Wl=incident, W2=reflection) and found that the pattern could be reproduced at specific amplitudes and frequencies. Thus, CUFF recordings of arterial pressure exhibit a marked resonance pattern in pts with severe AR, likely due to ventricular-vascular fluid mechanics interaction. This phenomenon should be useful in detecting and assessing AR during routine blood pressure recordings.


1994/11

A New Non-Invasive Method for Obtaining Arterial Pressure Waveforms: Assessment of Vascular Compliance and Validation with Catheter Data

Brinton TJ, Cotter B, Brown DL, Baddour P, Vuong A, Chio S-S, Calisi C, Demaria AN; UCSD, La Jolla, CA.

We evaluated a novel automated non-invasive technique (NI) developed to record waveforms (WAVE) of actual arterial pressure (AP) throughout the cardiac cycle. The algorithm derives pressures every 20 msec by an oscillometric cuff WAVE pattern recognition method. WAVE are derived assuming a T tube aorta, a straight tube artery, and that systolic and diastolic phases of the supra-systolic and sub-diastolic cuff waves best approximate the respective pressures. AP by NI were compared to those from the aorta (INV) in 26 catheterized pts. Systolic (146±3 vs 147±6) diastolic (75±2 vs 80±5) and mean (98±2 vs 100±4) pressures by INV and NI were similar (r=.94, .89, and .94). NI and INV WAVE were analyzed for peak positive (+) and negative (-) dp/dt (mmHg/sec), peak positive to negative time (sec), and the slope of pressure decay (mmHg/sec). NI local compliance was computed as 4πr(L+2r)/[(dp/dt)ppTpp] where r=radius, L=cuff length, and pp=distance between peak + and - values, and compared to INV systemic compliance (ml/mmHg). Results (mean±SD):

<table>
<thead>
<tr>
<th></th>
<th>dp/dt</th>
<th>-dp/dt</th>
<th>Slope</th>
<th>Tpp</th>
<th>COMPLIANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>NI</td>
<td>600±154</td>
<td>-466±135</td>
<td>-74±24</td>
<td>0.25±.04</td>
<td>0.37±.14</td>
</tr>
<tr>
<td>INV</td>
<td>508±138</td>
<td>-377±89</td>
<td>-74±22</td>
<td>0.25±.04</td>
<td>1.23±.44</td>
</tr>
<tr>
<td>r</td>
<td>0.87</td>
<td>0.68</td>
<td>0.96</td>
<td>0.85</td>
<td>0.73</td>
</tr>
</tbody>
</table>

Thus, measures of absolute pressures, their rate of change, and vascular compliance by a new non-invasive method show a good correlation with cath and should be of value in assessing cardiac and vascular properties.

Appendix A: *Quick guide to DynaPulse Hemodynamic Monitoring (DynaPulse-5200A/Pathway)*

**Part I. Blood Pressure Measurement**

Before you start installing DP-5200A/Pathway hardware and software, please check and make sure you have the following items ready:

- DP-5200A/Pathway monitor
- RS232 communication cable
- Blood Pressure cuff assembly (Include 3 adult-size cuffs)
- AC/DC adaptor, or optional 4 AA batteries (*Not included* in DP-5200A package)
- DP-5200A Pathway software for Windows CD (Include e-Manual User’s guide)
- A PC with Windows operation system (Windows 95, 98, NT, 2000 or XP), and an RS232 communication port. (For PC without RS232 port, an *optional* USB-RS232 converter is required.)

**Getting ready with DP-5200A/Pathway monitor and connect it to a PC:**

- Select a power source: Plug in the supplied AC/DC adaptor (110 Volts AC in USA), or install 4 AA batteries into the battery compartment.
- Connect Cuff assembly to DP-5200A (Use appropriate size cuff for each patient.)
- Connect RS232 cable, one end to DP-5200A and the other end to PC’s RS232 COM- port (*NOTE*: When using an optional USB-RS232 converter, make sure to install the *USB driver* provided by its manufacturer.)

*Equipment Layout – Shown a DP-5200A/Pathway monitor (battery operation) connected with a cuff assembly and to a PC’s RS232 communication port*
Install DP-5200M/Pathway software (a CD or DVD/CD drive is required):

- Insert DP-5200A/Pathway software CD to CD/DVD drive and closed
- Following the on-screen instruction, select correct Window version to install DP-5200A/Pathway software for blood pressure measurement.
- **Note:** First-time installation of DP-5200A software, an automatic COM check window will appear, click “Continue” to find and select an available COM port.
- Install Java Plug-in software for access to www.dynapulse.com web site and DynaPulse Analysis Center (DAC) server for hemodynamic analysis. (Optional service available to DP-5200A/Pathway user with active DAC account only. Contact us for more information.)

Ready and getting start with a blood pressure measurement:

- Go to “Patient” in Main Menu, select “Add” (for first time or a new user), and input patient’s Name and ID.
- Go to “Measure” in Main Menu, select “Start” and following the on-screen instructions to put on the cuff and pump up pressure and perform a blood pressure measurement. (For automatic multiple BP measurements, select “Cycle” to set interval and the total numbers of measurements.)
- A successful measurement will display the measured Systolic, Diastolic, Heart Rate and Pulse waveform, etc.. To keep this measurement, go to “File” and select “Save”. You may enter comments, such as before or after lunch, for this measurement.
Upper half displays:

**Left:**
Single pulse wave (at cursor)

**Right:**

**Blood Pressures:**
- Systolic
- Diastolic
- MAP
- Pulse Pressure (PP)

Heart Rate (HR)

---

Lower half displays:

**Top:**
- Measurement Timeline (28 sec)

**Center:**
- All pulses ( oscillometric waveform), Cursor & cuff pressure (81 mmHg at cursor)

**Bottom:**
- Systolic icon, MAP icon, Diastolic icon, and Cuff pressure

Where, MAP = Mean Arterial Pressure

- If an ERROR window appears, following the instruction, go to Measure” and adjusting the High or Low Range settings accordingly. Click “Start” to start another measurement.

**Other features for reviewing the recorded blood pressure data:**

- The Trend Display and Analysis – Go to “Options” and select “Show Trend Window”, a histogram display of previously recorded blood pressure data will be shown. Select “Analysis” to perform a statistic analysis.
- Go to “Record” in Main Menu and select “Personal Info”, would allow you to input and record, or edit general personal information.
- Go to “Record” in Main Menu and select “Record Table”, a tabulated display of previously recorded blood pressure measurement data will be displayed.
- For other advanced features, please read DP-5200A/Pathway e-manual (User’s guide) page 37-49.

**Note for DP-5200A owner and existing/registered users:**

- When you open the DP-5200A software, a “Patient List” window will display with default “Activated Patient” as “Guest”. Blood pressure measurement CANNOT be saved for the Guest!
- Find a patient name from the Patient List and double click to select it.
- Perform blood pressure measurement as described above.
Part II. DynaPulse online Hemodynamic Analysis

Note: A current and activated DAC (DynaPulse Analysis Center) account is required for uploading DP-5200A/Pathway data and performing DynaPulse online hemodynamic analysis. Please contact us at www.dynapulse.com or call (760) 842-8224 for more information.

Acquire DynaPulse Blood Pressure Data:
  • Make sure DP-5200A/Pathway is working properly, do a BP measurement and save the data as described in Part I for a selected Patient.  (If this patient has had BP already been measured and saved in DP-5200A/Pathway program, go to next step.)

Register a patient and login to DAC/clinical server:
  1. Make sure your PC is online, Java Plug-in was installed, and Pathway software is open and a patient is added (new patient) and selected.
  2. From Main menu, click on DAC > Analysis
  3. Check “cDAC.PulseMetric.com” is selected, fill in your DAC account’s “User Name” and “Password” and click “Login”
  4. Select and click on a Patient Name
  5. Click on Profile and input/edit patient profile information (Items with * must be entered)
  6. Click Update Server >OK and Update Local > OK and Close

Upload or Transmit Patient’s new Data for Hemodynamic Analysis:
  1. Following the above “Register a patient and login to DAC…” steps 1-4, check the patient has his/her “Registered” box marked “Yes”.
  2. Click on “Upload Data” (Wait for a message reporting success to appear)
  3. View and Print Hymodynamic Report: Now, the patient’s DynaPulse BP data has been successfully uploaded to DAC server for hemodynamic analysis. Only the registered DAC account and its authorized user (provided with its User Name and Password) can review or print the patient’s hemodynamic profile via Internet through www.dynapulse.com and login to cDAC as described above.

Note: DynaPulse hemodynamic analysis applies the proprietary Pulse Dynamics methodology of SS Chio’s invention. It analyzes the pulsation signal obtained from a cuff during routine blood pressure measuring cycle, from supra-systolic to sub-diastolic. Severe arrhythmia (irregular pulses) and/or artifacts due to arm movement, misplace of a cuff, etc., which affects the accuracy of blood pressure measurement and provides abnormal pulse waveform can result with ERROR or No hemodynamic parameters calculated. For further information and references on clinical studies and publications, please check our web site www.dynapulse.com or contact us.

******************************************************************************************
Appendix B: *DynaPulse Validation Studies*

Study 1: Blood pressure validation – *vs. Auscultatory*

**Pulse Dynamics vs. Auscultatory Method (ANSI/AAMI SP10-1987)**

<table>
<thead>
<tr>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Difference (Ausc. - PD)</td>
<td>-5</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>6</td>
</tr>
<tr>
<td>Standard Error of Estimation</td>
<td>5</td>
</tr>
<tr>
<td>Correlation Coefficient</td>
<td>0.96</td>
</tr>
</tbody>
</table>

**Experimental Conditions:**
1. Total Subjects: 132
2. Age Groups: (11-24) = 28 (25-44) = 38 (45-64) = 28 (65-85) = 38
3. Heart Rate Range: 45-115 BPM
4. Data represents a three measurement average.

---

110
Study 2: Blood pressure validation - *Systolic*

Pulse Dynamics vs. Auscultatory Method (ANSI/AAMI SP10-R-4/92)

**Systolic (Seated Position)**

Pulse Dynamics (mm Hg) vs. Auscultatory Method (mm Hg)

**Systolic (Standing Position)**

Pulse Dynamics (mm Hg) vs. Auscultatory Method (mm Hg)

**Systolic (Supine Position)**

Pulse Dynamics (mm Hg) vs. Auscultatory Method (mm Hg)

### Pulse Dynamics vs Auscultatory Method Systolic Summary

<table>
<thead>
<tr>
<th></th>
<th>Seated</th>
<th>Standing</th>
<th>Supine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Difference (Ausc. - PD)</td>
<td>-1</td>
<td>0</td>
<td>-2</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Standard Error of Estimation</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Correlation Coefficient</td>
<td>0.94</td>
<td>0.93</td>
<td>0.95</td>
</tr>
</tbody>
</table>

**Experimental Conditions:**

1. Total Subjects: 22
2. Age Groups: (17-24) = 4  (25-44) = 14  (45-64) = 3  (65-84) = 1
3. Data represents a three measurement average.
Study 2: Blood pressure validation - Diastolic

Pulse Dynamics vs. Auscultatory Method (ANSI/AAMI SP10-R-4/92)

Diastolic (Seated Position)

Diastolic (Standing Position)

Diastolic (Supine Position)

Pulse Dynamics vs. Auscultatory Method Diastolic Summary

<table>
<thead>
<tr>
<th></th>
<th>Seated</th>
<th>Standing</th>
<th>Supine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Difference (Ausc. - PD)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Standard Error of Estimation</td>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Correlation Coefficient</td>
<td>0.92</td>
<td>0.95</td>
<td>0.84</td>
</tr>
</tbody>
</table>

Experimental Conditions:
1. Total Subjects: 22
2. Age Groups: (17-24) = 4 (25-44) = 14 (45-64) = 3 (65-84) = 1
3. Data represents a three measurement average.
Study 3: Blood pressure validation – vs. Catheterization

Pulse Dynamics vs. Intra-Arterial Catheterization (UCSD Medical Center)

Systolic Pressure

Diastolic Pressure

Mean Arterial Pressure

Pulse Dynamics vs. Intra-Arterial Catheterization Summary

<table>
<thead>
<tr>
<th></th>
<th>Systolic</th>
<th>Diastolic</th>
<th>Mean Arterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Difference (Cath. - PD)</td>
<td>-2</td>
<td>-4</td>
<td>-1</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>9</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Standard Error of Estimation</td>
<td>9</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Correlation Coefficient</td>
<td>0.94</td>
<td>0.91</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Experimental Conditions:
1. Total Subjects: 36
2. Invasive Pressure Site: Descending Thoracic Aorta
3. Data represents a three measurement average.
Study 4: Cardiac output validation – vs. Thermo-dilution I (UCSD MC)

Comparison of DynaPulse CO and Thermodilution CO

Linear Regression

Bland-Altman Analysis

<table>
<thead>
<tr>
<th>Model</th>
<th>B (Unstandardized Coefficients)</th>
<th>Std. Error</th>
<th>Coefficients</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Constant)</td>
<td>3.558</td>
<td>0.710</td>
<td>4.969</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>XVAR</td>
<td>0.364</td>
<td>0.161</td>
<td>0.471</td>
<td>2.263</td>
<td>0.036</td>
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</tbody>
</table>

a. Dependent Variable: YVAR

Without Pulmonary Hypertension Patients

Linear Regression

Bland-Altman Analysis

<table>
<thead>
<tr>
<th>Model</th>
<th>B (Unstandardized Coefficients)</th>
<th>Std. Error</th>
<th>Coefficients</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Constant)</td>
<td>2.517</td>
<td>1.004</td>
<td>2.507</td>
<td>0.033</td>
<td></td>
</tr>
<tr>
<td>XVAR</td>
<td>0.494</td>
<td>0.204</td>
<td>0.528</td>
<td>2.421</td>
<td>0.038</td>
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</tbody>
</table>

a. Dependent Variable: YVAR
Study 4: Cardiac output validation – vs. Thermo-dilution II (UCSD MC)

**With Pulmonary Hypertension Patients**

**Linear Regression**

![Graph showing linear regression between Thermo-dilution CO (L/min) and DynaPulse CO (L/min).]

**Bland-Altman Analysis**

![Graph showing Bland-Altman analysis with mean difference (DIFF) and limits of agreement.]

<table>
<thead>
<tr>
<th>Model</th>
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<th>Standardized Coefficients</th>
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<th>Sig.</th>
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<tr>
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<td>XVAR</td>
<td>0.757</td>
<td>0.209</td>
<td>0.807</td>
<td>0.009</td>
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Dependent Variable: YVAR

**Study 5: Cardiac output validation – vs. FICK & Echo Doppler**

**DynaPulse in Comparison with Cardiac Output**

*Data from Beijing PLA Hospital, To be published*

**Linear Regression**

**FICK vs. DPCO**

- $y = 1.0783x - 0.1487$
- $R^2 = 0.4681$

![Graph showing linear regression between FICK and DynaPulse CO.]

**Echo vs. DPCO**

- $y = 0.7348x + 1.5172$
- $R^2 = 0.3737$

![Graph showing linear regression between Echo and DynaPulse CO.]

**Correlations**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pearson Correlation</th>
<th>Sig. (2-tailed)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>FICK</td>
<td>0.684</td>
<td>0.000</td>
<td>26</td>
</tr>
<tr>
<td>Echo</td>
<td>0.511</td>
<td>0.000</td>
<td>58</td>
</tr>
</tbody>
</table>

**Correlation is significant at the 0.01 level (2-tailed)**
Study 6: Cardiac output validation – vs. *Echo Doppler (UCSD Medical Center)*

**DynaPulse Cardiac Output vs. Echo Doppler during Dobutamine Stress Tests**

**Linear Regression**

\[ r = 0.87 \]
\[ p < 0.001 \]
\[ n = 94 \]

**Bland-Altman Analysis**

**Difference between DynaPulse and Echo Doppler CO (L/min)**

**Average of DynaPulse and Echo Doppler CO (L/min)**

******************************************************************************
Appendix C: DynaPulse Case Studies and Other Case Reports (Clinical Utilities)

Through the efforts of numerous worldwide clinical studies, collaborations, and independent patient participation, Pulse Metric, Inc. has also identified many interesting cases in which the DynaPulse hemodynamic monitoring technology has enabled clinicians to more effectively manage and treat patients with cardiovascular disease. In this Case Studies section, we share the findings of such cases. Included below, for references, are some published case reports that applied hemodynamic monitoring in cares of hypertension and related cardiovascular diseases.

* Reported by DynaPulse/Pulse Metric R&D team: Qiyi Xie, M.D., M.P.H., S. Lin-Liu, Ph.D., S-S. Chio, Ph.D., B.L. Tang, M.A. Kelley, R.N., B.S.N., C.C.R.C., A.S. Ng, J.J. Tsai, and DynaPulse users and contributors: J. Neutel, M.D., R. Gaston, MD, YL Chao, MD, and SJ. Chiu of CVM and patients, who contributed their DynaPulse data to these case studies.

DynaPulse Case Studies

2000-a
Case #1:

Patient Background & History: A 36-year-old male, Chinese, has experienced symptoms with shortness of breath and palpitations, on and off, since early February of 2000. His physician recorded the following: ECG showed left axis deviation and premature ventricular contraction. Echocardiogram examination revealed mild mitral regurgitation and mild tricuspid regurgitation. Stress test was negative. He was quite well until June 5th, when the episode of palpitations reoccurred. ECG then showed frequent PVC. Ambulatory 24 hours Holter ECG revealed 16597 isolated PVC and 20 couplets PVC but no short runs of VT. Mexitil was prescribed and the patient’s condition stabilized. Since May 15th, 2000, he was further advised to monitor cardiac, blood pressure, and hemodynamic functions using DynaPulse at home. The patient is currently stable and receiving medication with propafenone (Rytmonorm) 150mg b.i.d. under diagnosis of cardiac arrhythmia. Propafenone is a class 1C drug that has sodium channel blocking activity and also beta-adrenergic blocking properties.

DynaPulse Monitoring & Data Analysis: On May 15th, 2000, patient experienced an episode of arrhythmia. His physician, then, provided (prescribed) him with a DynaPulse 200M home monitoring device, and the patient was instructed to take a series of blood pressure measurements at home for a period of 15 days. Blood pressure and waveform data were collected by DynaPulse, and then transmitted to Pulse Metric’s DynaPulse Analysis Center (DAC) for hemodynamic analysis. Blood pressures, Pulse Pressures (PP), Heart Rate (HR) and other hemodynamic parameters were recorded and analyzed during the observation period. A cardiac event (angina) was captured. Trending of changes in blood pressure, cardiac function, and vascular condition were analyzed and later evaluated. When compared to their normal mean values, PP and HR percentage changes were significantly different. PP and HR (Fig.1) were then plotted. The trend of proportional changes corresponding to time and the occurrence of the cardiac event are displayed. The percentage change of the PP/HR ratio against the mean was calculated as:

\[
\frac{\text{ΔPP}}{\text{mean baseline PP}} : \frac{\text{ΔHR}}{\text{mean baseline HR}}
\]

Results & Observations: One day before the onset of the cardiac event (angina), over 40% elevation in PP was observed. Then, at 15 minutes before patient reported angina, a significant drop (50%), which is 10% below the mean, occurred. 15 min. later after patient reported the episode of angina, PP dropped another 35%. The PP stabilized in 30 min following the medication.

Comments & Opinions: The dramatic unidirectional shifting (85%) of PP within 24 hours from positive to negative vs. mean suggested the patient went from cardiovascular compensation to decompensation. The PP was stabilized following the medication in 30 min. Fig.2 shows the trend of PP/HR ratio changes. It indicates that before onset of the cardiac event, PP/HR ratio was significantly higher than the mean.
value (2 times > normal range). Using the trend ratio change as cardiac function index could objectively provide a quantified indicator for predicting an upcoming event particularly among outpatients.

**Patient History:** The patient is a 49-year-old hypertensive male who was diagnosed with paroxysmal atrial fibrillation in the fall of 1997. TEE was performed with successful DCC on December 11, 1997. However, the patient subsequently developed recurrent atrial fibrillation on December 20, 1997. Currently his symptoms persist and include occasional skipped beats, which occur mostly frequently during times of stress and fatigue. The patient experiences occasional dyspnea after the skipped beats and after climbing 2 flights of stairs. Other symptoms include fatigue, atypical left-sided chest discomfort described as a “dull ache” which is non-radiating in nature, and mild edema. Recently, persistent atrial fibrillation has occurred since August of 2000, resulting in episodes of awakening with a pause and jolt and periods of brief chest discomfort. The patient was treated with Amiodarone (800 mg/d) and Digoxin (0.25 mg/qd), which was discontinued due to side-effects that included difficulty in speaking and a dramatic reduction in heart rate (40 bps).

**Procedure:** The patient utilized the DynaPulse monitoring device to track his blood pressure and episodes of atrial fibrillation. A total of 212 DynaPulse hemodynamic measurements were obtained over a 9 month period, beginning in March of 2000. The hemodynamic measurements obtained included blood pressure (SBP, DBP, MAP, PP), cardiac function parameters (HR, LVdP/dt, LV contractility, and LV ejection time), systemic parameters (systemic vascular compliance and systemic vascular resistance), and brachial artery parameters (brachial artery compliance and brachial artery distensibility). In addition, pulse waveforms were also recorded for later morphological analysis. These data were obtained by the patient in his home and were analyzed retrospectively. A major focus of data analysis was to correlate associated hemodynamic changes with AF episodes over time. A blinded analysis of DynaPulse waveforms was performed to assess the device’s ability to detect AF episodes, and the results were then correlated with the patient’s actual documentation of such events.

**Results:** From a total of 212 DynaPulse measurements, 7 AF episodes were identified.

Normal Waveform AF Waveform Moreover, a significant reduction in LV contractility preceded all AF episodes, which was correlated to the patient’s reported atypical left-sided discomfort that also preceded the AF episodes. In all cases, the patient’s LV contractility dropped a minimum of 2 standard deviations from
the overall mean, which occurred between 3 and 8 hours prior to onset of the episode (mean = 5.5 hours prior to onset of the episode).

Comments: The sudden onset of atrial fibrillation (AF) may cause palpitations, angina pectoris and a decrease in cardiac output. Short-term predictability of the occurrence of AF for outpatients is difficult and has rarely been reported due to the lack of an appropriate tool to noninvasively measure hemodynamic changes. A decrease in LV contractility has been reported to occur during an AF event, and the results of this case study further indicate that a sudden decrease in LV contractility also occurs prior to the AF episode. Therefore, this study suggests that it may be possible to predict the occurrence of such cardiac events through the use of noninvasive hemodynamic monitoring technology.

Patient History: A 72-year-old white male has been diagnosed as hypertensive for about 30 years. Medical history includes prostate surgery in 1988, kidney stone removal in 1991, mini-stroke in 1992, chest pains in 1991 and 1998, and gallbladder removed in 1998. The patient’s daily medications include: Angiotensin II Inhibitor (Diovan®, Novartis 160mg/day), Diuretic (Aldactone® spironolactone 50mg/day) and beta blockade (Toprol-XL®, Zeneca) for blood pressure reduction. Other medications include: Levoxyl, Aspirin, and Zantac plus Multi-Vitamin. The blood chemistry readings were normal with the exception of a higher than normal glucose range in February of 1998 (193) and triglycerides in March of 2000 (264). Hematology and differential are normal. In addition to mild hypertension, which is now under control, the patient has also experienced irregular heartbeats since November of 2000.

Procedure: A total 372 DynaPulse measurements have been acquired over a period of 27 months, and include blood pressure (BP) other hemodynamic parameters such as Systemic Vascular Resistance (SVR), Brachial Artery Compliance (BAC), and Brachial Artery Distensibility (BAD). Measurements were collected by the patient himself at home and retrospectively analyzed. Results were compared to a normal population of males (N=877), and each individual parameter was trended and plotted against the patient’s medication history.

Results: The results demonstrate an overall improvement in blood pressure and hemodynamic parameters, all of which are statistically significant. Patient reported episodes of arrhythmia as indicated by abnormal DynaPulse waveforms and verified via Holter monitoring. The patient’s SVR, BAC, and BAD were compared to those obtained from the same age group within the normal population, demonstrating a lower initial BAC and higher initial SVR. The patient’s Hemodynamic condition improved (as measured by SVR, BAC, and BAD), and these improvements were correlated to medication adjustments. Angiotensin II (Diovan®, Novartis 160mg/day) alone did not result in significant changes of any parameter in the early treatment stage, however Angiotensin II combined with a diuretic (Aldactone® spironolactone 50mg/day) resulted in a clear reduction of SVR and elevation of BAC and BAD. The extra addition of beta blockade
(Toprol-XL®, Zeneca) to the drug treatment regime resulted in maintenance of the reduced SVR while simultaneously further improving the patient’s BAC and BAD.

**Comments:** Demonstration of the long-term effects of drug therapy on hemodynamic parameters has been scarcely reported largely due to the lack of appropriate tools and methodology. Monitoring changes in hemodynamic parameters such as SVR, BAC and BAD in chronic Cardiovascular Disease (CVD) patients over the course of treatment is essential for the optimization of therapy. Significant improvements in these hemodynamic parameters during the course of treatment were clearly documented in this case, demonstrating the clinical value of routine monitoring of blood pressure and hemodynamic changes.

Other Case Reports*: **Clinical utilities**

**Case A: Determining Whether Changes in the Medical Regimen are Warranted**

This 65 year old man with dilated cardiomyopathy of seven years duration, and a left ventricular ejection fraction of 12%, presented for a routine periodic evaluation. He denied any symptoms of heart failure over the preceding months, on a regimen of quinapril 20 mg bid, furosemide 80 mg qd, and digoxin 0.25 mg qd. The patient had been intolerant of beta-blockers in years past due to profound bradycardia. Physical examination was notable for a blood pressure of 120/90 mm Hg, a jugular venous pressure of 6 cm, a soft S₄ gallop, and a chronic grade I/IV mitral regurgitant murmur. Non-invasive hemodynamic analysis revealed a CI of 1.7 and an SVR of 2249. In spite of the patient’s asymptomatic state, this change in his hemodynamics led to a recommendation to increase his quinapril to 40 mg bid.
Upon repeat evaluation four weeks later, the blood pressure was 108/72 mm Hg, the jugular pressure 5 cm, and the cardiac examination unchanged. Non-invasive hemodynamic analysis showed a CI of 2.4 with a SVR of 1398. In view of achievement of these normal hemodynamic values, no changes were made in his medications on this visit. With the exception of minor changes in diuretic therapy, the patient has remained asymptomatic on this stable medical regimen for over two years.

**Case B: Assessing Hemodynamic Correlates of a Change in Symptoms**

This 71 year old woman with idiopathic dilated cardiomyopathy, an eight year history of symptomatic congestive heart failure, and an ejection fraction of 25% presented with complaints of fatigue, lethargy, and thirst on a regimen of lisinopril 20 mg qd, digoxin 0.125 mg qd, and bumetanide 2 mg qd. Examination showed a blood pressure of 84/60 mm Hg, a pulse in the 80s in chronic atrial fibrillation, a jugular pressure <5cm, clear lungs, no gallop, and no organomegaly or pedal edema. Non-invasive hemodynamics showed a CI of 2.5 with a SVR of 1497. As it was felt that her symptoms were likely related to volume depletion, diuretics were temporarily discontinued and she was scheduled for a follow up visit, with instructions to measure her weight daily in the interim.

Two weeks later she presented with complaints of abdominal fullness and a 1 lb weight gain, without dyspnea or peripheral edema. The blood pressure was 100/80 mm Hg, the pulse 85, and the neck veins now 12 cm in height. There was a grade I/VI mitral regurgitant murmur and moderate hepatomegaly, with no peripheral edema. Hemodynamics showed a CI of 1.6 with a SVR of 2883. Despite the minimal weight gain, it was apparent that the patient was significantly volume overloaded and bumetanide was resumed at its previous dose. She was also instructed to begin metoprolol 25 mg qd after resumption of the bumetadine.

Two weeks later a repeat evaluation revealed complaints of minimal dyspnea, with a blood pressure of 90/60 mm Hg, a heart rate of 90, a weight decrease of 1 lb down from the previous visit, and the neck veins now 8 cm in height. The CI was now 2.2 and the SVR 2710. Metroprolol was increased to 50 mg and subsequently to 100 mg daily.

Evaluation four weeks later showed a blood pressure of 96/60 mm Hg, a pulse rate of 80, a weight decrease of one more pound, and an otherwise unchanged examination. The CI at this time was 2.7 with an SVR of 1626. The patient’s symptoms, physical findings, and hemodynamics remained stable over the ensuing two years on this medical regimen.

**Case C: Tracking Trends in Hemodynamic Parameters After Alterations in Drug Therapy**

This 79 year old man presented to the outpatient clinic on continuous home dobutamine. After a 30 year history of progressive dilated cardiomyopathy, with an ejection fraction of <15%, he was hospitalized for progressive heart failure despite aggressive outpatient medical management. Pulmonary artery catheterization revealed a CI of 1.3, which
increased to 2.0 while on dobutamine. Multiple attempts at discontinuation of the drug proved futile and he was eventually discharged on an infusion of 5 mcg/kg/min of continuous dobutamine.

After six weeks of continuous home dobutamine he presented for an outpatient visit. In addition to dobutamine, he was on spironolactone 25 mg qd, lisinopril 10 mg qd, digoxin 0.25 mg qd, and furosemide 80 mg qd. He felt well, was able to walk one mile without dyspnea, and now denied any symptoms of heart failure. The blood pressure was 110/67 mm Hg, the pulse in the 80s in chronic atrial fibrillation, the central venous pressure normal, and the remaining exam notable only for a grade II/VI mitral regurgitant murmur. Non-invasive hemodynamics showed a CI of 2.8 and a SVR of 1081. In view of these excellent hemodynamics and the patient’s asymptomatic status, dobutamine was discontinued in the office while undergoing continuous hemodynamic monitoring. Surprisingly, over the ensuing hours his hemodynamics remained unaltered despite discontinuation of the dobutamine infusion. The patient was sent home off IV dobutamine and on escalating doses of metoprolol.

Over the ensuing weeks he remained clinically stable and repeat non-invasive hemodynamics showed a CI of 2.9 and SVR of 932, despite the reinstitution of metoprolol and the discontinuation of dobutamine.

Three months later, a periodic follow up was done with the patient on metoprolol 100 mg qd, lisinopril 20 mg qd, spironolactone 25 mg qd, digoxin 0.25 mg qd, and furosemide 80 mg qd. He complained of fatigue but was still able to walk one mile without dyspnea, and denied having orthopnea or pedal edema. Physical examination revealed no evidence of volume overload but non-invasive hemodynamics showed a CI of 1.8 and SVR of 1752. In view of the increased SVR and reduced CI, lisinopril was increased to 20 mg bid and, in hopes of achieving further sympathetic withdraw, metoprolol was increased to 150 mg qd. The patient has been stable on this clinical regimen and remains asymptomatic.

**Case D: Establishing Baseline Hemodynamic Parameters After Alterations in Drug Therapy**

This 37 year old woman was referred for management of chemotherapy induced dilated cardiomyopathy initially manifest as pulmonary edema and hypotension. The ejection fraction was demonstrated to be 20%. Symptomatically she improved on digoxin 0.125 mg qd, furosemide 40 mg qd, isosorbide mononitrate 60 mg qd, lisinopril 20 mg bid, and amiodarone. Physical examination revealed a blood pressure of 94/76 mm Hg with overt pulsus alternans, a pulse rate of 108 and a loud S4 gallop, but no jugular venous distention or edema. Non-invasive hemodynamics showed a CI of 1.4 with systemic vascular resistance of 2900. Metoprolol was begun at a dose of 25 mg daily.

One week later she returned, still complaining of fatigue but with no symptoms of dyspnea. The blood pressure was 80/60 mm Hg and the pulse 84; the pulsus alternans
had resolved and the S₄ gallop was unchanged. The CI was 2.1 and the SVR was 1500. Metoprolol was doubled to 50 mg daily.

Over the ensuing weeks the metoprolol was increased to 100 mg daily and the CI rose to 2.4 with a SVR of 1475. Orthostatic hypotension became problematic so lisinopril was reduced to 10 mg daily and isosorbide mononitrate was discontinued.

Over the next two months her symptoms improved and physical examination remained unremarkable except for a rise in the blood pressure to 130/60 mm Hg. At that point the CI was 2.4 with a SVR of 1338. Metroprolol was increased to 200 mg daily and digoxin was discontinued.

Over the ensuing two years the patient did well on continued medical therapy and the ejection fraction rose to 0.35. In view of this, and the fact that her hemodynamic parameters did not change, her lisinopril and furosemide doses were reduced by half. She remains clinically stable.

**Case E: Measuring Hemodynamics on Periodic Follow up Visits**

This 80 year old man with ischemic dilated cardiomyopathy was referred for optimal medical management because of continuing problems with fatigue despite therapy with furosemide 40 mg bid, losartan 50 mg bid, doxazosin 2 mg qd, and amiodarone. Physical examination revealed a blood pressure of 122/70 mm Hg, a pulse of 60, flat neck veins, a grade III mitral regurgitant murmur, and a S₄ gallop. There was no organomegaly or peripheral edema. Non-invasive hemodynamics showed a CI of 4.0 with a SVR of 770. It was recommended that he begin beta-blockade and in view of his low SVR, metoprolol (rather than carvedilol) was selected as the drug of choice, at an initial dose of 25 mg/day.

Two months later he returned complaining of lethargy on this new regimen. The blood pressure was 70/48 mm Hg, the pulse 58, and the cardiac exam notable only for a soft mitral regurgitant murmur and a S₄ gallop. The CI was 5.2 and the SVR was 428. Furosemide was discontinued and losartan was reduced to 50 mg qd.

On subsequent visits the blood pressure rose to 110/78 mm Hg, the pulse was 52, and the remaining cardiac exam unchanged. The CI was now 4.8 and the SVR 751. On this regimen the patient felt remarkably better.

Over the ensuing two years he remained clinically stable, on 100 mg of metoprolol daily, with unchanged hemodynamics.

**Case F: Using Hemodynamic Data in Patients with AV Sequential Pacemakers to Optimize Cardiac Output**

A 48 year old white female with a history of an aortic valve replacement and a right ventricular infarct requiring the insertion of a dual chamber pacemaker and heart failure
symptoms NYHA Functional Class III-IV was evaluated for a heart transplant. Upon examination she complained of chronic dyspnea on exertion, orthopnea, and fatigue with a decrease in exercise capacity limited to 50 feet. These symptoms started after the aortic valve replacement and became progressively worse in the last two years. Reviewing her medical records it was found that she had a right ventricular infarction secondary to a surgical sacrifice of the right coronary artery. The latter required the insertion of a dual chamber pacemaker. In addition, she previously had ventricular arrhythmias treated with amiodarone. She was admitted to the telemetry unit for evaluation. Her past medical history was also significant for hypothyroidism. Her physical examination revealed a blood pressure of 100/80 mm Hg in both arms, a heart rate of 60, a right ventricular lift, tricuspid regurgitation, jugular venous pressure of 10 cm, and bilateral lower extremity edema. Medication at the time of admission were: coumadin 5 mg/day, synthroid 0.1 mg/day, torsemide 20 mg twice a day, aldactone 100 twice a day, and cordarone 200 mg once a day. Her ECG revealed sinus rhythm with a rate of 58 and a right bundle branch block. An echocardiogram revealed a dilated right ventricle and right atrium, a normal functioning prosthetic valve in the aortic position, and a normal left ventricular function. A non-invasive assessment of hemodynamic parameters was performed and revealed a CA of 4.2 L/min and a CI of 2.1. Her laboratory tests were normal and her TSH was within the normal limits. The decision was made to non-invasively measure her hemodynamic parameters continuously and interrogate the pacemaker, to change the settings, in order to achieve a better CO. Upon interrogation of the pacemaker, several modifications in its settings were performed and hemodynamic parameters were measured at the same time. When the rate was modified to 85 bpm and the AV interval was modified to 180 msec, the CO increased to 6.0 L/min and the CI to 3.2. The changes represented a 30% increase in these hemodynamic parameters; the patient had a brief episode of flushing that abated quickly. She was discharged the next day and at the time, she was walking 250-300 feet without dyspnea or fatigue. Two months later the patient continued to do well and hemodynamic parameters remained normal (CI of 3.0).

Case G: Using hemodynamic data to help in the diagnosis of patients with “decompensated heart failure”

A 48 year old female with known history of dilated cardiomyopathy, hypertension, and an embolic stroke presented with worsening dyspnea on exertion for the previous three months. She also complained of weight loss, loose bowel movements, and occasional dizziness. In addition, she had multiple admissions in the recent past for decompensated heart failure. A previous evaluation included an echocardiogram and left heart catheterization. Both studies demonstrated an abnormal ventricular function with ejection fraction of 30% and normal coronary arteries. Despite adequate treatment for heart failure she continued to be symptomatic and, therefore, was being seen for further evaluation and treatment.

Physical examination was significant for sinus tachycardia (rate of 120), S3 gallop, and a slightly enlarged thyroid gland. A non-invasive assessment of hemodynamics was performed, revealing a CO of 11 L/min, CI of 5.0, and SVR of 640. Blood pressure was 130/70 mm Hg. Because of her history and as a result of her abnormal hemodynamic
status, thyroid function tests were performed and the results were: TSH < 0.08 mU/L (nl 0.047-5 mU/L), thyroid hormone 3 uptake (T3U) >55% (nl 24-39%), thyroid hormone 4 (T4) 22.8% (nl 5-11.4%). Based on these results and history, the diagnosis of hyperthyroidism was entertained and methimazole 10 mg per day was started. The patient was discharged home and after a three-month follow up, heart failure symptoms were resolved. Hemodynamic parameters measured non-invasively demonstrated a normalization of CO and systemic vascular resistance.

* referenced from ICD-9: 414.9 Chronic Ischemic Heart Disease; 428 Heart Failure; 786.5 Chest pain; 785.1 Palpitation, etc. sources, 2000-2003

Appendix D: DynaPulse Clinical Studies - 2013 Update

DynaPulse Clinical Studies – Update (January 7, 2013)
(23 papers added with links and abstracts)

Clinical Studies with DynaPulse

List of additional (23) papers published
(January 7, 2013)

Paper #23: Preventing Chronic Disease, Public Health Research, Practice and Policy (CDC publication) -http://www.cdc.gov/pcd/issues/2012/11_0134.htm

Predictors of Risk and Resilience for Posttraumatic Stress Disorder Among Ground Combat Marines: Methods of the Marine Resiliency Study

Dewleen G. Baker, MD; William P. Nash, MD; Brett T. Litz, PhD; Mark A. Geyer, PhD; Victoria B. Risbrough, PhD; Caroline M. Nievergelt, PhD; Daniel T. O’Connor, MD; Gerald E. Larson, PhD; Nicholas J. Schork, PhD; Jennifer J. Vasterling, PhD; Paul S. Hammer, MD; Jennifer A. Webb-Murphy, PhD; the MRS Team

Abstract: The Marine Resiliency Study (MRS) is a prospective study of factors predictive of posttraumatic stress disorder (PTSD) among approximately 2,600 Marines in 4 battalions deployed to Iraq or Afghanistan. We describe the MRS design and predeployment participant characteristics. Starting in 2008, our research team conducted structured clinical interviews on Marine bases and collected data 4 times: at predeployment and at 1 week, 3 months, and 6 months postdeployment. Integrated with these data are medical and career histories from the Career History Archival Medical and Personnel System (CHAMPS) database. The CHAMPS database showed that 7.4% of the Marines enrolled in MRS had at least 1 mental health diagnosis. Of enrolled Marines, approximately half (51.3%) had prior deployments. We found a moderate positive relationship between deployment history and PTSD prevalence in these baseline data.
**Introduction:** Chronic psychiatric illness such as posttraumatic stress disorder (PTSD) is a major public health problem among current and former military service members, especially those who have served in combat. The prevalence of PTSD among service members and veterans varies widely, but deployment to a war zone is consistently associated with an increased risk for PTSD by a factor of 1.5 to 3.5 across war eras (1). The Iraq and Afghanistan conflicts are no exception (2,3). Additionally, blast-related brain injuries, which are frequently associated with PTSD, are common (3,4). Although suicide rates among active duty personnel have risen since these conflicts started in 2003, reasons for the increase are not fully understood and are being investigated (5). PTSD and mild traumatic brain injury (TBI) appear to be risk factors for suicidal behavior (6). The number of veterans of the current conflicts seeking care at Veterans Health Administration (VHA) facilities has increased (7). Many of these veterans have met screening or diagnostic criteria for PTSD (20%–39%), often co-occurring with depression, anxiety, substance use disorders, and chronic pain (7,8). Associated long-term personal and societal costs are high.

Evidence-based therapies for PTSD have shown only modest efficacy in targeting war trauma (9). Increasingly, military resources are being invested in preventing PTSD. However, scientific advances in understanding the etiology and natural history of PTSD needed to develop effective prevention and treatments have been hampered by reliance on retrospective, cross-sectional research (10). Several prospective investigations of military cohorts have now been initiated (2,3,11). The Marine Resiliency Study (MRS) is singular among these investigations in its combined study of operational units and its biological, psychological, and social scope.

The objective of this article is to describe the research methods used in the MRS, a unique collaboration between the Marine Corps, Navy, Veterans Affairs (VA) Health Services Research and Development (HSR&D), and academia. The description of participant characteristics before deployment combined with future longitudinal data analysis may allow researchers to identify modifiable multisystem risk and resilience factors for combat-related PTSD. The potential factors under investigation are measures of arousal, cardiovascular and physical fitness, mental health, stress reactivity, genetics, neurocognitive function, deployment stressors, and social and military support.

**Paper #22:** Journal of the American College of Cardiology Vol. 59, No. 24, 2012 (P. 2206-16)

**Autonomic and Hemodynamic, Origins of Pre-Hypertension - Central Role of Heredity**

Jason T. Davis, MD,* Fangwen Rao, MD,* Dalal Naqshbandi, BA,* Maple M. Fung, MD,* Kuixing Zhang, MD,* Andrew J. Schork, BS,* Caroline M. Nievergelt, PHD,* Michael G. Ziegler, MD,* Daniel T. O'Connor, MD*†‡

UCSD Medical School, La Jolla, California, USA

**Objectives** The purpose of this study is to better understand the origins and progression of pre-hypertension.
Background Pre-hypertension is a risk factor for progression to hypertension, cardiovascular disease, and increased mortality. We used a cross-sectional twin study design to examine the role of heredity in likely pathophysiological events (autonomic or hemodynamic) in pre-hypertension.

Methods Eight hundred twelve individuals (337 normotensive, 340 pre-hypertensive, 135 hypertensive) were evaluated in a sample of twin pairs, their siblings, and other family members. They underwent noninvasive hemodynamic, autonomic, and biochemical testing, as well as estimates of trait heritability (the percentage of trait variance accounted for by heredity) and pleiotropy (the genetic covariance or shared genetic determination of traits) by variance components.

Results In the hemodynamic realm, an elevation of cardiac contractility prompted increased stroke volume, in turn increasing cardiac output, which elevated blood pressure into the pre-hypertension range. Autonomic monitoring detected an elevation of norepinephrine secretion plus a decline in cardiac parasympathetic tone. Twin pair variance components documented substantial heritability as well as joint genetic determination for blood pressure and the contributory autonomic and hemodynamic traits. Genetic variation at a pathway locus also indicated pleiotropic effects on contractility and blood pressure.

Conclusions Elevated blood pressure in pre-hypertension results from increased cardiac output, driven by contractility as well as heart rate, which may reflect both diminished parasympathetic and increased sympathetic tone. In the face of increased cardiac output, systemic vascular resistance fails to decline homeostatically. Such traits display substantial heritability and shared genetic determination, although by loci not yet elucidated. These findings clarify the role of heredity in the origin of pre-hypertension and its autonomic and hemodynamic pathogenesis. The results also establish pathways that suggest new therapeutic targets for pre-hypertension, or approaches to its prevention.


Korotkoff sound versus oscillometric cuff sphygmomanometers: comparison between auscultatory and DynaPulse blood pressure measurements

Shiu-Shin Chio, PhD, Elaine M. Urbina, MD, Jeffery LaPointe, BSA, Jeffrey Tsai, BSA, and Gerald S. Berenson, MD,*

Abstract

Listening to Korotkoff sounds (K-sounds) to determine systolic and diastolic blood pressure (BP) has been the standard for noninvasive BP measurement in medical practices for nearly 100 years. It is the essential tool used for evaluation and assessment of patients with hypertension and risks of cardiovascular diseases (CVD) by physicians and nurses despite limited understanding of the nature of K-sounds. Analyzing cuff oscillometric signals to obtain BP has been the foundation of most digital BP monitors available today. DynaPulse is an oscillometric digital BP monitor that records and analyzes subtle changes of pulse waveforms during the course of a BP measurement while cuff pressure slowly decreases from above systolic to below diastolic. This study compares systolic and diastolic readings obtained by K-sound method following the Bogalusa Heart Study protocol and BP measured by DynaPulse (DP2000A) monitor, in
order to better understand the nature and difference between K-sound and oscillometric methods. Analysis of means and differences is applied to BP data collected from 803 subjects examined in the Bogalusa Heart Study. The results indicated: 1) DynaPulse systolic was 9 mm Hg higher (P < .0001) than Phase 1 (K1) systolic, 2) DynaPulse diastolic was 5 mm Hg lower (P < .0001) than Phase 4 (K4), and 3) is less than 1 mm Hg higher than Phase 5 (K5) diastolic (P < .0001), when compared with K-sound auscultatory measurement. Understanding the methods and differences of DynaPulse oscillometric and K-sound BP measurements is important for clinic BP screening and self-BP monitoring, as well as future research to improve hypertension and CVD managements. J Am Soc Hypertens 2011;5(1):12–20.

Keywords: Korotkoff sounds; auscultatory; oscillometric; sphygmomanometer; DynaPulse; blood pressure measurement; Bogalusa Heart Study.

**Paper #20: J Pediatr 2011;158:715-21**

**Relationship between Elevated Arterial Stiffness and Increased Left Ventricular Mass in Adolescents and Young Adults**

Elaine M. Urbina, MD, MS, Lawrence M. Dolan, MD, Connie E McCoy, RVT, Philip R. Khoury, MS, Stephen R. Daniels, MD, PhD, and Thomas R. Kimball, MD

**Objective** To determine whether arterial stiffness relates to left ventricular mass (LVM) in adolescents and young adults.

**Study design** Demographic, anthropometric, laboratory, echo, carotid ultrasound and arterial stiffness data were obtained in 670 subjects 10 to 24 years of age (35% male, 62% non-Caucasian). Global stiffness index (GSI) was calculated from five measures of carotid artery stiffness, augmentation index, brachial distensibility, and pulse wave velocity (1 point if $95th% for subjects with body mass index <85th%). Stiff arteries (S = 73) were defined as GSI $95th%. Differences between flexible (F = 597) and S groups were evaluated by t tests. Models were constructed to determine whether GSI was an independent determinant of LVM index or relative wall thickness (RWT).

**Results** The S group had more adverse cardiovascular risk factors, higher LVM index and RWT (P # .05) with a trend for abnormal cardiac geometry. Independent determinants of LVM index were higher GSI, age, body mass index, systolic blood pressure, heart rate, glycated hemoglobin A1c, male sex, and sex–by–heart rate interaction (r2 = 0.52; P # .05). GSI was also an independent determinant of RWT.

**Conclusions** Increased arterial stiffness in adolescents and young adults is associated with LVM index independently of traditional cardiovascular risk factors. Screening for arterial stiffness may be useful to identify high risk adolescents and young adults.


**Cardiac and Vascular Consequences of Pre-Hypertension in Youth**

Elaine M. Urbina, MD, MS;1 Philip R. Khoury, MS;1 Connie McCoy, RVT;1 Stephen R. Daniels, MD, PhD;2 Thomas R. Kimball, MD;1 Lawrence M. Dolan, MD1
Hypertension is associated with increased left ventricular mass (LVM) and carotid intima-media thickness (cIMT), which predict cardiovascular (CV) events in adults. Whether target organ damage is found in pre-hypertensive youth is not known. The authors measured body mass index, blood pressure, fasting glucose, insulin, lipids and C-reactive protein, LVM/height^2.7 (LVM index), diastolic function, cIMT, carotid stiffness, augmentation index, brachial artery distensibility, and pulse wave velocity (PWV) in 723 patients aged 10 to 23 years (29% with type 2 diabetes mellitus). Patients were stratified by blood pressure level (normotensive: 531, pre-hypertensive: 65, hypertensive: 127). Adiposity and CV risk factors worsened across blood pressure group. There was a graded increase in cIMT, arterial stiffness, and LVM index and decrease in diastolic function from normotension to pre-hypertension to hypertension. In multivariable models adjusted for CV risk factors, status as pre-hypertension or hypertension remained an independent determinant of target organ damage for LVM, diastolic function, internal cIMT, and carotid and arterial stiffness. Pre-hypertension is associated with cardiovascular target organ damage in adolescents and young adults. J Clin Hypertens (Greenwich). 2011;13: 332–342.

**Paper #18:** Progress in Cardiovascular Diseases 53 (2011) 369–378

**Progress of Ambient Air Pollution and Cardiovascular Disease Research in Asia**

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**Abstract**

Asian countries are with deteriorating air quality accompanying the rapid economic and social development of the past decades, and the potential health impacts of air pollution have been noticed by researchers in the region. We reviewed the scientific literature on air pollution and cardiovascular diseases (CVD) published by Asian researchers in English since the 1980s to determine whether the findings in Europe and North America can be extrapolated to Asia. Epidemiological studies show that short-term particulate matter pollution is a strong predictor for CVD morbidity and mortality and suggestive on cerebrovascular morbidity and mortality in newly developed countries in Asia. Multicountry epidemiological studies are needed to fully appreciate the extent of air pollution on CVD in Asia, especially less developed Asian countries. New cohort studies should be initiated to improve our understanding of particulate matter's toxicological pathways, long-term exposure effects, and gene-environment interaction on CVD among the Asian population. (Prog Cardiovasc Dis 2011;53:369-378)
**Paper #17:** Journal of Hypertension 2010, 28:1692–1698

**Increased arterial stiffness is found in adolescents with obesity or obesity-related type 2 diabetes mellitus**

Elaine M. Urbinaa, Thomas R. Kimballa, Philip R. Khourya, Stephen R. Danielsb and Lawrence M. Dolana

**Objective** Adults with obesity or obesity-related type 2 diabetes (T2DM) are at higher risk for cardiovascular disease possibly due to increased arterial stiffness. We sought to determine if arterial stiffness is increased in youth with obesity or T2DM as compared with lean controls.

**Methods** Youth age 10–24 years (NU670, 62% non-Caucasian, 35% male) were examined. They were stratified by the 85th% of BMI as lean (LU241), obese (OU234) or obese with T2DM (T2DMU195). Questionnaire, anthropometric, BP, laboratory (fasting glucose, insulin, HbA1c, lipids, CRP), physical activity, and DXA were collected. Brachial artery distensibility (BrachD), pulse wave velocity (PWV) and augmentation index (AIx) were measured. Group differences were evaluated by ANOVA. General linear multivariate models were constructed to elucidate independent determinates of arterial stiffness.

**Results** CV risk profile deteriorated from L to O to T2DM group. There was a progressive increase in AIx and PWV-trunk with progressive decline in BrachD from L to O to T2DM individuals (all P<0.05). Group (status as L, O or T2DM) was an independent predictor of arterial stiffness even after adjusting for CV risk factors.

**Conclusion** Arterial stiffness is increased in young individuals with obesity and obesity-related T2DM even after correction for risk factors.

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**Development and Validation of a Noninvasive Method to Estimate Cardiac Output Using Cuff Sphygmanometry**

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**Summary**

**Background:** Obtaining cardiac output (CO) non-invasively during routine blood pressure measurement can provide additional clinical value and improve hypertension management. A new method has been developed that estimates cardiac output using pulse-waveform-analysis (PWA) from a brachial cuff sphygmanometer. This study evaluates the ability of PWA to track changes in CO as derived by Doppler ultrasound during dobutamine stimulation.

**Hypothesis:** This study aimed to validate the PWA CO estimation over a wider CO range as would be obtained during dobutamine stimulation with Doppler ultrasound evaluation.
**Method:** 48 patients undergoing standard dobutamine stress echocardiography testing for accepted clinical indications were enrolled. Among them, 44 patients (age 36-83, 18 females, 26 males) with good waveform data for analyses provided estimates of CO in this study. Noninvasive measurements of CO were performed using both Doppler ultrasound recordings and PWA techniques simultaneously at each stage of dobutamine infusion.

**Results:** A total of 207 simultaneous pulse-waveform-analyses and Doppler measurements were taken during dobutamine stress on 44 cardiac patients. Linear regression analysis revealed good intra-patient correlation between pulse-waveform-analysis and Doppler at different dobutamine induced CO with coefficients from r=0.69 to 0.98 (p<0.05). Analysis of all patients yielded an overall correlation of r=0.82 (p<0.001, bias = 0.4 L/min, standard deviation =1.8 L/min).

**Conclusion:** Non-invasive CO measured from a sphygmomanometer using this PWA method correlate well with those of Doppler through a range of dobutamine-stimulated levels. It should be useful for monitoring hemodynamic changes in hypertensive and cardiac patients during routine blood pressure measurement.

**Key Words:** CARDIAC OUTPUT, PULSE WAVEFORM ANALYSIS, THERMO-DILUTION, DOPPLER ULTRASOUND, DOBUTAMINE STIMULATION, HYPERTENSION

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**Arterial blood pressure measurement and pulse wave analysis—their role in enhancing cardiovascular assessment**

**Abstract.** The most common method of clinical measurement of arterial blood pressure is by means of the cuff sphygmomanometer. This instrument has provided fundamental quantitative information on arterial pressure in individual subjects and in populations and facilitated estimation of cardiovascular risk related to levels of blood pressure obtained from the brachial cuff. Although the measurement is taken in a peripheral limb, the values are generally assumed to reflect the pressure throughout the arterial tree in large conduit arteries. Since the arterial pressure pulse becomes modified as it travels away from the heart towards the periphery, this is generally true for mean and diastolic pressure, but not for systolic pressure, and so pulse pressure. The relationship between central and peripheral pulse pressure depends on propagation characteristics of arteries. Hence, while the sphygmomanometer gives values of two single points on the pressure wave (systolic and diastolic pressure), there is additional information that can be obtained from the time-varying pulse waveform that enables an improved quantification of the systolic load on the heart and other central organs. This topical review will assess techniques of pressure measurement that relate to the use of the cuff sphygmomanometer and to the non-invasive registration and analysis of the peripheral and central arterial pressure waveform. Improved assessment of cardiovascular function in relation to treatment and management of high blood pressure will result from future developments in the indirect measurement of arterial blood pressure that involve the conventional cuff
sphygmomanometer with the addition of information derived from the peripheral arterial pulse.

**Keywords:** arterial pressure, sphygmomanometer, hypertension, ageing, cardiovascular risk, pulse pressure, heart rate, pulse waveform, pulse wave analysis, transfer function, radial pulse, carotid pulse, central aortic pressure, arterial impedance, pulse wave velocity, arterial stiffness, pulse amplification, vascular haemodynamics

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**Gender differences in the relationships among obesity, adiponectin and brachial artery distensibility in adolescents and young adults**

E M Urbina, P Khoury, L J Martin, D D'Alessio and L M Dolan

**Abstract**

**Background:** Obesity-related cardiovascular diseases (CVDs) are a major cause of cardiovascular (CV) mortality. Obesity-related reduction in vascular protective adipose-derived proteins, such as adiponectin (APN), has an important role.

**Methods:** We compared brachial artery distensibility (BrachD) with APN, the level of adiposity and other CV risk factors (CVRFs) in 431 post-pubertal subjects (mean 17.9 years). Gender differences in average values were examined by *t*-tests. Correlations among BrachD, obesity and other CVRFs were examined. Regression analysis was performed to determine whether APN provided an independent contribution to BrachD, while controlling for obesity and other CVRFs.

**Results:** Male subjects had lower BrachD (5.72±1.37 vs 6.45±1.60% change per mmHg, *P*<0.0001) and lower APN (10.50±4.65 vs 13.20±6.53; all *P*<0.04) than female subjects. BrachD correlated with APN (*r*=0.25, *P*<0.0001). Both BrachD and APN correlated with measures of body size, including height, weight and body mass index (BMI). Both correlated with higher systolic blood pressure, glucose, insulin and lower high-density lipoprotein cholesterol (all *P*<0.01). In multivariate analysis, APN, gender, APN*gender and BMI z-score predicted BrachD (*r*²=0.305). On the basis of gender difference, only BMI z-score was significant for male subjects (*r*²=0.080), whereas APN and BMI z-score contributed for female subjects (*r*²=0.242, all *P*<0.0001).

**Conclusions:** BrachD is independently influenced by obesity in both male and female subjects. In female subjects, APN exerts an additional independent effect even after adjusting for blood pressure (BP), lipid levels and insulin. Differences in the effect of
the APN–adiposity relationship on obesity-related vascular disease may be one reason for gender differences in the development and progression of atherosclerosis.

**Keywords:** elasticity, pediatrics, sex, risk factors, brachial artery

**Paper #13:**

http://hyper.ahajournals.org/cgi/content/abstract/54/5/919?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=EM+Urbina%2C+2009&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT

*Hypertension. 2009; 54:919-950*

**Noninvasive Assessment of Subclinical Atherosclerosis in Children and Adolescents - Recommendations for Standard Assessment for Clinical Research: A Scientific Statement From the American Heart Association**

Elaine M. Urbina, MD, FAHA, Chair; Richard V. Williams, MD; Bruce S. Alpert, MD, FAHA; Ronnie T. Collins, MD; Stephen R. Daniels, MD, PhD, FAHA; Laura Hayman, PhD, RN, FAHA; Marc Jacobson, MD, FAHA; Larry Mahoney, MD, FAHA; Michele Mietus-Snyder, MD; Albert Rocchini, MD, FAHA; Julia Steinberger, MD, MS; Brian McCrindle, MD, MPH, FAHA on behalf of the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young

Deterioration in endothelial function and arterial stiffness are early events in the development of cardiovascular diseases. In adults, noninvasive measures of atherosclerosis have become established as valid and reliable tools for refining cardiovascular risk to target individuals who need early intervention. With limited pediatric data, the use of these techniques in children and adolescents largely has been reserved for research purposes. Therefore, this scientific statement was written to (1) review the current literature on the noninvasive assessment of atherosclerosis in children and adolescents, (2) make recommendations for the standardization of these tools for research, and (3) stimulate further research with a goal of developing valid and reliable techniques with normative data for noninvasive clinical evaluation of atherosclerosis in pediatric patients. Precise and reliable noninvasive tests for atherosclerosis in youth will improve our ability to estimate future risk for heart attack and stroke. Currently, large longitudinal studies of cardiovascular risk factors in youth, such as the Bogalusa and Muscatine studies, lack sufficient adult subjects experiencing hard outcomes, such as heart attack and stroke, to produce meaningful risk scores like those developed from Framingham data.

**Key Words:** AHA Scientific Statements • pediatrics • elasticity imaging technique • brachial artery • risk factors • vasculature • carotid arteries

**Paper #12:**

http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6WDS-4WM052N-2&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&_docanchor=&view=c&_searchStrId=1140895210&_rerunOrigin=google&_acct=C000050221&_version=1&_userid=10&md5=2f20017c29921dcba99e3a127e27210

*Environmental Research Volume 109, Issue 7*, October 2009, Pages 900-905
Effects of environmental noise exposure on ambulatory blood pressure in young adults


Abstract

Epidemiological studies have demonstrated that environmental noise exposure is associated with hypertension in middle-aged and older populations, but the relationship in the young subpopulation and between the genders is still unclear. This panel study investigated effects of environmental noise exposure on 24-h ambulatory blood pressure in 60 adults aged 18–32 years. Individual noise exposure and personal blood pressure were measured simultaneously for 30 males and 30 females. Linear mixed-effects regression models were applied to estimate effects. Total subjects (56.6±16.5 A-weighted decibels (dBA)) had transient elevations of 1.15 (95% CI=0.86–1.43) mmHg SBP and 1.16 (0.93–1.38) mmHg DBP at daytime, as well as 0.74 (0.21–1.26) mmHg SBP and 0.77 (0.34–1.20) mmHg DBP at nighttime, significantly associated with a 5-dBA increase in noise exposure. Such effects on SBP and DBP still persisted at the 30- and 60-min time-lagged noise exposure. Per 5-dBA increase in 24-h average noise exposure was significantly associated with sustained increments of 1.15 (0.76–1.54) mmHg SBP and 1.27 (0.96–1.58) mmHg DBP in males (57.4±16.0 dBA), as well as the higher levels of 1.65 (1.36–1.94) mmHg SBP and 1.51 (1.27–1.75) mmHg DBP in females (55.9±17.0 dBA). We found that environmental noise exposure may have elevated effects on adults’ blood pressure. Young females are more susceptible to noise exposure than males.

Keywords: Blood pressure; Hypertension; Noise exposure; Panel study; Young adults

Abbreviations: 95% CI, 95% confidence interval; dBA, A-weighted decibel; DBP, diastolic blood pressure; OR, odds ratio; SBP, systolic blood pressure

Paper #11:

doi: 10.1097/MBP.0b013e3283057ae4 Analytical Methods and Statistical Analyses

Reproducibility of systemic hemodynamics in stable chronic hemodialysis: a pilot study

Vij, Rajiv S.; Motiwala, Shaheen; Peixoto, Aldo J.

Abstract

Objective: Hemodynamic measurements are important in the understanding of hemodialysis (HD) hypertension and intradialytic hypotension. The reproducibility of hemodynamic measurements in HD patients is not known and is the objective of this report.
Methods: We enrolled 13 male patients (mean age 63±13 years) on stable chronic HD. Blood pressure (BP) and hemodynamic variables were obtained with a pulse dynamic technology device. Measurements were taken before and after HD, in the supine and standing positions over a 2-week period.

Results: Ranges for the average intraindividual standard deviation for each hemodynamic variable before and after HD in both supine and standing positions were: 8.3-14.5 mmHg for oscillometric systolic BP; 4.1-10.7 mmHg for oscillometric diastolic BP; 10.7-14.5 mmHg for manual systolic BP; 5.4-8.8 mmHg for manual diastolic BP; 131.4-188.9 mmHg/s for left ventricular dP/dtmax; 0.17-0.27 L/min/m² for cardiac index; 142.4-222.6 dynes/s/cm² for systemic vascular resistance; 0.59-1.13%/mmHg for brachial artery distensibility; and 0.09-0.15 ml/mmHg for systemic vascular compliance. Repeated measures analysis of variance results showed no significant variability in measures. Intraclass correlation coefficient ranges were 0.58-0.72 for oscillometric systolic BP, 0.46-0.83 for oscillometric diastolic BP, 0.41-0.62 for manual systolic BP, 0.57-0.84 for manual diastolic BP, 0.10-0.78 for left ventricular dP/dtmax, 0.63-0.84 for cardiac index, 0.47-0.80 for systemic vascular resistance, 0.40-0.84 for brachial artery distensibility, and 0.62-0.88 for systemic vascular compliance. No correlation was observed between interdialytic weight gain and hemodynamic variability.

Conclusion: In this pilot study, hemodynamic variables have acceptable reproducibility in chronic stable HD patients. Our results are relevant to the use of hemodynamic monitoring in HD practice and research.


Ambulatory blood pressure monitoring: a useful tool to diagnose hypertension and supervise it's treatment.

Shrestha B, Dhungel S, Pahari SK.

Automatic ambulatory blood pressure monitoring (ABPM) for the diagnosis and treatment of hypertension (HTN) is not common in Nepal. The purpose of this study is to evaluate various characteristics of hypertensive patients undergoing ABPM before starting antihypertensive treatment and evaluate the adequacy of the blood pressure (BP) control during antihypertensive treatment. ABPM was performed in 108 consecutive patients attending the hypertension clinic of Nepal Medical College Teaching Hospital from 1st March 2005 to 30th April 2007 with DynaPulse 5000A (version 3.20q) for approximately 24 hours. Male female ratio was 59:49 and age (mean +/- SD) was 47.8 +/- 16.4 years. The maximum use of ABPM (25.9%) was noted in the age group of 40-49 years. Body mass index was 25.7 +/- 3.8. Diabetes was noted in 13% patients. Maximum use of ABPM was observed in Newar ethnic group (56.5%). ABPM was used for the diagnosis of HTN in 62.0% patients and for follow up
in 38.0% patients. Severe HTN was seen in approximately half (47.2%) of the hypertensive patients. Majority of the patients (88.0%) had dipper type of HTN. Beta-blocker (35.6%), ACE inhibitor/Losartan (31.1%) and calcium channel antagonist (26.7%) were the usual antihypertensive agents used. Single antihypertensive agent was used in the majority of patients (64.1%). In a small number of patients (42, 38.9%) undergoing ABPM during antihypertensive therapy, the adequacy of control of HTN was very poor.

**Paper #9:** [http://cjasn.asnjournals.org/cgi/content/full/3/1/184](http://cjasn.asnjournals.org/cgi/content/full/3/1/184)


**Vascular Stiffness: Its Measurement and Significance for Epidemiologic and Outcome Studies**

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Arterial stiffness is recognized increasingly as an important component in the determination of cardiovascular risk, particularly in chronic kidney disease and ESRD populations. Although the technique has been around for nearly 100 yr, in the past 20 to 25 yr, pragmatic noninvasive approaches have allowed the incorporation of arterial stiffness measurements, usually in the form of aortic pulse wave velocity (PWV), into clinical assessment of patients. In populations with high cardiovascular risk, especially those with ESRD, aortic PWV measurements provide predictive utility independent of the standard brachial arterial BP measurements. This review briefly discusses the history of vascular dynamics, the determinants of PWV, and some of the available technologies in current use and concludes with a section on the relevance of arterial stiffness measurements in populations of particular interest to nephrologists.


Critical Care Medicine: February 2007 - Volume 35 - Issue 2 - pp 422-429; doi: 10.1097/01.CCM.0000254722.50608.2D

Clinical Investigations
Nurse-physician perspectives on the care of dying patients in intensive care units: Collaboration, moral distress, and ethical climate *

Hamric, Ann B. PhD, RN, FAAN; Blackhall, Leslie J. MD, MTS

Abstract
Objective: To explore registered nurses' and attending physicians' perspectives on caring for dying patients in intensive care units (ICUs), with particular attention to the relationships among moral distress, ethical climate, physician/nurse collaboration, and satisfaction with quality of care.
Design: Descriptive pilot study using a survey design.
Setting: Fourteen ICUs in two institutions in different regions of Virginia.
Subjects: Twenty-nine attending physicians who admitted patients to the ICUs and 196 registered nurses engaged in direct patient care.
Interventions: Survey questionnaire.
Measurements and Main Results: At the first site, registered nurses reported lower collaboration ($p < .001$), higher moral distress ($p < .001$), a more negative ethical environment ($p < .001$), and less satisfaction with quality of care ($p = .005$) than did attending physicians. The highest moral distress situations for both registered nurses and physicians involved those situations in which caregivers felt pressured to continue unwarranted aggressive treatment. Nurses perceived distressing situations occurring more frequently than did physicians. At the second site, 45% of the registered nurses surveyed reported having left or considered leaving a position because of moral distress. For physicians, collaboration related to satisfaction with quality of care ($p < .001$) and ethical environment ($p = .004$); for nurses, collaboration was related to satisfaction ($p < .001$) and ethical climate ($p < .001$) at both sites and negatively related to moral distress at site 2 ($p = .05$). Overall, registered nurses with higher moral distress scores had lower satisfaction with quality of care ($p < .001$), lower perception of ethical environment ($p < .001$), and lower perception of collaboration ($p < .001$).
Conclusions: Registered nurses experienced more moral distress and lower collaboration than physicians, they perceived their ethical environment as more negative, and they were less satisfied with the quality of care provided on their units than were physicians. Provider assessments of quality of care were strongly related to perception of collaboration. Improving the ethical climate in ICUs through explicit discussions of moral distress, recognition of differences in nurse/physician values, and improving collaboration may mitigate frustration arising from differences in perspective.

Paper #7:

C-reactive protein, an 'intermediate phenotype' for inflammation: human twin studies reveal heritability, association with blood pressure and the metabolic syndrome, and the influence of common polymorphism at catecholaminergic/beta-adrenergic pathway loci
Abstract
Background: C-reactive protein (CRP) both reflects and participates in inflammation, and its circulating concentration marks cardiovascular risk. Here we sought to understand the role of heredity in determining CRP secretion.

Methods: CRP, as well as multiple facets of the metabolic syndrome, were measured in a series of 229 twins, both monozygotic (MZ) and dizygotic (DZ), to estimate trait heritability ($h^2$). Single nucleotide polymorphism (SNP) genotyping was done at adrenergic pathway loci. Haplotypes were inferred from genotypes by likelihood methods. Association of CRP with hypertension and the metabolic syndrome was studied in a larger series of 732 individuals, including 79 with hypertension.

Results: MZ and DZ twin variance components indicated substantial $h^2$ for CRP, at $56 \pm 7\%$ ($P < 0.001$). CRP was significantly associated ($P < 0.05$) with multiple features of the metabolic syndrome in twins, including body mass index (BMI), blood pressure (BP), leptin and lipids. In established hypertension, elevated CRP was associated with increased BP, BMI, insulin, HOMA (index of insulin resistance), leptin, triglycerides and norepinephrine. Twin correlations indicated pleiotropy (shared genetic determination) for CRP with BMI ($P = 0.0002$), leptin ($P < 0.001$), triglycerides ($P = 0.002$) and systolic blood pressure (SBP) ($P = 0.042$). Approximately 9800 genotypes (43 genetic variants at 17 loci) were scored within catecholaminergic pathways: biosynthetic, receptor and signal transduction. Plasma CRP concentration in twins was predicted by polymorphisms at three loci in physiological series within the catecholamine biosynthetic/β-adrenergic pathway: TH (tyrosine hydroxylase), ADRB1 (β1-adrenergic receptor) and ADRB2 (β2-adrenergic receptor). In the TH promoter, common allelic variation accounted for up to 6.6% of CRP inter-individual variance. At ADRB1, variation at Gly389Arg predicted 2.8% of CRP, while ADRB2 promoter variants T-47C and T-20C also contributed. Particular haplotypes and diplotypes at TH and ADRB1 also predicted CRP, though typically no better than single SNPs alone. Epistasis (gene-by-gene interaction) was demonstrated for particular combinations of TH and ADRB2 alleles, consistent with their actions in a pathway in series. In an illustration of pleiotropy, not only CRP but also plasma triglycerides were predicted by polymorphisms at TH ($P = 0.0053$) and ADRB2 ($P = 0.027$).

Conclusions: CRP secretion is substantially heritable in humans, demonstrating pleiotropy (shared genetic determination) with other features of the metabolic syndrome, such as BMI, triglycerides or BP. Multiple, common genetic variants in the catecholaminergic/β-adrenergic pathway contribute to CRP, and these variants (especially at TH and ADRB2) seem to interact (epistasis) to influence the trait. The results uncover novel pathophysiological links between the adrenergic system and inflammation, and suggest new strategies to probe the role and actions of inflammation within this setting.
Remote Anesthetic Monitoring Using Satellite Telecommunications and the Internet

Stephen W. Cone, MD*, Lynne Gehr, MD, Russell Hummel, MS*, and Ronald C. Merrell, MD, FACS*

Abstract
Remote collaboration for anesthesia requires considerable sharing of physiologic data, audio, and images on a consistent data platform. A low-bandwidth connection between Ecuador and the United States supported effective joint management of operative plan, airway, intraoperative decisions, and recovery. Transmission with a 64-Kbps InMarSat satellite telephone (Thrane & Thrane, Denmark) connection from hospitals in Macas and Sucúa, Ecuador, to Richmond, Virginia, included preoperative patient evaluations, video of endotracheal intubations, electrocardiogram waveforms, pulse oximetry measurements, arterial blood pressure readings, capnography readings, and auscultation of breath sounds.

Ventriculo-vascular interactions in patients with β thalassaemia major

Y F Cheung1, S Y Ha2, G C F Chan2

Abstract
Objectives: To determine potential interactions between the heart and arterial system in patients with β thalassaemia major.
Design and patients: Vascular compliance, systemic vascular resistance, and left ventricular (LV) contractility was determined in 34 asymptomatic thalassaemia patients at 2–4 hours after blood transfusion and also in 34 age and sex matched controls using a non-invasive device. The results were compared between groups and inter-relationships between LV contractility and indices of vascular load were explored.
Setting: Tertiary paediatric cardiac centre.
Results: When compared with controls, patients had greater systemic vascular resistance (1633 (259) v 1377 (276) dynes/s/cm², p < 0.001) and effective arterial elastance (E_a) (1.86 (0.25) v 1.65 (0.29) mm Hg/ml, p = 0.001), an index of combined pulsatile and static vascular load. On the other hand, their systolic blood pressure (104 (9) v 112 (13) mm Hg, p = 0.006), pulse pressure (45 (9) v 57 (10) mm Hg, p < 0.001), adjusted systemic vascular compliance (1.21 (0.09) v 1.37 (0.14), p < 0.001), adjusted brachial artery distensibility (21 (0.29) v 7.95 (0.29)%/mm Hg, p < 0.001) and LV+dP/dt (1059 (183) v 1239 (237) mm Hg/s, p = 0.001) were significantly lower. Significant determinants of LV contractility, as reflected by LV+dP/dt, were age (standardised β = −0.24, p = 0.003), body mass index (standardised β = −0.34, p = 0.004), systolic blood pressure (standardised β = 0.90, p < 0.001), and effective E_a (standardised β = −0.50, p <
0.001) (model $R^2 = 0.69$). No significant correlation existed between serum ferritin concentration and any of the cardiac or vascular indices.

**Conclusion:** An unfavourable ventriculo-vascular interaction, as characterised by impaired cardiac contractility and increased static and pulsatile vascular load, occurs in patients with β thalassaemia major.

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**Paper #4:** [http://heart.bmj.com/content/91/6/773.1.extract](http://heart.bmj.com/content/91/6/773.1.extract)

*Heart 2005; 91:773 doi:10.1136/hrt.2004.04470; Miscellanea*

**Left ventricular pseudoaneurysm in a child**

*S S Kothari, A Roy, G Sharma;*

*Images in cardiology*

A 14 year old girl presented with a history of fatigue, atypical chest pain, and breathlessness for one month. Her haemoglobin was 8.3 g/dl and erythrocyte sedimentation rate (ESR) was 48 mm in the first hour. She had …

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**Paper #3:** [http://ntr.oxfordjournals.org/cgi/content/abstract/7/4/581](http://ntr.oxfordjournals.org/cgi/content/abstract/7/4/581)

*Nicotine & Tobacco Research 2005 7(4):581-590; doi:10.1080/146222005000185199*

**The Influence of Gender, Race, and Menthol Content on Tobacco Exposure Measures**

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Massachusetts College of Pharmacy and Health Sciences Boston, MA
Palo Alto Center for Pulmonary Disease Prevention Palo Alto, CA and Division of Pulmonary & Critical Care Medicine, Department of Medicine, Stanford University School of Medicine Stanford, CA
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**Abstract**

Research has suggested that race, gender, and menthol cigarette use influence tobacco-smoke exposure measures and smoking-related disease risk. For example, a high proportion of Black smokers prefer menthol cigarettes and, despite smoking fewer cigarettes per day (CPD) than do Whites, tend to have higher cotinine levels. Additionally, Black males are more at risk for smoking-related lung cancer. High cotinine levels and smoking menthol cigarettes may lead to higher toxin intake, which contributes to increased disease risk. We explored the relationship between tobacco exposure variables (i.e., cotinine, CPD, carbon monoxide [CO], nicotine content, and nicotine dependence) with respect to race, gender, and menthol content in a sample of 307 smokers recruited from the greater Boston area to participate in a smoking cessation treatment trial. The pattern of correlations between tobacco exposure measures and
cotinine showed a consistently positive correlation between cotinine and CO in all smokers and a correlation between cotinine and CPD in those who smoked nonmenthol cigarettes. Cotinine and CPD correlations varied by gender and race among menthol cigarette smokers. Consistently, we found a significant genderxracexmenthol interaction on salivary cotinine level as well as cotinine/CPD ratio. These findings suggest that the relationship between number of cigarettes consumed and salivary cotinine is more complex than previously believed. It is not sufficient to look at race alone; researchers and clinicians need to look at race and gender concurrently, as well as type of cigarette consumed.


**A novel intelligent sphygmogram analyzer for health monitoring of cardiovascular system**

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**Abstract**

A novel sphygmogram analyzer (SGA) with embedded medical advisory system is proposed to conquer the drawbacks of the existing commercial systems such as clumsy volume, awkward user-interface, and weak intelligence, etc. Firstly, benefited from the advanced embedded systems and micro-processing chips, the elementary components of SGA can be condensed into a tiny micro-system, which will greatly contribute to the wearable health monitoring devices. Secondly, the proposed SGA is distinguished due to the embedded medical advisory system, which can provide the comparative medical services while adaptive to the source restricted embedded platforms. In this paper, the hemodynamic analysis of sphygmogram is firstly introduced and then, the implementation of SGA, including data acquiring and analyzing unit (DA2U), embedded medical advisory system (e-MAS) boosted for the application of soft computing, and the distributed information exchanging framework, is addressed in detail.

**Keywords:** Sphygmogram analyzer; Embedded systems; Medical advisory system; Health monitoring

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Paper #1: [http://www.nature.com/ajh/journal/v15/n3s/abs/ajh2002368a.html](http://www.nature.com/ajh/journal/v15/n3s/abs/ajh2002368a.html)

**P-78: Cardiovascular reactivity and diurnal arterial compliance during nebivolol treatment of young obese essential hypertensives**

Sergey A. Golubev1,2, Jeffrey J. Tsai1,2, Maxim N. Mily1,2 and Vyacheslav V. Afanassiev1,2
Abstract
To evaluate changes in systemic and peripheral hemodynamics in resting, under stress tests and daily life conditions during short-term treatment with nebivolol in a special high-risk population twelve randomly selected verified never treated essential hypertensives (aged 38.6 ± 8.4 years, body mass index 31.2 ± 5.2 kg/m2) underwent ambulatory blood pressure monitoring (DynaPulse 5000A; Pulse Metric, Inc., USA), standard mental arithmetic (MT) and cold pressor (CT) tests before and 4 weeks after treatment with nebivolol (5 mg once daily). Systemic and local (brachial artery) vascular hemodynamics parameters were derived blindly from each measurement by previously validated web-based pulse dynamics analysis technology. Ambulatory BP and HR were significantly reduced by nebivolol without excessive nighttime falls and variability affecting. 24-hour, but not resting systemic vascular compliance was significantly improved (1.19 ± 0.11 vs. 1.36 ± 0.16 mL/mm Hg; p<0.05) without changes in brachial artery compliance. Nebivolol reduced diastolic BP response to MT (17.0 ± 8.5 vs. 14.0 ± 11.2 mm Hg; p<0.05), and enhanced the rise in systemic vascular resistance during CT (1.5 ± 1.6 vs. 4.7 ± 3.3 mm Hg; p<0.05).
Thus, in the studied overweight young essential hypertensives, under significant short-term antihypertensive effects of nebivolol during daily life and MT, favorable changes in systemic but not in brachial artery compliance are registered, probably due to main peripheral points of nitric oxide modulating. The last might result in some discrepancies registered in hemodynamics and compliance changes between different stress tests, resting and 24-hour conditions. Daily arterial compliance evaluation is useful for comprehensive judgement about vascular effects of antihypertensive agents.

Keywords: Nebivolol, Arterial Compliance, Cardiovascular Reactivity
Appendix E: *Samples of DynaPulse Hemodynamic Profile Report*

**Sample 1**

DynaPulse Analysis Cloud

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**Hemodynamic Report**


**Dynapulse Hemodynamic Profiling Service - Physician Name: n/a n/a**

**Patient ID:**

**Patient Name:**

Birthdate | Sex: 12/25/1944 | Male

**Body Mass Index (BMI):** 25.0

**Auscultatory Systolic/Diastolic (K1/K4):**

120 / 75

**HR:** 71 bpm

---

**CENTRAL BP PARAMETERS**

- End Systolic (mmHg): 133
- End Diastolic (mmHg): 72
- MAP (mmHg): 88
- PP (mmHg): 61

**CARDIAC PARAMETERS**

- LV Ejection Time (sec): 0.251
- LV DP/dt Max (mmHg/s): 1,556
- LV Contractility (L/L): 16.82
- Cardiac Output (L/min): 5.57
- Cardiac Index (L/min/m²): 3.12
- Stroke Volume (mL): 74.3
- Stroke Vol Index (mL/m²): 41.6

**SYSTEMIC VASCULAR PARAMETERS**

- SV Compliance (mL/mmHg): 1.22
- SV Resistance (dynes*sec/cm²): 1,263

**BRACHIAL ARTERY PARAMETERS**

- BA Compliance (mL/mmHg): 0.074
- BA Distensibility (%/mmHg): 5.78
- BA Resistance (kdynes*sec/cm²): 168

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Sample 2

Patient List | Upload | Export | Administration | Working Org

>> Home >> Patients >> Patient List >> Hemodynamic Table Report

Hemodynamic Report


DynaPulse Hemodynamic Profiling Service - Physician Name: n/a n/a

Patient ID: 

Patient Name: 

Birthdate | Sex: 9/21/1953 | Male


Body Mass Index (BMI): 33.9

Auscultatory eq. Systolic/Diastolic (K1)/(K4)/(K5)

153 / 93 | 88 mmHg

HR: 72 bpm

The red, yellow and blue markers are for End Syst., MAP and End Dia.

CENTRAL BP PARAMETERS

End Systolic (mmHg) 165
End Diastolic (mmHg) 88
MAP (mmHg) 110
PP (mmHg) 77

CARDIAC PARAMETERS

LV Ejection Time (sec) 0.207
LV DP/dt Max (mmHg/s) 1,531
LV Contractility (1/s) 15.30
Cardiac Output (l/min) 4.96
Cardiac Index (L/min/m²) 2.81
Stroke Volume (mL) 67.8
Stroke Vol Index (mL/m²) 38.4

SYSTEMIC VASCULAR PARAMETERS

SV Compliance (mL/mmHg) 0.88
SV Resistance (dyne*sec/cm²) 1,775

BRACHIAL ARTERY PARAMETERS

BA Compliance (mL/mmHg) 0.066
BA Distensibility (%) (mmHg) 4.50
BA Resistance (dyne*sec/cm²) 178

[Normal Range(Male)]

105 - 143
54 - 83
70 - 101
39 - 72

[0.207 - 0.300]
[847 - 1506]
[12.39 - 19.08]
[4 - 8]

[2.5 - 4.2]
[60 - 130]

[30 - 65]

[1.02 - 2]
[770 - 1500]

[0.056 - 0.132]
[4.38 - 9.28]

[80 - 317]

Measured value out of normal range. Evaluate if high blood pressure persists.

Measured value out of normal range. Evaluate for other CV condition(s) or artifacts.

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**Sample 3**

Patient List | Upload | Export | Administration | Working Org

---

**Hemodynamic Report**

**Patient ID:** n/a n/a
**Physician Name:** n/a

**Measurement Time:** 1/26/2008 16:06

**Auscultatory Systolic/Diastolic:**

<table>
<thead>
<tr>
<th>141</th>
<th>82</th>
<th>79 mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR:</td>
<td>83</td>
<td>bpm</td>
</tr>
</tbody>
</table>

The red, yellow and blue markers are for End Syst., MAP and End Dia.

### CENTRAL BP PARAMETERS
- End Systolic (mmHg): 156
- End Diastolic (mmHg): 79
- MAP (mmHg): 103
- PP (mmHg): 77

### CARDIAC PARAMETERS
- LV Ejection Time (sec): 0.237
- LV dp/dt Max (mmHg/sec): 1.575
- LV Contractility (1/sec): 16.64
- Cardiac Output (L/min): 5.66
- Cardiac Index (L/min/m²): 3.39
- Stroke Volume (mL): 68.0
- Stroke Vol Index (mL/m²): 40.7

### SYSTEMIC VASCULAR PARAMETERS
- SV Compliance (mL/mmHg): 0.88
- SV Resistance (dynes*sec/cm²): 1,455

### BRACHIAL ARTERY PARAMETERS
- BA Compliance (mL/mmHg): 0.044
- BA Distensibility (%/mmHg): 4.49
- BA Resistance (kdynes*sec/cm²): 275

### Notes:
- Measured value out of normal range. Evaluate if high blood pressure persists.
- Measured value out of normal range. Evaluate for other CV condition(s) or artifacts.

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Vista, California, USA