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Application of Static Pressure Change in Estimation of Elastic Parameters of Rabbit's Artery by Doppler Ultrasound

Backgrounds/Objectives: Noninvasive evaluation of elastic properties of vessel wall is hampered by the absence of methods to directly asse ss local elasticity. In order to invasively record the static pressure of carotid artery dur ing cardiac cycle in rabbit s and compare it with noninvasive technique, T-shaped tubes have been designed and constructed and calibrated. A noninvasive method to measure static pressure in arteries and finally estimate the elasticity of vessels is provided.

Materials and Methods: In male white rabbits, we estimated the static pressure changes in carotid artery noninvasively by measuring blood flow velocities throughout cardiac cycle using Color Doppler Ultrasound. The blood flow ve locities were converted to static pressure changes by using energy conservation low. The st atic pressure changes of arterial wall were estimated. These parameters were compared wi th measured actual static pressure changes using a T-shaped tube, that was inserted into the carotid artery and the static pressure change was measured in the side br anch of the tube. The elastic parameters in both methods were calculated and compared by pa ired t-test statistical analysis.

Results: Statistical analysis of static pressure c hanges and elastic parameters in both methods showed that there was no significant difference between the two methods.

Conclusion: By applying this noninvasive approach, we can estimate elastic parameters in arteries of normal people and patients with, or at risk of developing atherosclerosis for determination of disease extent. We propose this noninvasive method as an accurate and safe way suitable for screening of large popula tions of young and symptom-free individuals.

Keywords: Doppler ultrasound, static pressure change, elastic parameters, carotid artery

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Received Deember 10, 2004;
Accepted after revision April 12, 2005.

June 2005; 2:141-146

Introduction

Cardiovascular disease is responsible for over 50% of all deaths in the Western world. [1] The normal artery has a three-layer structure: the intima, which is a thin membrane of squamous epithelium in contact with the blood; the media, which consists of smooth muscle and elastic tissue; and the adventitia, which is the outer layer composed of fibrous tissue. Disease progression in arteries is associated with thickening of the intimal layer, lipid deposition, plaque formation, and reduction in the luminal diameter, with eventual vessel occlusion.

The study of dynamic properties of the wall of large arteries such as the carotid is becoming more common, since the mechanical and structural properties of the arterial wall may change before the occurrence of clinical symptoms of cardiovascular disease, and noninvasive measurement of arterial wall stiffness may be useful in identifying individuals at risk of cardiovascular disease. [2-5]

Many studies have been performed to show brachial artery pressure diameter relationship *in vivo* and *in vitro*, either invasively or noninvasively, in animal as well as in human. [3, 6-9] The application of ultrasound in vascular imaging has been commenced since 1950s and its role as an appropriate method for obtaining the dynamics of vascular system has been appreciated.

Many investigations have been conducted to measure the arterial diameter changes during the cardiac cycle with the use of ultrasound waves. Such measurements are of interest in fundamental studies of physiology and disease development, as well as clinically for determination of disease location and extent. Arterial stiffness indices have been estimated by measuring brachial artery blood pressure directly and arterial diameter changes during cardiac cycle using ultrasonography. [6, 10-14] However, there are controversial reports about the amount of estimated pressure-strain elastic modulus in arteries of different people [10,13,15,16], which may be due to the application of brachial arterial changes instead of arterial static pressure in calculation of pressure-strain elastic modulus. Because of the gradual diminution of pressure-wave towards the peripheral arteries, the maximum pressure in the brachial artery is different from the main arterial pressure so that the intraarterial pressure noninvasively is about 10 percent less than the measured pressure changes, which causes underestimation of arterial stiffness. [10, 17] The effect of increased blood pressure on mean velocity of blood flow [18], and maximum velocity of blood flow has been studied and it has been showen that higher blood pressures make significant increases in blood flow velocity.

The effect of atherosclerosis on distensibility of arteries has been investigated by measuring brachial pressure changes. It was showen that atherosclerosis may have some effect on the mechanical properties of arterial wall; however, its disadvantage was using brachial artery for estimations of the carotid artery blood pressure. [1, 19] Therefore, a noninvasive method to estimate static pressure changes of arterial wall seems quite essential.

In this study, in order to estimate the static pressure of carotid arterial wall, the static pressure changes of arterial wall in laboratory rabbits was determined noninvasively using color Doppler ultrasound, and with regard to the energy conservation law, the blood flow velocity was related to static pressure. To investigate the probality of changes in estimating the static pressure changes and ultimately elastic parameters by Doppler ultrasound, the static pressure was measured invasively by introduction of cannula inside rabbit artery.

Materials and Methods

The mean velocity of blood flow at the first part of the aorta is 40 cm/s. The velocity of aortic blood flow ranges between 120 cm/s in the systolic phase and a negative value at the time of blood recoil before aortic valve closure in the diastole. The blood flow velocity in the systolic phase is also higher than that in the diastolic phase. But the flow is continuously directed forward because the vessel's wall which was recreated during the systolic phase, would transfer its elastic return force to the blood during the diastolic phase which is called Wind vessel. [20]

Based on the energy conservation law, total fluid energy per unit volume of blood equals the sum of the pressure, plus a factor related to the influence of gravity, plus the kinetic energy:

$$P_t = P + \rho gh + \rho V^2/2 \qquad (1)$$

In the above equation, P_t is the total pressure of fluid; P is the static pressure; ρ is the fluid density; g is the gravitation acceleration; h is the height above or under a reference level; and V is the flow velocity.

The arterial pressure can be calculated by an intraarterial cannula, an electronic manometer, and appropriate calibration. If the artery is interrupted distal to the cannula, the end pressure would be recorded. So that, the blood flow would be interrupted and all the kinetic energy of blood converted to pressure energy. By inserting a T-shaped tube, the pressure at the side tube could be determined. If the resistance is negligible, the side pressure would equal the static pressure. This pressure is less than the end pressure as much as the kinetic energy of blood flow. The measurement of blood pressure in a supine subject is not accompanied by hydrostatic pressure; however, when the patient is sitting or standing, the hydrostatic pressure must be considered.

For noninvasive estimation of static pressure changes of carotid artery, we studied 16 laboratory white male rabbits (*Oryctolagus-Cuniculus*) with an average weight of 2,092

were purchased from the Pasteur Institute of Iran and kept as a group and were fed sufficiently before they surgery.

The anasthtic drugs, Ketamin 10% (Alafsan Co.) and Chanazine 2% (Chanelle Co.) were injected into the rabbit's peritoneal cavity at a dose 0.5 ml/kg of weight. After the rabbits were anesthesized and stabled, color Doppler ultrasonography (GE logic 500 MD, 5 MHz, mechanical array probe) was performed. The blood flow velocities of the carotid artery during the systolic and diastolic phases were recorded (Figure 1). Considering equation 2, the blood flow velocity was related to the static pressure changes:

$$\Delta P_s = \rho \, (V_2{}^2 - V_1{}^2)/2 \qquad (2)$$

In this equation, V_1 and V_2 are defined as the peak systolic and end diastolic velocities in the right common carotid artery respectively, and ρ is the density of blood.

Results

The data acquisition system consistedg of a personal computer and multimedia board (video blaster SE Creative Tech.) for monitoring and grabbing the changes in blood flow velocity and carotid artery cross-sectional area in each cardiac cycle. For every ultrasound examination, matching longitudinal views of the common carotid artery were located, and frames representing a minimum of two cardiac cycles were grabbed. The cross-sectional area of the right common carotid artery was measured by color Doppler imaging throughout a cardiac cycle (Fig 1).

Application of the computerized multi-frame image processing method to all the processeable frames generated a sequence of measurements on the cross-sectional area of the carotid artery over two cardiac cycles. The maximum and minimum cross-sectional areas at the proximal right common carotid artery were determined over each cardiac cycle. To measure the velocities throughout a cardiac cycle, a transducer was placed with the least possible pressure, allowing expansion of the carotid artery in all directions. Peak systolic and end-diastolic velocities were determined in the right common carotid artery at a point near to the bifurcation. Five milliliters of the rabbit' s carotid artery blood was obtained with a disposable heparinized syringe and blood density was measured by a Sartorius accurate balance (accuracy of 0.001 milligram). Using the equation 2, the static pressure changes of carotid artery were noninvasively estimated.

In order to invasively record the carotid artery static pressure in rabbit and compare the results with the noninvasive technique, T-shaped tubes were designed and constructed (stainless steel tube, outter diameter of 1.5±0.1 mm). After calibration, they were used to measure the carotid artery static pressure at each cardiac cycle (Figure 2). For a correct correlation, both static pressure measurements were carried out simultaneously.

The anesthetics were administrated intraperitoneally. After the rabbits were anesthesized and stabled, the operational surgery was performed and the T- tube was placed inside the carotid artery with the use of a light microscope (Wild M and Heerbrugg) (Figure 3). The T-shaped tube was connected to the pressure transducer (1000B, Narco Bio-system) for

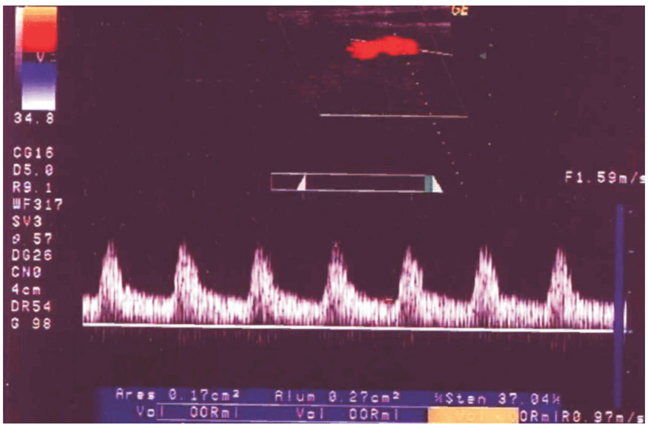

Fig 1. Color Doppler image of right common carotid artery: blood velocities component in beam direction is color coded.

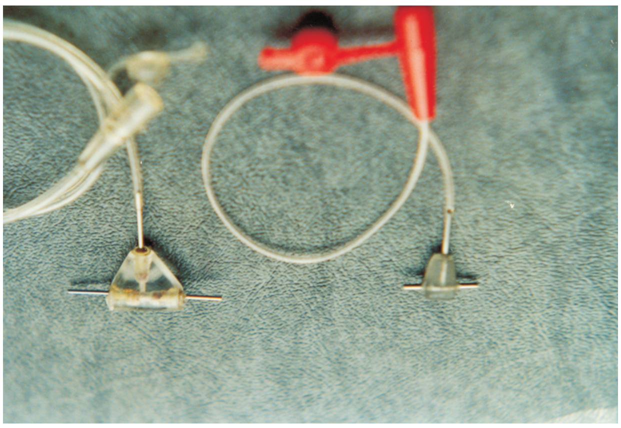

Fig 2. T-shaped tubes for static pressure measurement.

Fig 3. Setting up of the T- shaped tube in a rabbit's carotid artery.

measuring the static pressure and blood pressure at each cardiac cycle. The pressure transducer was emptied of air by heparinized saline in order to prevent coagulation and to record the precise pressure. The transducer was connected to physiograph system (Physiograph MK-111-P, accuracy of 0.2 mmHg) to record the curve of static pressure changes exerted to the arterial wall. After recording static pressures in systolic and diastolic states, the carotid artery was interrupted at the cannula entry and the end (overall) pressure was also recorded. In this state, the arterial blood flow was disrupted; therefore, all the kinetic energy of blood was converted to pressure energy that was blood pressure. The mean time of anesthesia was 3 hours up to the recording of static pressure and 4 hours up to the recording of the end pressure.

With measuring the arterial diameter and the cross sectional area in diastole (d_0 and A_0) and the diameter changes of carotid artery during cardiac cycle (Δd and ΔA), the amount of relative displacement ($\Delta d/d$: Strain) and relative cross section change ($\Delta A/A_0$) of the arterial wall was obtained. The static pressure-strain elastic modulus (E_p), cross-section compliance (Cc) and distensibility (D) were estimated and compared in two states, noninvasively and invasively:

$$E_p = \text{Stress}/\text{Strain} \qquad (3)$$

$$Cc = \Delta A/\text{Stress} \qquad (4)$$

$$D = [\Delta A/A_0]/\text{Stress} \qquad (5)$$

For a statistical comparison between the two methods, a paired t-test was performed on the average static pressure change, static pressure-strain elastic modulus, cross-section compliance and distensibility, as determined by both methods.

Results

The data obtained from noninvasive examination of rabbits are given in Table 1. In this Table, the peak systolic velocity and end-diastolic velocity were estimated by color Doppler ultrasound from right common carotid artery at a point near the bifurcation (1cm). The arterial cross-sectional areas in the diastole and systole were measured by color Doppler ultrasound. Then, the diastolic diameter and diameter changes of the carotid artery throughout a cardiac cycle were calculated. It should be noticed that the density of rabbit blood was estimated 1,060 kg/m^3.

In Table 2, the results of invasive measurements of systolic (P_s) and diastolic (P_d) static pressure by T-shaped cannulation in the right common carotid artery at the point near the bifurcation are shown.

The carotid artery was interrupted at the cannula entry and systolic and diastolic blood pressures were recorded.

Statistical analysis of static pressure changes of carotid artery by both methods showed that there was no significant difference between the measured static pressure changes with invasive and noninvasive methods ($P \leq 0.05$). In Table 3, static pressure-strain elastic modulus, cross-section compliance and distensibility by both invasive and non-invasive methods are shown.

Statistical analysis of static pressure-strain elastic modulus, cross section compliance and distensibility of carotid arterial wall by both methods ($P<0.05$) showed that there was no significant difference between these two methods and Doppler ultrasound can be used as an alternative to estimate the elastic properties of the arterial wall and diagnose the normal from the diseased artery.

Table 1. The results of evaluation of arterial parameters by noninvasive method (mean ± SD).

Systolic velocity V_s (cm/s)	Diastolic velocity V_d (cm/s)	Blood density ρ (kg/m^3)	Minimum carotid diameter d_0 (mm)	Relative diameter Change($\Delta d/d_0$)	Relative cross section change($\Delta A/A_0$)	Static pressure change ΔP_s(N/m^2)
52.4±4.9	13.8±4.9	1060	1.12±0.20	0.41±0.25	1.15±0.79	135.43±19.45

Table 2. The results of evaluation of pressure parameters by invasive method (mean ± SD).

Systolic static pressure P_s (N/m^2)	Diastolic static pressure P_d (N/m^2)	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Heart rate per minute	Static pressure change ΔP_s(N/m^2)
1587.60±165.29	1440.97±162.63	82±21	50±14	281±17	146.63±20.00

Table 3. The means and standard deviations of static pressure-strain elastic modulus, cross-section compliance and distensibility of right common carotid artery by invasive and noninvasive methods.

Methods	Static pressure-strain elastic modulus (pa)	Cross-section compliance (mm^2.Kpa^{-1})	Distensibility (K pa^{-1})
Noninvasive (Doppler ultrasound)	391.01±53.33	7.77±2.58	8.01±4.53
Invasive (cannulation)	361.15±51.87	6. 45±1.42	7.81±4.33

Discussion

There is no consensus on the methodology of obtaining pulse pressure (static blood pressure minus diastolic blood pressure) used in the calculation of elastic parameters. Various ultrasonic methods proposed for noninvasive assessment of local pulse pressure are not reliable. In most studies, the measurement of brachial artery blood pressure changes has been adopted to estimate the elastic parameters of arterial wall. [11, 21, 22] In some studies, arterial wall thickening or appearance of calcifications has been related to the disease. However, in elastic properties, considering the structural changes of arterial wall, there is no difference between the intact and diseased artery at the preliminary stage. [5, 23]

In this study, we estimated the local static pressure changes in the common carotid artery of rabbits with invasive (cannulation) and noninvasive (color Doppler ultrasound) approaches. Comparison of mean static pressure changes and related elastic parameters of rabbit arterial wall with an invasive (Table 1) and a noninvasive method (Table 2) show that they are compatible.

The compression waves in each cardiac contraction both the pressure (or pulse) wave and the associated velocity wave (detected by Doppler) travel at a rate somewhat greater than the velocity of the column of blood. Pressure and velocity waves fluctuate between a minimum and a maximum, each with distinct waveforms. For the purposes of this discussion, we will ignore the changes in the more complex velocity waves.

Estimation of static pressure changes with Bernoulli's principle, the method requires that resistance of the arterial system does not change significantly. There are three primary factors that determine the resistance to blood flow within a single vessel: diameter (or radius), length, and blood viscosity.

Vessel resistance is directly proportional to the length (L) of the vessel and the viscosity (η) of the blood, and inversely proportional to the radius to the fourth power (r^4) (Poiseuill's equation) [15]. Vessel length does not change appreciably in vivo and, therefore, can be generally considered constant. Blood viscosity normally does not change very much; however, it can be significantly altered by changes in the hematocrit, temperature, and by low flow states. Therefore, vessel resistance is exquisitely sensitive to changes in diameter. In the normal arterial circulation, the resistance of large arteries is very low [1]. The arterial diameter of carotid is large; therefore, we can ignore changing resistance of carotid artery in this study.

The subtle difference between the results of both methods could be due to physiological condition of the rabbits and the fact that the time of anesthesia varied. In the noninvasive method, we required the resistance of the arterial system, but arterial resistance was ignored, because the diameter of carotid artery is large. Doppler ultrasonography was carried out when the rabbits were drowsy; but during cannulation, the rabbits were quite unconscious. It should be noted that there is another important reason for the difference between ultrasonography and cannulation, i.e. the overestimation of velocities by Doppler systems. [12, 24] That is, making the connection with the T-shaped tube would have influenced static pressure measurements.

Conduction examinations on dog's arterial wall have shown that the static pressure is approximately 7mmHg (~933 N/m^2) and that it does not go beyond 1 mmHg (~133N/m^2) in the resting state.[10] The rabbits were anesthetized during both Doppler ultrasonography and surgery, so that the amount of static pressure changes in the carotid artery was quite compatible with the previous experiences.

In summary, this paper describes a new method to noninvasively measure the elastic properties in an artery. Although the properties of large arteries have been studied for several decades, the field of clinical arterial biomechanics remains in its infancy. The clinical value of any of the available techniques has yet to be proven convincingly, and no single elastic parameter can ever be expected to describe all the clinically relevant arterial wall properties. Therefore, we have estimated static pressure-strain elastic modulus, cross-section compliance and distensibility that are useful in comparing arteries of different sizes. This study was based on measuring static pressure change using the Bernoulli principle. The static pressure change was used to quantify arterial elastic parameter under invasive and noninvasive conditions. The results showed that there was no significant difference between the invasive and noninvasive methods. By applying this noninvasive method, we can estimate elastic parameters in arteries of normal and diseased people and those at risk of developing atherosclerosis, as a means to determine the event of the disease.

We propose this noninvasive method as an accurate and safe method for screening large populations of young and symptom-free individuals.

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