The Carotid-Femoral (Aortic) Pulse Wave Velocity and Paraoxonase 1 Activity: Review

Karotid-Femoral (Aortik) Nabız Dalga Hızı ve Paraoksonaz 1 Aktivitesi

Mustafa YILDIZ, MD, Assoc.Prof.[a]

[a]Department of Cardiology, Kartal Koşuyolu Yüksek İhtisas Educational and Research Hospital, İstanbul

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Yazışma Adresi/*Correspondence:* Mustafa YILDIZ, MD, Assoc.Prof. Kartal Koşuyolu Yüksek İhtisas Educational and Research Hospital, Department of Cardiology, İstanbul, TÜRKİYE/TURKEY
mustafayilldiz@yahoo.com

ABSTRACT Measurement of arterial pulse wave velocity is a good technique in which large artery elasticity is assessed from analysis of the peripheral arterial waveform. Pulse wave velocity is an index of arterial stiffness and a surrogate marker for atherosclerosis. It is inversely correlated with arterial elasticity and relative arterial compliance. The carotid-femoral (aortic) pulse wave velocity predicts cardiovascular morbidity and mortality in high risk patients with hypertension and hemodialysis. Aortic distensibility is reduced in the presence of coronary artery disease and left ventricular hypertrophy. A 1 m/s of increase in aortic pulse wave velocity increases risk of cardiovascular events approximately 39%. Serum lipids and lipoproteins such as oxidized low-density lipoprotein and paraoxonase 1 are important in atherosclerotic disease. Paraoxonase 1 is synthesized primarily in the liver and is secreted into the plasma, where it is closely associated with high density lipoproteins. Paraoxonase 1 prevents the formation of oxidized low density lipoprotein and it protects phospholipids in high density lipoprotein that has a potential cardio-protective function from oxidation. The association of paraoxonase 1 with pulse wave velocity is controversial. According to current data, there are a few studies in connection with activity of paraoxonase 1 and pulse wave velocity in the literature. Therefore, this connection was assessed in this review manuscript.

Key Words: Aryldialkylphosphatase; heart rate

ÖZET Arteriyel nabız dalga hızı ölçümü periferal arteriyel dalga şeklinin incelenmesi ile büyük arterlerin elastikliğinin değerlendirildiği iyi bir tekniktir. Nabız dalga hızı arteriyel sertliğin bir göstergesidir ve ateroskleroz için bir belirteçtir. Arteriyel esneklik ve göreceli arteriyel kompliyans ile ters orantılıdır. Karotid-femoral (aortik) nabız dalga hızı hipertansif ve hemodiyalize giren yüksek riskli hastalarda kardiyovasküler morbidite ve mortaliteyi öngördürür. Koroner arter hastalığı ve sol ventrikül hipertrofisi varlığında aortik esneklik azalır. Aortik nabız dalga hızındaki 1 m/s artış kardiyovasküler olay riskini yaklaşık %39 artırır. Okside düşük yoğunluklu lipoprotein ve paraoksonaz 1 gibi serum lipidleri ve lipoproteinleri aterosklerotik hastalıkta önemlidir. Paraoksonaz başlıca karaciğerde sentezlenir ve yüksek-yoğunluklu lipoproteinlerle yakın ilişkili olduğu plazmaya salınır. Paraoksonaz 1 okside düşük yoğunluklu lipoprotein oluşumunu önler ve potansiyel kardiyo-protektif işlevi olan yüksek yoğunluklu lipoproteinlerdeki fosfolipidleri oksidasyondan korur. Paraoksonaz 1 ve nabız dalga hızı arasındaki ilişki tartışmalıdır. Mevcut verilere göre, literatürde paraoksonaz 1 aktivitesi ve nabız dalga hızı bağlantısı ile ilgili az sayıda çalışma vardır. Bu derlemede bu bağlantı değerlendirildi.

Anahtar Kelimeler: Arildialkilfosfataz; kalp hızı

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THE CAROTID-FEMORAL (AORTIC) PULSE WAVE VELOCITY

Atherosclerotic cardiovascular disease is characterized by thickening of the arterial wall.[1] This disease can be observed in different stages by use of some invasive and non-invasive techniques.[2-14] One of

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these non-invasive ultrasound techniques is carotid-femoral pulse wave velocity (PWV) which is defined as arterial pulse velocity of moving along vessel wall. It is used as an indicator of arterial stiffness and plays an important clinical role in describing patients under high cardiovascular risk.[5-14] PWV is inversely correlated with arterial elasticity and relative arterial compliance. Theoretically, the wave velocity (C0), in a thin-walled, uniform, elastic vessel containing an incompressible viscous fluid, with no reflections, can be expressed by the Moens-Korteweg equation: $C0= \sqrt{Eh/2\rho R}$ (E: Young's modulus of elasticity, h: wall thickness, R: mean radius, ρ: blood density).[15,16] Following Bramwell and Hill, equation of Moens-Korteweg also can be expressed as $C0= \sqrt{dP\ V/dV\ \rho}$ (P: pressure, V: volume of tube per unit length, dV/VdP: volume compliance of the tube).[17] In this equation, the square of the wave velocity is inversely related to the volume compliance that represents the total arterial stiffness.

A number of studies have investigated the effects of the different factors such as age, sex, weight, height, blood pressure and heart rate on the PWV.[6-14,18-20] In fact, the most important factor contributing to increased aortic PWV in humans is age because it causes increased arterial stiffness due to decreased elastin fiber, increased collagenous material and loss of arterial elasticity.[21-23] Increased medial calcification and endothelial dysfunction are also characteristics of arterial aging.[21] In addition to aging, PWV also depends on blood pressure since it gets higher at a high blood pressure and lower at a low blood pressure.[14,24,25] However, varying correlation coefficients have been reported between PWV and systolic, diastolic and mean blood pressures.[14] Although the arterial blood pressure is determined by cardiac output and total peripheral resistance which is composed of the arterioles, pulse pressure is influenced by the left ventricular ejection, elasticity of the large arteries, the timing of reflected waves and heart rate.[26,27] Elastic large arteries absorb energy during the systole and thereby reduce the cardiac work for a given cardiac output. With the resultant increase in arterial stiffness with advancing age, this buffer effect is lost and this leads to an increase in systolic blood pressure. In addition, the normal elastic recoil during diastole does not occur and the diastolic blood pressure tends to fall. Because coronary perfusion occurs predominantly in diastole, a reduction in diastolic blood pressure may cause myocardial ischemia.[10,28]

THE CAROTID-FEMORAL (AORTIC) PULSE WAVE VELOCITY MEASUREMENTS BY COMPLIOR DEVICE

We used Complior Colson (France) device to study carotid-femoral (aortic) PWV. The carotid-femoral PWV and arterial blood pressure were measured by the same observer in each subject in the supine position after at least 20 minutes of rest. Clinic blood pressure was measured using a mercury sphygmomanometer with a cuff appropriate to the arm circumference (Korotkoff phase I for systolic blood pressure and V for diastolic blood pressure). In each subject, two blood pressure measurements were performed, and their average was used for analysis.

Pulse pressure= Systolic blood pressure-Diastolic blood pressure

Mean blood pressure= [Systolic blood pressure + 2 x Diastolic blood pressure]/3

Arterial stiffness was determined by an automatic carotid-femoral PWV measurement using the Complior Colson (France) device. The technical characteristics of this device have been described, and indicate inter-and intra-observer repeatability coefficients >0.9.[14] PWV is calculated from measurements of pulse transit time and the distance traveled by the pulse between two recording sites (the right femoral and common carotid arteries): PWV= Distance (m)/Transit time (ms) (Figure 1). Different factors such as Doppler, pressure and diameter can be used for measurement of PWV. In this study, we used the TY-306 pressure transducer (Fukuda Co). This transducer has a large frequency bandwidth ranging from less than 0,1 Hz to more than 100 Hz, which mostly covers the principal frequency harmonics of the pressure

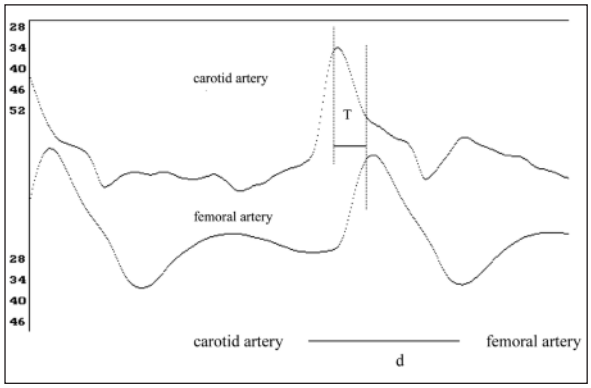

FIGURE 1: Measurement of carotid-femoral (aortic) pulse wave velocity [d: distance (m), T: propagation time (ms) from the point of maximum upstroke of the signal as used in the Complior system)].

wave at different heart rates and thus allows its application for PWV measurement. For automatic measurement of PWV, pressure waveforms are digitized at different rates according to the distance between the recording sites; the sampling acquisition frequency is 500 Hz for carotid-femoral PWV. The two pressure waveforms are stored in a recirculating memory buffer, half of which is displayed at any given time. During preprocessing analysis, the gain of each waveform was adjusted to obtain an equal signal for the two wave forms. During PWV measurements, when pulse waveforms of sufficient quality were recorded, the digitization process was initiated by the operator and automatic calculation of the time delay between two upstrokes was started. The measurement was repeated over 10 different cardiac cycles, and the mean value was used for the final analysis.

PARAOXONASE

Serum lipids and lipoproteins such as total cholesterol, high density lipoprotein, low density lipoprotein, oxidized low-density lipoprotein, apolipoprotein A1 and apolipoprotein B are important in atherosclerotic disease.[29,30] While higher high density lipoprotein and apolipoprotein A1 levels, the major receptor for nonesterified cholesterol from the peripheral tissues, are associated with decreased risk for atherosclerotic disease. Oxidized low-density lipoprotein is taken into macrophages through scavenger receptors without any down regulation and causes formation of foam cells. Oxidation products of low-density lipoprotein are cytotoxic and these cytotoxic products are especially dangerous for endothelial cells.

Paraoxonase (PON; aryldialkylphosphatase) 1 is a member of a family proteins which also include PON2 and PON3.[31,32] PON1 is composed of 354 amino acids with a molecular mass of 43 kDa. The PON1 gene is located on the long arm of human chromosome 7 (q21.22) with other members of its supergene family. PON1 is synthesized primarily in the liver and is secreted into the plasma, where it is closely associated with high density lipoproteins.[31] PON1 prevents the formation of oxidized low density lipoprotein and inactivates low density lipoprotein-derived oxidized phospholipids when it is formed.[31] PON1 also protects phospholipids in high density lipoprotein that has a potential cardio-protective function from oxidation.[33] PON1 is located in a subfraction of high density lipoprotein that contains apolipoprotein A1 and clusterin (apoJ).[34,35] This subfraction of high density lipoprotein may function to protect cell membranes generally against lipid peroxidation and other toxic effects.[36] These effects of PON1 may play a role in cardiovascular diseases and chronic inflammation.

Decreased activity of serum PON1 enzyme was reported as a risk factor for development of atherosclerosis.[37,38] Apolipoprotein A1 is the major protein of high-density lipoprotein. It was reported that Apolipoprotein A1 was required for the anti-inflammatory function of high-density lipoprotein and PON1 activity.[34,35] According to current data, there are a few studies in the literature in which connection of PON1 with PWV were evaluated.[18,39,40] Recently, we investigated the mechanism of the effect of valproic acid, carbamazepine, and valproic acid+carbamazepine by determining serum levels of oxidized low-density lipoprotein, apolipoprotein A1, homocysteine, folic acid, vitamin B12, PON1, total antioxidant capacity, malondialdehyde, nitric oxide and thyroid hormones in pediatric epileptic patients.[18] Besides the level of apolipoprotein A1, the activity of PON1 remained unaffected in pediatric patients who used antiepileptic drugs. Unaffected PON1 activity may

be associated with unchanged levels of apolipoprotein A1. In addition, we did not find any correlation with PON1 and carotid-femoral (aortic) PWV.

Lambrinoudaki et al. investigated the association of common polymorphisms involved in apolipoprotein B 3500, apolipoprotein E (E2/E3/E4), cholesterol 7 alpha-hydroxylase A-204C, cholesterol ester transfer protein B1/B2, glycoprotein IIIa leu33pro, integrin beta 3 PLA1/PLA2, plasminogen activator inhibitor 1 4G/5G, PON1 gln192 arg, and methylenetetrahydrofolate reductase ala222val and indices of endothelial function and arterial elasticity via radial and femoral PWV and augmentation index in healthy postmenopausal women.[39] They found that only cholesterol 7 alpha-hydroxylase A-204C polymorphism was positively associated with subclinical atherosclerosis.

In a cross-sectional study, Charakida et al. compared vascular function and structure with high density lipoprotein properties in patients with antiphospholipid syndrome and controls, and found a relationship between vascular function and structure and PON activity levels.[40] They found an association between paraoxonase activity of high density lipoprotein cholesterol and carotid intima media thickness and PWV in antiphospholipid syndrome, which suggests a possible interaction between antiphospholipid antibodies and PON, leading to reduced PON activity, a concept that was demonstrated in experimental studies.[41]

In conclusion, studies which evaluated the association of PON1 and PWV in the literature are controversial. While significant association was reported in some studies, a similar relationship could not be shown in the other studies. Studies in the literature were performed on a limited number of patients, therefore further investigations are necessary.

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