

The Effects of Traditional Dual Chamber Cardiac Permanent Pacemaker on Arterial Distensibility Using Carotid-Femoral (Aortic) Pulse Wave Velocity in Patients with Angiographically Normal Coronary Arteries

Klasik Çift Odacıklı Kalıcı Kalp Piliinin Anjiyografik Olarak Normal Koroner Arterleri Olan Hastalarda Karotis-Femoral (Aortik) Nabız Dalga Hızı Aracılığıyla Ölçülen Arteriyel Distansibilite Üzerine Etkileri

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ABSTRACT

Introduction: The traditional dual chamber cardiac permanent pacemakers are widely used for symptomatic bradycardia. Pulse wave velocity (PWV) is an index of arterial stiffness and a marker of cardiovascular events. This study aims to investigate arterial distensibility using carotid-femoral (aortic) PWV measurements in patients with traditional dual chamber cardiac permanent pacemakers and angiographically normal coronary arteries.

Patients and Methods: We recruited 17 paced patients and 17 age and sex matched controls. Aortic PWV was determined using an automatic device, the Complior Colson (France), which

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allowed on-line pulse wave recording and automatic calculation of PWV. PWV is calculated from measurements of pulse transit time and the distance travelled by the pulse between two recording sites, according to the following formula:

$$PWV (m/s) = \text{Distance (m)} / \text{Transit time (s)}$$

Results: The carotid-femoral PWV (10.20 ± 2.00 , 9.06 ± 0.94 m/s, $p=0.04$) was increased in patients with dual chamber pacing as compared with age and sex-matched control group. Multiple regression analysis between PWV and clinical parameters (age, sex, weight, height, systolic blood pressure, diastolic blood pressure, pulse pressure, mean blood pressure, heart rate) showed that PWV correlated positively with age ($r^2=0.31$; $p=0.007$). Similar results were obtained in the paced patients (age, $r^2=0.36$; $p=0.03$) and control (age, $r^2=0.33$; $p=0.04$) subgroups when analyzed separately.

Conclusion: Arterial distensibility is increased in patients with traditional dual chamber cardiac permanent pacemakers and angiographically normal coronary arteries, as compared with age and sex matched controls.

Key Words: Angiography; pacemaker, artificial; blood pressure; carotid arteries; vascular stiffness.

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ÖZET

Giriş: Klasik çift odacıklı kalıcı kalp pili semptomatik bradikardide geniş bir şekilde kullanılmaktadır. Nabız dalga hızı (NDH) arteriyel sertleşmenin bir indeksi ve kardiyovasküler olayların bir belirteçidir. Bu çalışmanın amacı, klasik çift odacıklı kalıcı kalp pili ve anjiyografik olarak normal koroner arterleri olan hastalarda karotis-femoral (aortik) NDH aracılığıyla arteriyel distansibiliteyi araştırmaktır.

Hastalar ve Yöntem: Çalışmaya 17 kalp pili hastası ile cinsiyet ve yaş yönünden uyumlu 17 kontrol grubu alındı. Aortik NDH, online nabız dalgası kaydeden otomatik Complior Colson (Fransa) cihazıyla belirlenip otomatik olarak hesaplandı. NDH, nabızın ilerlediği iki kaydedici bölge arasındaki mesafenin nabız geçiş zamanına oranı olarak; "NDH (m/s) = Mesafe (m) / Geçiş zamanı (s)" formülü ile hesaplandı.

Bulgular: Karotis-femoral NDH (10.20 ± 2.00 , 9.06 ± 0.94 m/s, $p=0.04$) cinsiyet ve yaş yönünden uyumlu kontrol grubu ile karşılaştırıldığında, çift odacıklı kalp pili bulunan hastalarda daha yüksekti. NDH ve klinik değişkenler (yaş, cinsiyet, vücut ağırlığı, boy, sistolik kan basıncı, diyastolik kan basıncı, nabız basıncı, ortalama kan basıncı, kalp hızı) arasında çoklu regresyon analizi yapıldığında NDH ile yaş arasında pozitif ilişki gözlemlendi ($r^2=0.31$; $p=0.007$). Alt grup analizi yapıldığında benzer sonuçlar kalp pili bulunan hastalarda (yaş, $r^2=0.36$; $p=0.03$) ve kontrol grubunda (yaş, $r^2=0.33$; $p=0.04$) da izlendi.

Sonuç: Arteriyel distansibilite, klasik çift odacıklı kalıcı kalp pili ve anjiyografik olarak normal koroner arterleri olan hastalarda, yaş ve cinsiyet yönünden benzer kontrollere göre daha yüksektir.

Anahtar Kelimeler: Anjiyografi; kalp pili, yapay; kan basıncı; karotid arter; vasküler sertlik.

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INTRODUCTION

Non-invasive ultrasound techniques are used to evaluate arterial system and cardiovascular condition. One such technique, carotid-femoral pulse wave velocity (PWV), which is defined as arterial pulse's velocity of moving along vessel wall, as an indicator of arterial stiffness, plays an important clinical role in describing patients under high cardiovascular risk⁽¹⁻⁴⁾. PWV is inversely correlated with arterial distensibility and relative arterial compliance. Theoretically, the wave velocity (C0), in a thin-walled, uniform, elastic vessel containing an incompressible, inviscous fluid, with no reflections, can be expressed by the Moens-Korteweg equation^(5,6): $C0 = \sqrt{(Eh/2\rho R)}$ (E: Young's modulus of elasticity, h: Wall thickness, R: Mean radius, ρ : Blood density). Following Bramwell and Hill, equation of Moens-Korteweg also can be expressed as $C0 = \sqrt{(dP.V/p.DV)} \rho$ (P: pres-

sure, V: volume of tube per unit length, dV/VdP: volume compliance of the tube)⁽⁷⁾. In this equation, the square of the wave velocity is associated with the inverse of the volume compliance that represents the total arterial stiffness.

Traditional dual chamber cardiac permanent pacemakers which are widely used for symptomatic bradycardia offer the theoretical benefit of mimicking the normal electrical sequence of the heart, pacing the right atrial appendage first and the apex of the right ventricular chamber second^(8,9). The use of dual-chamber pacing modes allows the maintenance of atrioventricular synchrony, the preservation of sinus node control over heart rate, and the potential for normal ventricular activation over the His-Purkinje system. Although the main reasons for traditional right ventricle apical pacing the easy implantation and the stability of passive-fixation leads in the apical trabeculae,

the clinical trial evidence suggests that traditional dual chamber cardiac pacing may be harmful⁽¹⁰⁻¹²⁾. It produces frequent, unnecessary right ventricular pacing and worse clinical outcomes⁽¹³⁾. These undesirable results had forced to search for effective points to pace the ventricles such as right ventricular outflow tract⁽¹³⁻¹⁵⁾. Through the undesirable findings of traditional right ventricular apical pacing, we investigated arterial distensibility using carotid-femoral (aortic) PWV measurements in patients with traditional dual chamber cardiac permanent pacemakers and angiographically normal coronary arteries.

PATIENTS and METHODS

Patient Population

Seventeen patients (mean age: 50.1 ± 11.8 years, 11 women, mean pacemaker duration: 2.6 ± 0.7 years) implanted with dual chamber (pacing the right atrial appendage first and the apex of the right ventricular chamber second) cardiac pacemakers (DDD pacemakers) for complete AV block ($n=17$), and 17 age and sex matched controls (mean age: 50.2 ± 7.5 years, 11 women) were included in the study. The coronary angiography of all patients were normal. All subjects gave their consent for inclusion in the study. The investigation conforms with the principles outlined in the Declaration of Helsinki. Exclusion criteria were a previous myocardial infarction, hypertension, constrictive or dilated cardiomyopathy, heart failure, severe valvular heart disease, diabetes mellitus, dyslipidaemia, peripheral arterial disease, cerebrovascular disease, renal failure, anemia (Hct $< 30\%$), body mass index ($\geq 35 \text{ kg/m}^2$) and waist / hip ratio ≥ 1 . None of our patients was treated at the time of examination with angiotensin converting enzyme inhibitors, nitrates, diuretics, alpha blockers, beta-blockers, statins and non-steroidal anti-inflammatory drugs. All subjects were nonsmokers.

Study Protocol

Blood pressure and pulse wave velocity measurements: 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 measurement were performed, and their mean was considered for analysis.

Pulse pressure = Systolic blood pressure-Diastolic blood pressure

Mean blood pressure = $[\text{Systolic blood pressure} + 2 \times \text{Diastolic blood pressure}] / 3$

Arterial stiffness was assessed by 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 coefficient values > 0.9 ⁽¹⁶⁾. 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): $\text{PWV} = \text{Distance (meters)} / \text{Transit Time (seconds)}$. Different factors can be used for measurement of PWV such as Doppler, pressure, diameter^(17,18). In this study we used the TY-306 pressure transducer (Fukuda Co); this transducer has a large frequency bandwidth from less than 0.1 Hz to more than 100 Hz, which largely covers the principal frequency harmonics of the pressure 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, after pulse waveforms of sufficient quality were recorded, the digitisation process was initiated by the operator and automatic calculation of the time delay between two upstrokes was started. Measurement was repeated over 10 different cardiac cycles, and the mean value was used for the final analysis.

Statistical Analysis

Statistics were obtained using the ready-to-use programme of SPSS version 8.0. All the values were expressed as mean \pm standard deviation. The obtained results were assessed by independent samples t test. Correlations were calculated with the Pearson test. Multiple regression test was used for analysis between PWV and clinical parameters (age, sex, weight, height, systolic blood pressure, diastolic blood pressure, pulse pressure, mean blood pressure, heart rate). The significance level was set at a value of $p < 0.05$.

RESULTS

The carotid-femoral PWV (10.20 ± 2.00 , 9.06 ± 0.94 m/s, $p=0.04$) was increased in patients with dual chamber pacing as compared with sex-matched control group

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Table 1. Antropometric and hemodynamic values in control subjects and paced patients

	Paced patients	Controls	p
Age (years)	50.1 ± 11.8	50.2 ± 7.5	0.97
Weight (kg)	67.05 ± 11.58	70.76 ± 13.81	0.40
Height (cm)	160.17 ± 8.50	162.70 ± 11.47	0.47
Systolic blood pressure (mmHg)	125.00 ± 12.50	119.70 ± 12.17	0.22
Diastolic blood pressure (mmHg)	77.35 ± 5.03	74.41 ± 4.63	0.08
Pulse pressure (mmHg)	47.64 ± 10.47	45.29 ± 12.17	0.55
Mean blood pressure (mmHg)	93.23 ± 6.67	89.50 ± 5.55	0.08
Heart rate (beat/minute)	69.41 ± 11.95	67.52 ± 10.13	0.62
Pulse wave velocity (m/s)	10.20 ± 2.00	9.06 ± 0.94	0.04*
LVEDd (mm)	50.94 ± 3.41	49.00 ± 3.46	0.11
LVESd (mm)	32.52 ± 3.04	31.70 ± 3.13	0.44
Ejection fraction (EF%)	64.82 ± 4.14	65.47 ± 5.00	0.68
IVSd (mm)	10.94 ± 0.89	10.70 ± 0.84	0.43
LVPWd (mm)	10.47 ± 0.51	10.12 ± 0.95	0.20
Mitral E velocity (cm/s)	1.26 ± 0.19	1.27 ± 0.13	0.96
Mitral A velocity (cm/s)	0.95 ± 0.10	0.89 ± 0.15	0.19

* p < 0.05.

LVEDd: Left ventricle end-diastolic diameter, LVESd: Left ventricle end-systolic diameter, IVSd: Interventricular septum thickness in diastole, LVPWd: Left ventricle posterior wall thickness in diastole.

Table 2. The correlation between pulse wave velocity and antropometric and hemodynamic values

	p	r
PWV-Age (years)	0.003*	0.49
PWV-Weight (kg)	0.13	0.26
PWV-Height (cm)	0.77	-0.05
PWV-Systolic blood pressure (mmHg)	0.03*	0.35
PWV-Diastolic blood pressure (mmHg)	0.26	0.19
PWV-Pulse pressure (mmHg)	0.07	0.30
PWV-Mean blood pressure (mmHg)	0.05	0.33
PWV-Heart rate (beat/minute)	0.31	0.17
PWV-LVEDd (mm)	0.88	-0.02
PWV- LVESd (mm)	0.18	0.23
PWV-EF%	0.06	-0.32
PWV-IVSd (mm)	0.95	-0.01
PWV-LVPWd (mm)	0.97	-0.006
PWV-Mitral E velocity (cm/s)	0.08	-0.29
PWV-Mitral A velocity (cm/s)	0.33	0.17

*p < 0.05.

PWV: Pulse wave velocity, LVEDd: Left ventricle end-diastolic diameter, LVESd: Left ventricle end-systolic diameter, EF%: Ejection fraction, IVSd: Interventricular septum thickness in diastole, LVPWd: Left ventricle posterior wall thickness in diastole.

(Table 1). There were significant correlation between PWV and age and systolic blood pressure ($p= 0.003$, $r= 0.49$; $p= 0.03$, $r= 0.35$ respectively) (Table 2). Multiple regression analysis between PWV and clinical and hemodynamic parameters (age, sex, weight, height, systolic blood pressure, diastolic blood pressure, pulse pressure, mean blood pressure, heart rate, left ventricle end-diastolic diameter, left ventricle end-systolic diameter, ejection fraction, interventricular septum thickness in diastole, left ventricle posterior wall thickness in diastole, mitral E velocity, mitral A velocity) showed that PWV correlated positively with age ($r^2= 0.31$; $p= 0.007$). Similar results were obtained in the paced patients (age, $r^2= 0.36$; $p= 0.03$) and control (age, $r^2= 0.33$; $p= 0.04$) subgroups when analyzed separately.

DISCUSSION

In this study we found that carotid-femoral PWV is increased in patients with traditional dual chamber pacing, as compared with age and sex matched controls. Therefore, our results suggest that patients with traditional dual chamber pacing have a higher arterial stiffness than control subjects. Although the electric treatment of symptomatic bradycardia by an implanted pacemaker is necessary, electrical stimulation of the traditional right ventricle pacing may have disadvantages which produces frequent, unnecessary pacing⁽⁸⁻¹³⁾. The conventional pacing in the right ventricular apex causes a modification of the ventricular activation pattern and can result in impeded left ventricular filling and ejection. Activation delays within the left ventricular itself can cause decreased efficiency of contraction, increased mitral regurgitation, and abnormal ventricular remodelling⁽¹⁰⁻¹³⁾.

Unnecessary right ventricular pacing may increase arterial stiffness. There are various reports on the relationship between aortic PWV and heart rate. Observational studies imply a statistically significant positive link between high heart rate and high arterial stiffness, suggesting that arterial stiffness per se may be influenced by heart rate⁽¹⁹⁾. Indeed, Stefanadis et al. reported decreased aortic stiffness, measured using ultrasound, during incremental ventricular pacing⁽²⁰⁾. But some investigators did not observe any significant change in the timing of the reflected wave during pacing that provides a measure of the aortic PWV^(21,22). Wilkinson et al. reported a significant, inverse, linear relationship between heart rate and augmentation index is a measure of systemic arterial stiffness derived from the ascending aortic pressure waveform in patients with permanent atrial or dual chamber pacing⁽²³⁾.

Patients receiving ventricular pacemakers have a higher sympathetic nerve activity^(1,24). An exaggerated response of the sympathetic tone to a decreased stroke volume on the peripheral arterial system may increase PWV. Sympathetic neural control affects small resistance arteries and the mechanical properties of large arteries; activation of the sympathetic nervous system has been shown to reduce distensibility of small and medium size arteries in animals^(25,26). Boutouyrie et al. showed that increase in sympathetic stimulation is associated with a reduction of radial artery distensibility that is inversely correlated with arterial PWV in humans⁽²⁷⁾.

In this study, multiple regression analysis between PWV and clinical parameters (age, sex, weight, height, blood pressure, heart rate) showed that PWV correlated positively with age. In fact, the most important factor contributing to increased PWV in human populations is age because of increased arterial stiffness caused by medial calcification, increase in collagenous material and loss of arterial elasticity⁽²⁸⁻³⁰⁾. In addition to the role of age, PWV also depends on blood pressure level (PWV becomes higher at high blood pressure and lower at low blood pressure). However, varying correlation coefficients have been reported between PWV and systolic, diastolic, and mean blood pressures⁽¹⁸⁾. In our study multiregression analysis showed that arterial blood pressure was not associated with PWV which is widely used as an index of arterial distensibility⁽¹⁶⁾. Although the mean arterial blood pressure is determined by cardiac output and total peripheral resistance composed by the arterioles, pulse pressure is influenced by the left ventricular ejection, elasticity of the large arteries, the timing of reflected waves and heart rate⁽³¹⁻³³⁾. Elastic large arteries absorb energy during the systole and thereby reduce the cardiac work for a given cardiac output⁽¹⁶⁾. With the resultant increase in arterial stiffness with advancing age this buffer effect is lost and this lead to an increase in systolic blood pressure. Also, the normal elastic recoil during diastole does not occur and the diastolic blood pressure tends to fall⁽³²⁾. Because of coronary perfusion occurs predominantly in diastole, a reduction in diastolic blood pressure may cause myocardial ischaemia^(32,34).

In our study sex, weight, height and heart rate did not significantly influence carotid-femoral PWV. There are conflicting reports on the relationship of some of these factors with the stiffening of large arteries on humans. Albaladejo et al. reported, using cardiac pacing in 11 subjects a non-significant positive trend between PWV and heart rate⁽³⁵⁾. Some studies have shown significant differences in PWV

and body mass index and sex⁽³⁶⁻⁴⁰⁾. Barinas-Mitchell et al. demonstrated that moderate weight loss improves arterial stiffness in type 2 diabetes⁽⁴¹⁾.

In our study showed that arterial distensibility was assessed by automatic carotid-femoral PWV measurement is increased in patients with traditional dual chamber cardiac permanent pacemakers and angiographically normal coronary arteries, as compared with age and sex matched controls.

Study Limitations

Despite the method measures the stiffness of the aorta indirectly, it is the best described method [The pressure wave forms are easily recorded in both areas, the distance between two areas is long enough, and elasticity of arterial wall could have been reflected on a large scale as in aorta, measurement of carotid-femoral pulse wave velocity was preferred⁽¹⁶⁾]. We took great care to exclude subjects with known cardiovascular disease or risk factors, such as a previous myocardial infarction, hypertension, constrictive or dilated cardiomyopathy, heart failure, severe valvular heart disease, diabetes mellitus, dyslipidaemia, peripheral arterial disease, cerebrovascular disease, renal failure, anemia (Hct < 30%), body mass index ($\geq 35 \text{ kg/m}^2$) and waist/hip ratio ≥ 1 . The other limitation, we didn't use a new laboratory data and didn't measure sympathetic activity. For exclusion criteria, we used files data of the patients. Finally, these conclusions may not extend to the great population, therefore; the results of this study will need confirmation in larger studies.

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