Assessment of P-wave dispersion in patients with isolated bicuspid aortic valve and its relationship with aortic elasticity

İzole biküspit aort kapak hastalarında P dalga dispersiyonunun değerlendirilmesi ve aort esnekliği ile ilişkisi

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**ABSTRACT**

Objectives: We evaluated P-wave duration and P-wave dispersion (PWD) in patients with isolated bicuspid aortic valve (BAV) without significant valve dysfunction and investigated the relationship between P-wave measurements and aortic elasticity.

Study design: This prospective study consisted of 39 patients with isolated BAV with normal ejection fraction and 29 age- and gender-matched healthy subjects. P-wave duration and P-wave dispersion were calculated on 12-lead electrocardiograms. Echocardiographic examination was performed and aortic elasticity parameters were calculated including aortic strain, aortic stiffness index, aortic distensibility, and aortic elastic modulus.

Results: Patients with BAV had significantly greater \( P_{\text{max}} \) and PWD compared to controls (128±11 vs. 115±11 msec, \( p=0.006 \); 70±10 vs. 66±13 msec, \( p=0.02 \), respectively), whereas \( P_{\text{min}} \) was similar. Aortic strain and distensibility were significantly lower and aortic stiffness index and aortic elastic modulus were significantly greater in patients with BAV (for all, \( p=0.0001 \)). In correlation analysis, \( P_{\text{max}} \) was significantly correlated with aortic strain (\( r=-0.30, p=0.01 \), aortic distensibility (\( r=-0.27, p=0.02 \), aortic stiffness index (\( r=0.36, p=0.004 \)), and aortic elastic modulus (\( r=0.38, p=0.003 \)), while PWD was correlated with aortic strain (\( r=-0.23, p=0.05 \)) and aortic elastic modulus (\( r=0.25, p=0.05 \)).

Conclusion: Our data showed that isolated BAV without valve dysfunction was associated with prolonged P-wave duration and increased PWD, both of which were related to aortic elasticity parameters.

**ÖZET**

Amaç: Bu çalışmada, kapak işlevinde önemli bozukluk olmayan izole biküspit aort kapaklı (BAK) hastalarda P dalga süresi ve P dalga dispersiyonu değerlendirildi ve P dalga ölçümleri ile aort esneklik parametreleri arasındaki ilişki araştırıldı.

Çalışma planı: İleriye dönük bu çalışmaya izole BAV olan ve ejeksiyon.fraksiyonu normal 39 hasta ve yaş ve cinsiyet uyumlu 29 sağlıklı birey alındı. P dalga süresi ve P dalga dispersiyonu 12 derivasyonlu elektrokardiografi kayıtlarından hesaplandı. Tüm olgulara ayrıntılı ekokardiografi incelemesi yapıldı ve aort gerilimi, aort sertlik indeksi, aort gerilebilirliği ve aort esneklik katsayısı gibi aort esneklik parametreleri hesaplandı.

Bulgular: En yüksek P dalga süresi ve P dalga dispersiyonu hasta grubunda kontrol grubuna göre anlamlı derecede yüksek bulundu (sirasıyla, 128±11 vs. 115±11 msec, \( p=0.006 \); 70±10 vs. 66±13 msec, \( p=0.02 \),分别地），whereas P min was similar. Aortic strain and distensibility were significantly lower and aortic stiffness index and aortic elastic modulus were significantly greater in patients with BAV (for all, \( p=0.0001 \)). In correlation analysis, \( P_{\text{max}} \) was significantly correlated with aortic strain (\( r=-0.30, p=0.01 \), aortic distensibility (\( r=-0.27, p=0.02 \), aortic stiffness index (\( r=0.36, p=0.004 \)), and aortic elastic modulus (\( r=0.38, p=0.003 \)), while PWD was correlated with aortic strain (\( r=-0.23, p=0.05 \)) and aortic elastic modulus (\( r=0.25, p=0.05 \)).

Sonuç: Bulgularımız, kapak fonksiyonu normal izole BAK hastalarında P dalga süresi ve dispersiyonunda artış olduğunu, bunların her ikisinin de aort esneklik parametreleri ile ilişkili olduğunu gösterdi.
Bicuspid aortic valve is the most common congenital heart defect, affecting 0.5% to 2% of the general population. Congenital fusion of two cusps with a fibrous raphe is the most frequent pathologic mechanism. Recent studies have shown that BAV is associated with abnormal aortic elasticity, however, it still remains undefined whether BAV without significant valve dysfunction is associated with inhomogeneous atrial conduction.

P-wave dispersion, defined as the difference between the longest and shortest P-wave durations recorded from the surface electrocardiogram leads, indicates heterogeneous intra-atrial and inter-atrial conduction, providing a substrate that favors reentry mechanisms.

Recently, many studies have demonstrated the relationship between arterial stiffness and left ventricular diastolic function. Likewise, reduced aortic wall elasticity and LV diastolic dysfunction have been shown in patients with BAV. We hypothesized that impaired aortic elasticity and diastolic function could induce electrocardiographic conduction abnormalities in patients with BAV. In this study, we aimed to evaluate P-wave duration and PWD in patients with isolated BAV without significant valve dysfunction, together with the relationship between P-wave measurements and aortic elasticity.

**PATIENTS AND METHODS**

**Patients and controls**

We prospectively involved 39 patients with isolated BAV and 29 age- and gender-matched healthy subjects in the study. Exclusion criteria were the presence of the following conditions: aortic valve stenosis and more than mild aortic regurgitation, previous cardiac surgery, concomitant dysfunction (>mild degree) of other heart valves, cardiomyopathy, LV systolic dysfunction (LV ejection fraction <50%), arrhythmias, Marfan’s syndrome, other congenital heart defects, hypertension, coronary artery disease, diabetes mellitus, current smoking, use of any cardiovascular drugs, hypercholesterolemia, prior pacemaker implantation, atrioventricular or intraventricular conduction disturbances.

The study was approved by the local ethics committee. Informed consent was obtained from each participant.

**Abbreviations:**

- BAV: Bicuspid aortic valve
- LV: Left ventricular
- PWD: P-wave dispersion

**Electrocardiography**

Twelve-lead electrocardiograms were obtained from each subject in the supine position with a standardized paper speed of 50 mm/sec and signal size of 10 mm/mV. P-wave duration was measured manually with the use of a caliper by two cardiologists who were blind to echocardiography findings and clinical data. Subjects with measurable P waves in nine or fewer electrocardiographic leads were excluded from the study. P-wave duration was measured in all leads. The beginning of the P wave was defined as the point where the first atrial deflection crossed the isoelectric line and the end of the P wave was defined as the point where the atrial deflection returned to the isoelectric line. The difference between maximum and minimum P-wave durations (P_max and P_min) was defined as PWD. Any lead where the onset and termination of the P wave could not be identified was excluded from the analysis.

**Echocardiography**

Echocardiography was performed using a GE Vivid 7 system (GE Vingmed Ultrasound AS, Norten, Norway) with a 2.5-MHz phased array transducer. All measurements were made by two investigators blind to the clinical data of the subjects. The morphology of the aortic valve was assessed in the parasternal short axis view. Two-dimensional echocardiographic criteria for BAV included partial or complete fusion of two of the aortic valve leaflets resulting in partial or complete absence of a functional commissure between the fused leaflets. Recordings were taken in the left lateral decubitus position. An average of three beats was analyzed. M-mode traces were recorded at a speed of 50 mm/sec and Doppler signals were recorded at a speed of 100 mm/sec. Simultaneous electrocardiographic recordings were also taken. Systolic and diastolic ascending aortic diameters were measured on M-mode tracings at 3 cm above the aortic valve. Systolic diameter was measured at the maximal anterior motion of the aorta, while diastolic diameter was measured at the peak of the QRS complex on the simultaneous electrocardiogram. Systolic and diastolic pressures of the right brachial artery were recorded as the average of three consecutive measurements immediately after the echocardiographic study with a conventional sphygmomanometer. Aortic elasticity parameters were calculated using the following formulas:

\[
\text{Aortic strain} \% = \frac{(\text{Aortic systolic} - \text{diastolic diameter}) \times 100}{\text{Aortic strain}}
\]

\[
\text{Aortic stiffness index} = \frac{\text{Systolic}}{\text{Diastolic blood pressure}} \div \text{Aortic strain}
\]
Aortic distensibility \( (\text{cm}^2.\text{dyne}^{-1}.10^{-6}) = 2 \times \text{Aortic strain} / (\text{Systolic} – \text{Diastolic blood pressure}) \)

Aortic elastic modulus \( (\text{dyne} \cdot \text{cm}^{-2}.10^6) = (\text{Systolic} – \text{Diastolic pressure}) / \text{Aortic strain} \)

Left ventricular ejection fraction was calculated by the biplane Simpson’s method. Interventricular septum thickness, posterior wall thickness, LV end-diastolic and end-systolic diameters, left atrial volume index were also measured. Echocardiographic LV relative wall thickness was determined using the formula: \( 2 \times \text{posterior wall thickness} / \text{LV end-diastolic diameter} \). Mitral inflow velocity pattern was recorded from the apical four-chamber view with the pulsed-wave Doppler sample volume positioned at the tips of the mitral leaflets during diastole. Peak early (E) and late (A) diastolic velocities, deceleration time, isovolumetric relaxation time were measured. Early diastolic annular velocity (E’) was measured by means of tissue Doppler imaging at the septal border of the mitral annulus.

Statistical analysis

Data analysis was performed using the SPSS for Windows 11.5 statistical software. Normal and continuous variables were expressed as mean and standard deviation, whereas categorical variables were expressed as number and percentage. The Student’s t-test and Mann-Whitney U-test were used to compare differences between continuous variables. To determine the relation between two variables Pearson’s or Spearman’s correlation analyses were used. Statistical significance was accepted as \( p<0.05 \). The Bland-Altman test and intra-class correlation coefficient (ICC) were used to evaluate inter- and intraobserver variability for continuous variables. Limits of agreement were also calculated using the Bland-Altman, (MedCalc, ver. 9.3.0.0, because this test was not available on the SPSS).

Inter- and intraobserver reproducibility showed perfect agreement for both aortic diastolic diameter (ICC 0.93, 0.89-0.95; Bland-Altman mean difference 0.11, -0.27-0.48) and aortic systolic diameter (ICC 0.94, 0.91-0.96; Bland-Altman mean difference: -0.19, -0.52-0.13).

RESULTS

Clinical and echocardiographic characteristics, and data on P-wave duration and PWD of the patient and control groups are presented in Table 1. There were no significant differences between the two groups with respect to age, gender, heart rate, blood pressure, LV end-diastolic and end-systolic dimensions, interven-tricular septum thickness, posterior wall thickness, LV relative wall thickness, and LV ejection fraction.

Aortic strain and distensibility were significantly lower in patients with BAV than in controls (3.7±2.5% vs. 8.0±4.4%, \( p=0.0001 \) and 1.1±0.8 vs. 2.7±1.5 cm².dyne⁻¹.10⁻⁶, \( p=0.0001 \), respectively). Aortic stiffness index and aortic elastic modulus were significantly greater in patients with BAV (12.8±8.0 vs. 6.6±3.1, \( p=0.0001 \) and 44.5±25.6 vs. 23.5±11.6 dyne.cm⁻².10⁶, \( p=0.0001 \), respectively). Patients with BAV also had significantly higher E/E’ ratio and left atrial volume index (Table 1).

Among electrocardiographic parameters, \( P_{\text{max}} \) and PWD were significantly greater in BAV patients compared to controls (128±11 vs. 115±11 msec, \( p=0.006 \) and 70±10 vs. 66±13 msec, \( p=0.02 \), respectively), whereas \( P_{\text{min}} \) was similar (Table 1).

In correlation analysis (Table 2), \( P_{\text{max}} \) was significantly correlated with aortic strain (\( r=-0.30, p=0.01 \)), aortic distensibility (\( r=-0.27, p=0.02 \)), aortic stiffness index (\( r=0.36, p=0.004 \)), and aortic elastic modulus (\( r=0.38, p=0.003 \)) and PWD was correlated with aortic strain (\( r=-0.23, p=0.05 \)) and aortic elastic modulus (\( r=0.25, p=0.05 \)).

DISCUSSION

To our knowledge, this is the first study to assess the relationship between aortic elasticity, LV diastolic function, and PWD in patients with isolated BAV without significant valvular dysfunction, where BAV was found to be associated with prolonged P-wave duration and increased PWD compared to controls. In addition, increases in PWD was related to aortic elasticity parameters.

P-wave duration and PWD are markers of inter-atrial and intra-atrial conduction disorders of sinus impulses, and inhomogeneous atrial conduction.[5] It has been demonstrated that PWD on the electrocardiogram has a predictive value for atrial fibrillation.[6] Increased P-wave duration and PWD have been reported in various clinical settings, including coronary artery disease, hypertension, rheumatic mitral stenosis, mitral annular calcification, hypertrophic cardiomyopathy, obstructive sleep apnea, and obesity.[8-14] It has also been shown that patients with prehypertension may have increased P-wave duration and PWD.[15]

The mechanisms of increased PWD are not well established. However, several studies have suggested
that increased P-wave duration and PWD may be associated with myocardial ischemia,[16] altered autonomic control,[17] aortic elasticity,[18] LV diastolic dysfunction,[19] enlarged left atrial dimension and elevated left atrial pressure,[20,21] and left atrial fibrosis.[22]

Recently, many studies have demonstrated a significant relationship between arterial stiffness and LV diastolic function.[23,24] Likewise, reduced aortic wall elasticity has been shown in patients with BAV, which is not only a disorder of valvulogenesis, but also represents a genetic disorder of the aorta and cardiac development.[25] An association between PWD and LV diastolic dysfunction has also been reported. Gündüz et al.[19] demonstrated increased PWD in patients with diastolic dysfunction, but this increase was unrelated to the severity or cause of diastolic dysfunction. Our study patients showed impaired diastolic function with a higher E/E’ ratio and left atrial volume index, but the E/A ratio and deceleration time were not different between the two groups. Increases in the left atrial volume may change the geometry of atrial fibrils and this might explain the increase in PWD and P_max in the current study. Besides, both LV diastolic dysfunction related to increased aortic stiffness and primary myocardial impairment have been shown in patients with isolated BAV.[7] We hypothesized that, like in many different conditions, increased aortic stiffness and LV diastolic dysfunction might increase PWD in patients with isolated BAV. Increased PWD causing atrial fibrillation could be a subject of another study in patients with isolated BAV.

Data are limited on the relation between atrial inhomogeneity of electrical activity and arterial elasticity parameters. Çelik et al.[18] demonstrated that young patients with prehypertension had increased PWD and arterial stiffness and these parameters were correlated with each other. In the present study, there was also a significant relation between aortic elasticity and P_max.

### Table 1. Clinical and echocardiographic characteristics, together with P-wave duration and P-wave dispersion in patients with isolated bicuspid aortic valve and in controls

<table>
<thead>
<tr>
<th></th>
<th>Bicuspid aortic valve (n=39)</th>
<th>Controls (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.5±11.3</td>
<td>34.6±11.2</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>25</td>
<td>17</td>
</tr>
<tr>
<td>Female</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.8±0.3</td>
<td>1.8±0.3</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>117.5±12.2</td>
<td>116.6±8.11</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>74.3±9.6</td>
<td>75.1±5.7</td>
</tr>
<tr>
<td>Left ventricle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic diameter (cm)</td>
<td>4.6±0.1</td>
<td>4.6±0.4</td>
</tr>
<tr>
<td>End-systolic diameter (cm)</td>
<td>2.6±0.6</td>
<td>2.7±0.3</td>
</tr>
<tr>
<td>Systolic aortic diameter (cm)</td>
<td>3.3±0.6</td>
<td>2.9±0.3</td>
</tr>
<tr>
<td>Diastolic aortic diameter (cm)</td>
<td>3.2±0.6</td>
<td>2.7±0.4</td>
</tr>
<tr>
<td>Aortic strain (%)</td>
<td>3.7±2.5</td>
<td>8.0±4.4</td>
</tr>
<tr>
<td>Aortic distensibility (cm².dyne⁻¹.10⁻⁶)</td>
<td>1.1±0.8</td>
<td>2.7±1.5</td>
</tr>
<tr>
<td>Aortic stiffness index</td>
<td>12.8±8.0</td>
<td>6.6±3.1</td>
</tr>
<tr>
<td>Aortic elastic modulus (dyne.cm².10⁶)</td>
<td>44.5±25.6</td>
<td>23.5±11.6</td>
</tr>
<tr>
<td>E/A</td>
<td>1.5±0.4</td>
<td>1.4±0.5</td>
</tr>
<tr>
<td>E/E’</td>
<td>8.3±2.6</td>
<td>6.9±1.5</td>
</tr>
<tr>
<td>Left atrial volume index (ml/m²)</td>
<td>24.2±5.8</td>
<td>21.7±4.1</td>
</tr>
<tr>
<td>Maximum P-wave duration (msec)</td>
<td>128±11</td>
<td>115±11</td>
</tr>
<tr>
<td>Minimum P-wave duration (msec)</td>
<td>58±7</td>
<td>58±8</td>
</tr>
<tr>
<td>P-wave dispersion (msec)</td>
<td>70±10</td>
<td>66±13</td>
</tr>
</tbody>
</table>
and PWD in the BAV group. Recently, the concept of disease continuity has been proposed to describe the relationship between the arteries and the rest of the cardiovascular system.[23,24] Thus, our results suggest that increased PWD, impaired aortic elasticity parameters and LV diastolic parameters might be early findings of subclinical cardiovascular involvement in our patient group.

**Study limitations**

This study has some limitations. It involves a small sample of patients with BAV. However, this BAV group was an exceptional population because of having no valvular dysfunction. As it was a cross-sectional study, it did not include a rhythm follow-up. Thus, we do not know whether increased PWD predicts atrial arrhythmias in our patient group. We measured P_{max} and P_{min} manually using a caliper instead of using a computer-assisted P-wave calculating system. Although manual PWD measurements are criticized in some studies, it has been shown that manual measurement could be done with little error with standardized signal size and paper speed.[26]

In conclusion, our study showed that isolated BAV without significant valve dysfunction was associated with prolonged P-wave duration and increased PWD, the mechanisms of which may include reduced aortic elasticity, increased left atrial volume index, and impaired LV diastolic function.

**Conflict-of-interest issues regarding the authorship or article: None declared**

**REFERENCES**


**Table 2. Correlation analysis for P-wave parameters and echocardiographic aortic elasticity parameters in patients with isolated bicuspid aortic valve**

<table>
<thead>
<tr>
<th></th>
<th>Maximum P-wave duration</th>
<th>Minimum P-wave duration</th>
<th>P-wave dispersion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
</tr>
<tr>
<td>Aortic strain</td>
<td>-0.30</td>
<td>0.01</td>
<td>0.004</td>
</tr>
<tr>
<td>Aortic distensibility</td>
<td>-0.27</td>
<td>0.02</td>
<td>-0.003</td>
</tr>
<tr>
<td>Aortic stiffness index</td>
<td>0.36</td>
<td>0.004</td>
<td>0.10</td>
</tr>
<tr>
<td>Aortic elastic modulus</td>
<td>0.38</td>
<td>0.003</td>
<td>0.05</td>
</tr>
</tbody>
</table>
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Key words: Aortic valve abnormalities; echocardiography; elasticity; electrocardiography/methods; heart conduction system; heart defects, congenital.

Anahtar sözcüklер: Aort kapağı/anormallik; ekokardiyografi; esneklik; elektrokardiyografi/yöntem; kalp iletim sistemi; kalp defekti, doğuştan.