# Evidence of Early Left Ventricular Dysfunction in Bicuspid Aortic Valve Patients Identified by MRI-Based Wave Intensity Analysis

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**Purpose**: There is an energetic and elastic interdependence between the left ventricle (LV) and arterial systems in normal physiology, termed ventricular-arterial coupling, which is altered by aging (due to increased arterial stiffness) and conditions such as congestive heart failure, hypertension and aortic stenosis.[1] One approach to assessing ventricular-arterial coupling is with wave intensity analysis (WIA), which traditionally utilizes ultrasound techniques; however, a method for measuring forward traveling waves in the aorta with 2D phase-contrast MRI (PC-MRI) has been recently described.[2] **The forward compression wave (FCW) that occurs in early systole has been correlated with the rate of ventricular pressure rise (LV *dp/dt*) and is considered to be a marker of LV systolic function**.[3] In a study of patients with congenital aortic stenosis evidence of early myocardial fibrosis was detected despite the LV being otherwise normal, suggesting that there may be sequela of congenital valvular disease related to increased left ventricular afterload, which are not detected by conventional echocardiographic evaluation. The most common cause of congenital aortic valve stenosis is bicuspid aortic valve (BAV). There are several possible sources of inefficient ventricular energetics (i.e. energy loss) in BAV patients including disorganized systolic flow patterns[5,6] and increased afterload due to valvular stenosis or increased arterial stiffness.[7] **We hypothesized that there may be disturbances in ventricular function, related to altered ventricular-arterial coupling, which precede echocardiographic abnormalities in BAV patients.**

| | Patient Characteristics | | |
|---|---|---|---|
| **Variable** | **Normal (n=10)** | **BAV** | **p-value** |
| Age (y) | 31.2 ± 10.7 | 34.0 ± 15.3 | 0.49 |
| Sex (male/female) | 4/6 | 29/24 | 0.5 |
| Pulse wave velocity (m/s) | 3.5 ± 0.3 | 4.1 ± 0.2 | 0.12 |
| FCW (10^-5m/s) | 4.43 ± 1.62 | 2.59 ± 2.73 | **<0.002** |
| Maximum Diameter (cm) | 2.7 ± 0.3 | 3.6 ± 0.8 | **<0.001** |
| | **FCW Correlations** | | |
| **Variable** | **Pearson's *r*** | ---------- | **p-value** |
| Age (y) | -0.47 | - | **<0.001** |
| Maximum Diameter (cm) | -0.67 | - | **<0.001** |
| Pulse wave velocity (m/s) | -0.37 | - | **0.01** |
| Aortic stenosis | -0.26 | - | **0.09** |
| | **Regression Results** | | |
| **Predictors of FCW** | **Coefficient** | **SE** | **p-value** |
| Maximum Diameter (cm) | -1.27 | 0.11 | **<0.001** |
| Pulse wave velocity (m/s) | -1.21 | 0.18 | **<0.001** |
| Body Surface Area | 1.48 | 0.27 | **<0.001** |
| Aortic insufficiency severity | 0.28 | 0.08 | **<0.002** |
| Aortic stenosis | -0.19 | 0.08 | **0.24** |

**Methods**: Bicuspid aortic valve patients (n=53) and "normal" patients without cardiovascular disease (n=10) who has undergone cardiac MRI including 2D-PC sequences (temporal resolution <30ms) in the tubular ascending aorta were identified by chart review. Various clinical variables were collected by chart review. Valvular dysfunction severity and ventricular function (EF) were determined by transthoracic echocardiography (TTE) reports. Luminal segmentation of 2D cine PC-MRI data was performed using free software (Segment, Medvisio) and maximal aortic diameter was measured. WIA software (Matlab, Mathworks) was used to calculate pulse wave velocity (PWV) and FCW using the flow-area (QA) method.[2] Patients with PVW >10 m/s were excluded from analysis, due to low change aortic area over the cardiac cycle (*dA/A*) above this level, which precludes accurate measurement of FCW by the QA method. Statistical analysis included t-tests, ANOVA, Fisher's Exact test, Pearson's correlations and multiple linear regression.

**Results**: All BAV patients had normal ventricular function by TTE (EF: 66.5 ± 7.4%). Maximal aortic diameter was larger in BAV patients versus normal patients, although there was no significant difference in age between these groups (see table). Average FCW values were lower in BAV patients compared to normal patients, but there were no difference in age or sex (see table). There were several statistically significant correlations between FCW and clinical/demographic parameters including age, maximal diameter and PWV (see table). Multiple linear regression identified five variables that predicted FCW (see table) (adjusted $R^2$=0.84).

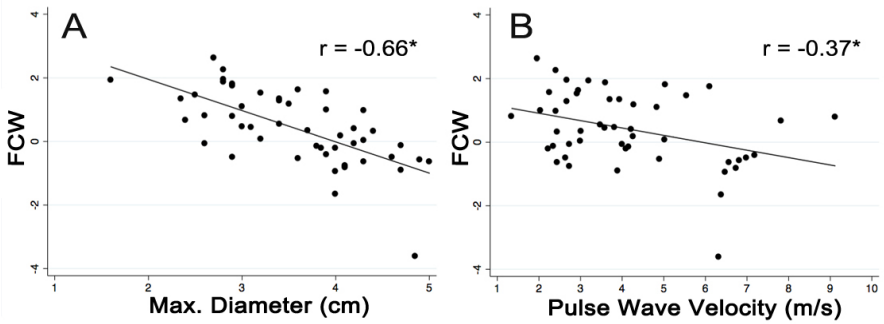


Figure: Negative correlations were seen between forward compression wave ln(FCW) and maximum diameter (**A**) as well as between ln(FCW) and pulse wave velocity (PWV)(**B**). * p<0.001.

**Discussion**: We demonstrated **differences in FCW between BAV and normal patients that are not revealed by conventional analyses.** Decreased FCW intensity was predicted by increases in maximal aortic diameter and aortic stiffness (PWV), even in the absence of valvular dysfunction, suggesting that the presence of aortic dilation and stiffening in BAV patients may lead to early changes in left ventricular function which precede echocardiographic abnormalities. The lower average FCW values in BAV patients may be explained by the increased hemodynamic stress of long-standing inefficient flow patterns in the setting of ascending aortic dilation[5,6] and/or chronically increased afterload in the setting of aortic stiffening.

**Conclusion**: Two features of bicuspid valve-related aortopathy, larger aortic dimensions and increased aortic stiffness, were found to predict decreases in ventricular function, as measured by FCW. **Wave intensity analysis may identify early and adverse changes in ventricular-arterial coupling in patients with BAV that would otherwise go unnoticed**, possibly leading to better medical and surgical treatment.

References:
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