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Is There a Relationship between P Wave Dispersion and Aortic Elasticity Parameters in Ankylosing Spondylitis?

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ABSTRACT

Background : The stiffened arteries in ankylosing spondylitis (AS) may be the cause of the higher cardiovascular burden. P-wave dispersion (PWD), measured from surface electrocardiogram (ECG) leads, has been demonstrated as a reliable indicator of the onset of atrial fibrillation (AF).

Objective: We aim to examine PWD in AS and establish how it relates to aortic elasticity.

Patients and methods: A case-control study was conducted on 136 participants. They were classified into two groups; control (Group I) 46 volunteers, AS (Group II) 90 cases were subjected to aortic elasticity parameters and assessed by m-mode, stiffness index (SI), D (Distinsibility) and tissue doppler imaging (TDI) on aortic systolic velocity ($AO_{S)}$. PWD duration by surface (ECG); lipid profile and blood pressure were assessed.

Results: SI was higher in AS than in the control [25.62±5.68 vs. 11.18±2.19, respectively (P<0.001)]. AO_S was lower in AS than in the control [12.3±2.2 vs. 16.1±0.96, respectively (P<0.001)]. PWD was higher in AS group than in the control. PWD and SI correlated positively (r= 0.831, P<0.001).

Conclusion: Prolonged PWD was correlated with impaired aortic elasticity indexes. A higher risk of having AF may result from the increased PWD duration.

Keywords: Ankylosing spondylitis, P-wave dispersion, Stiffness index, Aortic systolic velocity.

INTRODUCTION

Even after accounting for conventional risk variables, ankylosing spondylitis (AS), an inflammatory illness is linked to a greater risk of cardiovascular death [(1)]. In addition, this patient group has been found to have structural and functional cardiac abnormalities [(2-5)].

The stiffness of the arteries developed by chronic inflammation, which is associated with an increase in cardiovascular events, maybe the cause of the increased cardiovascular burden in AS [(6)]. It has been established that aortic stiffness is a sign of subclinical disease and that it occurs before the onset of hypertension [(7)].

Structure alterations and increased arterial stiffness are caused by elastin fragmentation, increased collagen buildup, and arterial calcification are independent of cardiovascular risk variables adjustment [(8)]. Aortic stiffness can predict incident events such as coronary disease, heart failure, stroke, and cardiovascular mortality [(9)].

Clinically, a number of methods, including arteriography, MRI [(10)], CT angiography [(11)], and pulse wave velocity (PWV) [(12,13)], can evaluate arterial elasticity. However, some techniques cannot be easily used due to allergy to the contrast agent and possible radiation risks. Doppler echocardiographic technique is helpful since it is an easy-to-use, non-invasive imaging method with great repeatability. The ultrasonic technique known as "tissue doppler imaging" (TDI) was created to assess the slow movement of tissue. Previous research had demonstrated that arterial stiffness can be measured accurately with tissue Doppler imaging [(14,15)]. Aortic stiffness has been shown to affect the diameter

of the left atrium and increase the patient's risk of AF, which can lead to an embolic stroke [(16)].

P-wave dispersion (PWD), measured from surface electrocardiogram (ECG) leads, has been investigated in AS before as a possible precursor of arrhythmia [(17)]. It has been demonstrated that a rise in PWD is a reliable indicator of the onset of AF [(18)]. Yet, to our knowledge, the relative association of aortic elasticity parameters in AS patients to a risk of AF development has not been investigated before.

We aimed to examine PWD from ECG and evaluate how it relates to aortic elasticity in AS patients.

PATIENTS AND METHODS

The current case-control study was carried out on 136 participants in the Echocardiography Unit of Cardiovascular Department, and Rheumatology and Rehabilitation Department of Zagazig University Hospital and Cardiovascular Department of Al-Ahrar Teaching Hospital from November 2022 to May 2023.

Sample size and technique: Using an open epi program, power 80% CI 95%The minimal required sample was calculated to be 136 (90 cases, 46 control). Participants were classified into two groups; control (Group I) 46 volunteers and AS (Group II) 90 cases. Based on the modified New York criteria, AS was diagnosed [(19)] and control healthy volunteers were included. Patients with coronary heart disease,

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diabetes, dyslipidemia, hypertension, AF, atrial flutter, or any other atrial tachy-arrhythmias, any atrioventricular (AV) conduction abnormalities, significant valvular lesions, low ejection fraction (EF) <50%,and any aortic disease; coarctation of the aorta, Marfan's syndrome and aortic aneurysm were excluded from the study.
All participants had undergone the following:

Blood pressure (BP) was measured 3 times, each 5 minutes apart. Using a mercury sphygmomanometer and the participant seated, measurements were taken in the right arm. Systolic BP and Diastolic BP were determined [(20)].

Lipid profile was withdrawn from all participants.

Conventional transthoracic 2-dimensional echocardiography using a 1.5–3.6 MHz multifrequency phased array probe (GE Vivid 95, Horton, Norway) was done. The participant was positioned in the left lateral posture, left ventricular EF M-mode, and Simpson, parasternal, and apical images were obtained.

Aortic elasticity parameters: The aorta was imaged using M-mode at a level about 3 cm superior to the aortic valve in the parasternal long axis view, and the aorta's systolic and diastolic diameters (A s and A d, respectively) were noted. A d was recorded at the apex of QRS, and As was recorded when the aortic valve was fully open. Five cardiac cycles were measured for each measurement, and the average was calculated. An aneroid sphygmomanometer was used to measure the Systolic BP and Diastolic BP in the cuff of the brachial artery simultaneously [(21)].

- D (Distinsibility) = 2 (As− Ad) / (Ad(Ps− Pd))
- SI (Stiffness Index) = ln (Ps/Pd) / ((As− Ad)/Ad)
- Ep (Pressure strain elastic modulus) = ((Ps− Pd) / ((As− Ad)/Ad), respectively, where, As is the diameter of the aorta at its end-systole, Ad is its diameter at its end-diastole, Pd is the diastolic BP and Ps is the systolic BP.

Tissue Doppler imaging (TDI) was used**,** in order to measure peak velocities during systole (AOs), early (AO_E), and late (AO_A) peak velocities at diastole, a sampling volume was placed at the same site of the aforementioned aorta [(22)].

Figures 1 and 2 represent case demonstration of the studied groups.

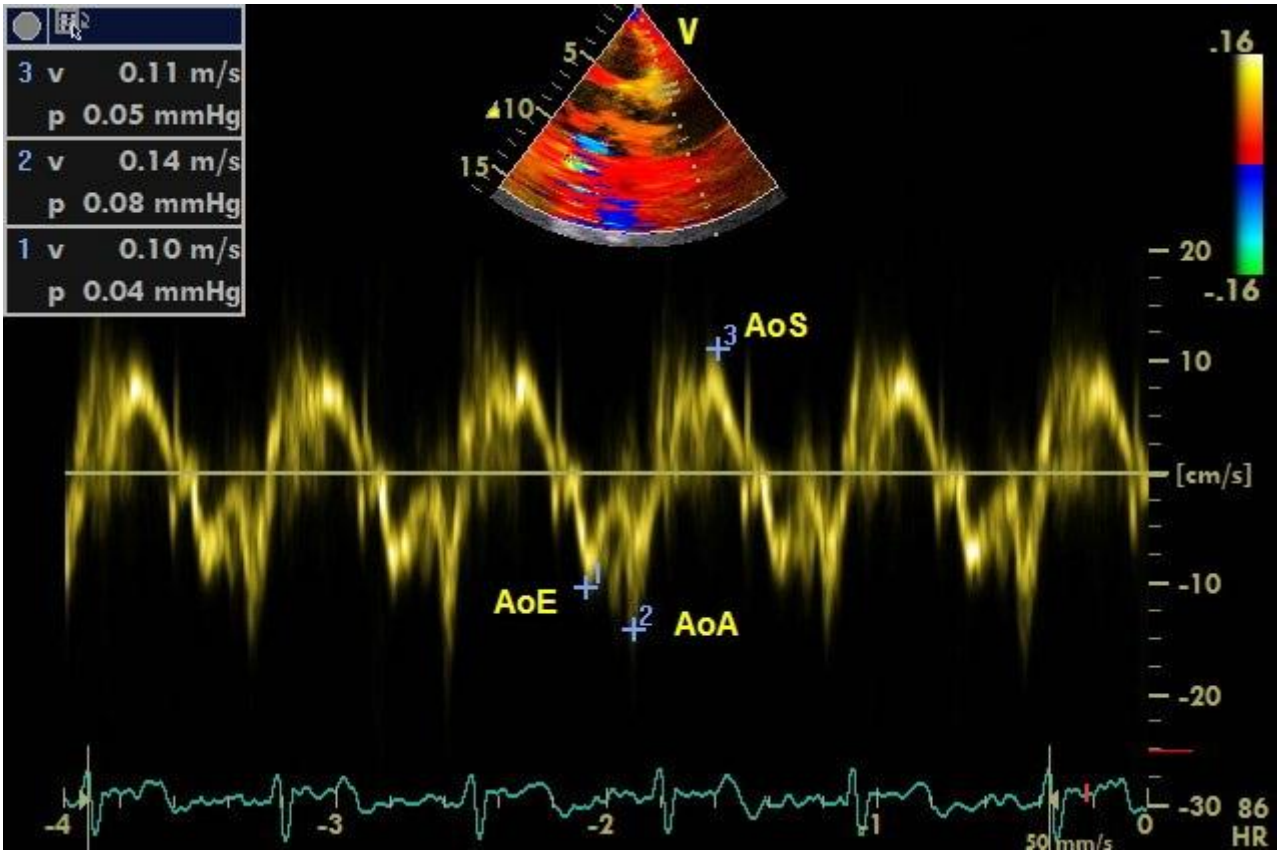

Figure (1): Case demonstration of TDI on ascending aorta waves in control group I showing systolic (AoS) peak velocity 0.11m\s, early diastolic (AoE):0.10m\s , and late diastolic (AoA):0.14m\s.

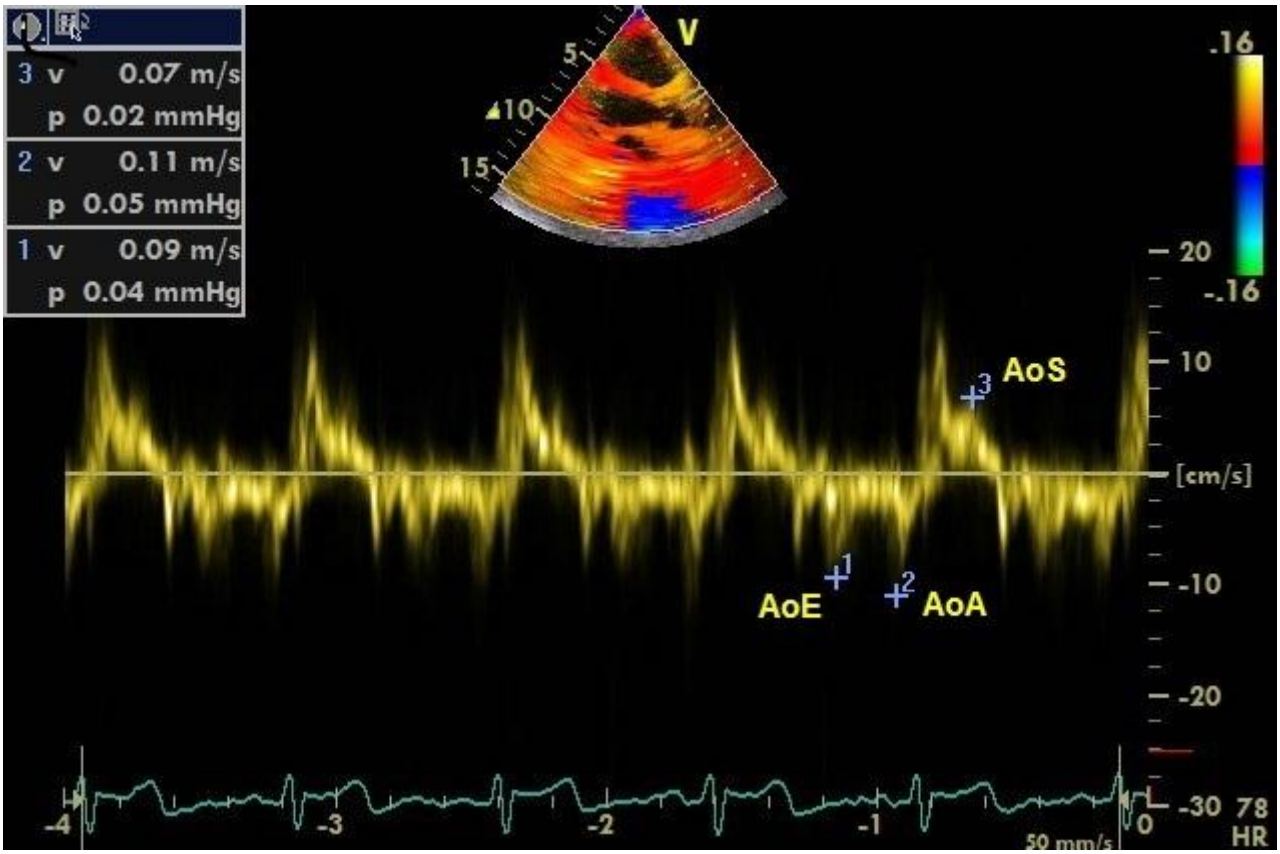

Figure (2): Case demonstration of TDI on ascending aorta waves in AS group II showing systolic (AoS) peak velocity 0.0.07m\s, early diastolic (AoE):0.09m\s , and late diastolic (AoA):0.11m\s.

For the assessment of mitral EA, Ee, the average velocities assessed from the septal and lateral mitral annuli on the four-chamber view were taken [(23)].

Twelve leads surface electrocardiography (ECG) (Hewlett Packard M1700A) was used. Two cardiologists blinded to the individuals' clinical information manually measured P wave duration (Pdur) on a higher-resolution computer screen using digital calipers.

The ECGs were four times amplified using Adobe Photoshop. The first atrial deviation from the isoelectric line was used to identify the P-wave beginning, and the end was the atrial signal returning to the isoelectric line. The mean Pdur was calculated as the mean value in each lead. PWD ms (P maximum-P minimum) was used to define the difference between the maximum and minimum Pdur [(24)].

Ethical Approval:

This study was ethically approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University, Egypt (No. ZU-IRB # 10136/20-11-2022). Written informed consent was obtained from all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical analysis

The collected data were introduced and statistically analyzed by utilizing the Statistical Package for Social Sciences (SPSS) version 17 for windows. Qualitative data were defined as numbers and percentages. Chi-Square test was used for comparison between categorical variables. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as mean and standard deviation (SD), and independent sample t-test was used for comparison between groups. To evaluate the link between different study variables, Pearson correlation was used. P value ≤0.05 was considered to be statistically significant.

RESULTS

There was no significant difference regarding age, and sex, while LDL was lower in AS group than in control group (**Table 1).**

Table (1): Demographic, laboratory characteristics of the studied groups:

Variable	Group I Control group (n=46)		Group II Ankylosing Spondylitis (n=90)		P-value
Age (years) Mean±SD Range	36.33±6.43 (20-50)		34.12±7.71 (20-60)		0.106
Variable	**No**	**(%)**	**No**	**(%)**	**P-value**
Sex • **Male** • **Female**	24 22	52.2 47.8	51 39	56.7 43.3	0.618
BMI(kg\m2) Mean±SD	29.76±3.6		27.54±1.89		**<0.001**
Total Cholesterol (mg\dl) Mean±SD	100.26±19.17		104.31±16.12		0.181
HDL(mg\dl) Mean±SD	56.57±9.56		54.84±6.22		0.174
LDL(mg\dl) Mean±SD	121.5±30.71		102.48±17.45		**<0.001**
TG (mg\dl) Mean±SD	115.4±7.63		134.82±21.4		**<0.001**

BMI: Body mass index; **SD**: Standard deviation **TG**: Triglycerides; **LDL**: Low densitylipoprotein**; HDL**: High density lipoprotein.

Systolic and diastolic function parameters were presented in **Table 2.**

Table (2): Conventional LV assessment study of the studied groups:

Variable	Group I Control (n=46)	Group II Ankylosing Spondylitis (n=90)	P-value
M-Mode Mean±SD Range	66.58±8.2 (55-79)	65.97±5.93 (55-77)	0. 28
ESV Mean±SD Range	46.89±14.26 (23-67)	49.66±12.49 (23-67)	0.14
EDV Mean±SD Range	77.17±14.96 (55-140)	80.11±16.86 (58-140)	0.327
EF simpson Mean±SD Range	66.76±5.24 (55-79)	64.92±5.5 (53-75)	0.062
MV E/A Mean±SD Range	0.84±0.15 (0.68-1.4)	1.08±0.27 (0.64-1.8)	<0.001
Septal e (m/s) Mean±SD Range	13.1±2.1 (9-17)	12.7±0.25 (0.9-1.8)	0.454
Lateral e (m/s) Mean±SD Range	15.3±2.1 (9-19)	14.5±2.9 (9-19)	0.119
MVE/e average Mean±SD Range	5.1±0.57 (4.5-6.5)	5.76±0.98 (3.9-7.9)	<0.001

MV; Mitral Valve, **E**; peak velocity of early diastolic transmitral inflow, **A**; peak velocity of late transmitral flow **e**; peak velocity of early diastolic mitral annular motion, **ESV;** end-systolic volume, **EDV**; end-diastyolic volume, **EF**; ejection fraction.

Systolic blood pressure was higher in AS than in the control [123±7.71 vs.119.78±9.06, respectively (P=0.02)]. SI was higher in AS than in the control [25.62±5.68 vs. 11.18±2.19, respectively (P<0.001)]. D was lower in AS than in the control [3.64±0.63 vs. 6.79±1.08, receptively (P<0.001)]. AO_S was lower in AS than in the control [12.3±2.2 vs. 16.1±0.96, respectively (P<0.001)] **(Table 3).**

Table (3): Aortic elasticity parameters of the studied groups:

Variable	Group I Control group (n=46)	Group II Ankylosing Spondylitis (n=90)	P-value
AOdiastolic diameter(cm)			
Mean±SD	1.9870±0.284	1.97±0.282	0.81
Range	(13-25)	(14-25)	
AOsystolic diameter(cm)			
Mean±SD	2.25±0294	2.24±0.292	0.88
Range	(16-28)	(17-27)	
DC(cm)			
Mean±SD	0.26±0.10	0.28±0.13	0.49
Range	(0.1-0.6)	(0.1-1)	
SBP(mmHg)			
Mean±SD	119.78±9.06	123±7.71	**0.028**
Range	(110-130)	(110-130)	
DBP(mmHg)			
Mean±SD	75.65±4.79	75.94±5.7	0.771
Range	(70-80)	(70-90)	
PP(mmHg)			
Mean±SD	44.13±9.56	46.5±6.51	0.073
Range	(30-60)	(30-60)	
SI	11.18±2.19	25.62±5.68	**<0.001**
Mean±SD	(10-48)	(11-45)	
D (10^{-3}mmHg^{-1})			
Mean±SD	6.79±1.08	3.64±0.63	**<0.001**
Range	(1-8)	(1-5)	
Elastic Modulus			
Mean±SD	418.11± 221.3	421.98±233.52	0.926
Range	(175-1000)	(175-1080)	
AOs **(cm\s)**			
Mean±SD	16.1±0.96	12.3±2.2	**<0.001**
Range	(10-18)	(6-16)	
AO_E **(cm\s)**			
Mean±SD	11.9±1.98	12±2.3	0.805
Range	(8-15)	(6-15)	
AO_A **(cm\s)**			
Mean±SD	10. 31±3.2	10.8±2.3	0.266
Range	(8-15)	(7-17)	

AO: Aortic; **DC**: diameter change; **SBP**: systolic blood pressure; **DBP**: diastolic blood pressure; **PP**: pulse pressure**;** **SI**: stiffness index; **D**: Distensibility; **AOs**: Aortic wall systolic velocity; **AO_E:** Aortic wall early diastolic velocity. **AO_A:** Aortic wall late diastolic velocity.

PWD duration was prolonged in AS group than in the control (30 vs. 20, respectively with P<0.001) (**Table 4).**

Table (4): ECG data of the studied groups:

Variable	Group I Control (n=46)	Group II Ankylosing spondylitis (n=90)	P-value
P maximum(ms) Mean±SD Range	100.22±7.15 (90-110)	111.67±5.25 (100-120)	<0.001
P minimum(ms) Mean±SD Range	82.39±7.05 (80-110)	81±8.35 (70-100)	0.346
PWD(ms) Median (IQR)	20 (10-20)	30 (30-40)	<0.001
HR (bpm) Mean±SD Range	79.89±4.01 (70-90)	80.17±4.27 (70-90)	0.718

PWD: P wave dispersion, **HR**:heart rate **, bpm**:beat per min

- SI and AOs correlate negatively (r= -0.4, P<0.001) [**Figure 3].**
- PWD and SI had a strong positive connection. (r= 0.831, P<0.001) [**Figure 4].**
- PWD and D had a strong negative correlation (r= - 0.748, P<0.001) [**Figure 5].**
- PWD and AOs had a negative correlation (r= - 0.268, P<0.001) [**Figure 6].**
- Intra and inter-observer variabilities were non-significant. Two blinded investigator (E.H.S and S.W) randomly selected ECG recordings of 45 participants (33%) for inter-observer agreement, 1 week later (E.H.S) investigated the same ECG for intra-observer agreement; for P maximum the intra and inter-observer variabilities were 2.6 and 3%, respectively, and for PWD were 3.8 and 4.1%, respectively.

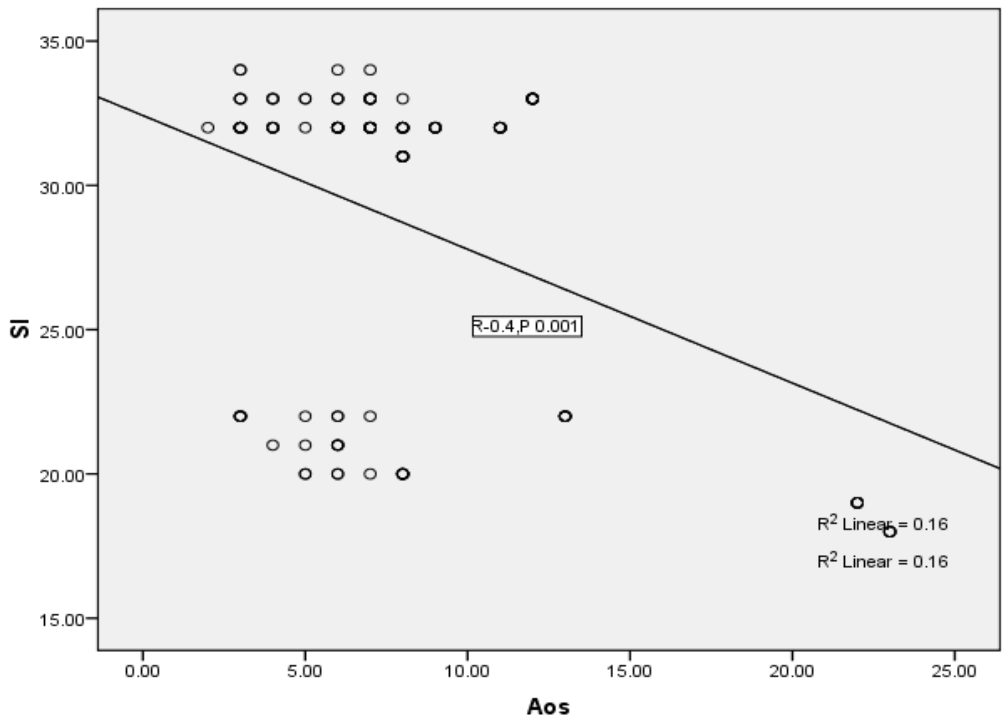

Figure (3): Correlation between SI, $AO_{S.}$ **[SI**: stiffness index, $\mathbf{AO_{S.}}$ aortic systolic wave].

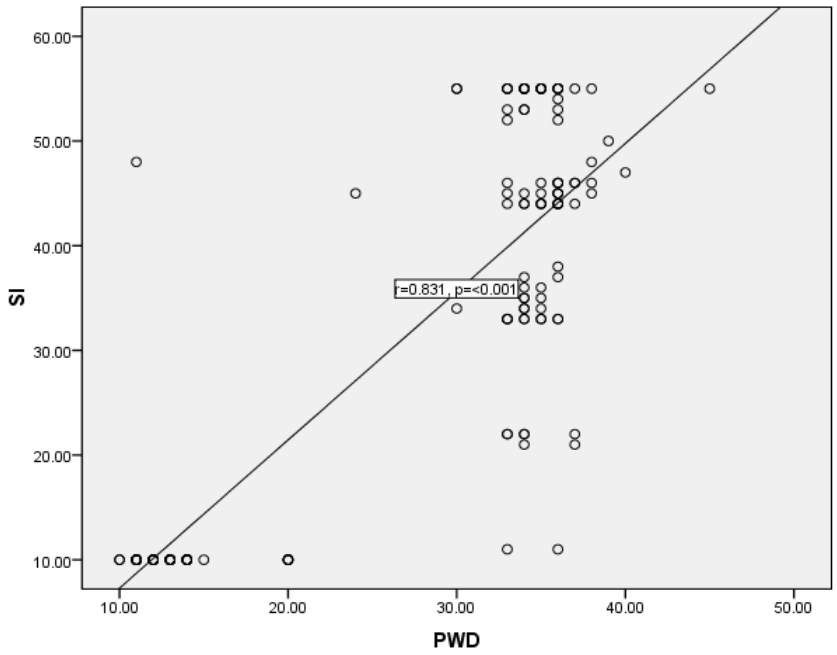

Figure (4): Correlation between SI and PWD **[SI**: stiffness index, **PWD**: P wave dispersion**]**.

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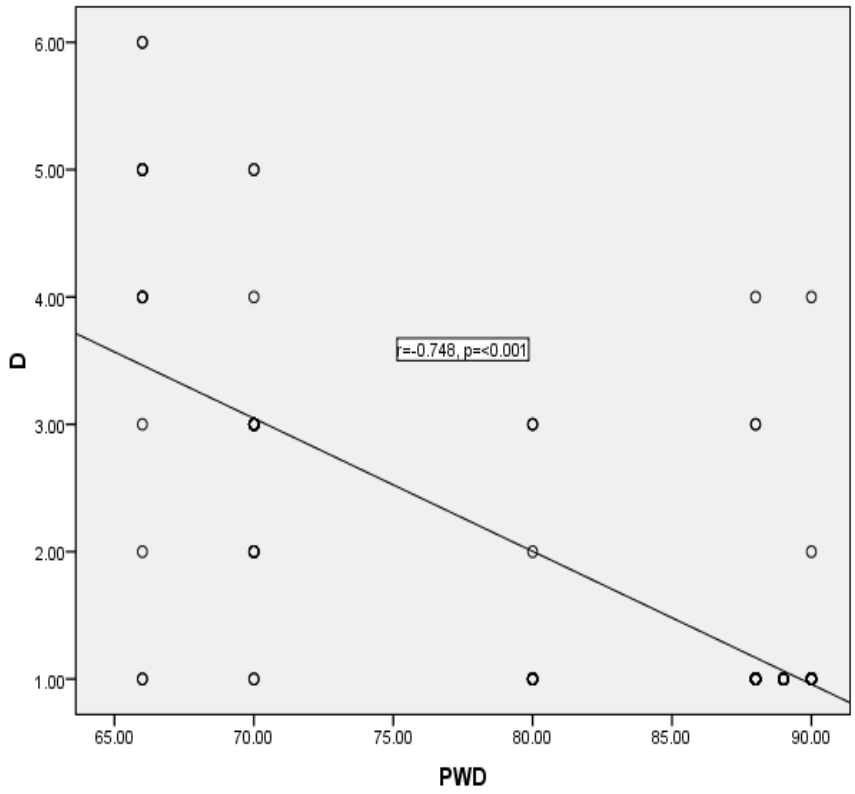

Figure (5): Correlation between distensibility and PWD **[D**: distensibility, **PWD**: P wave dispersion].

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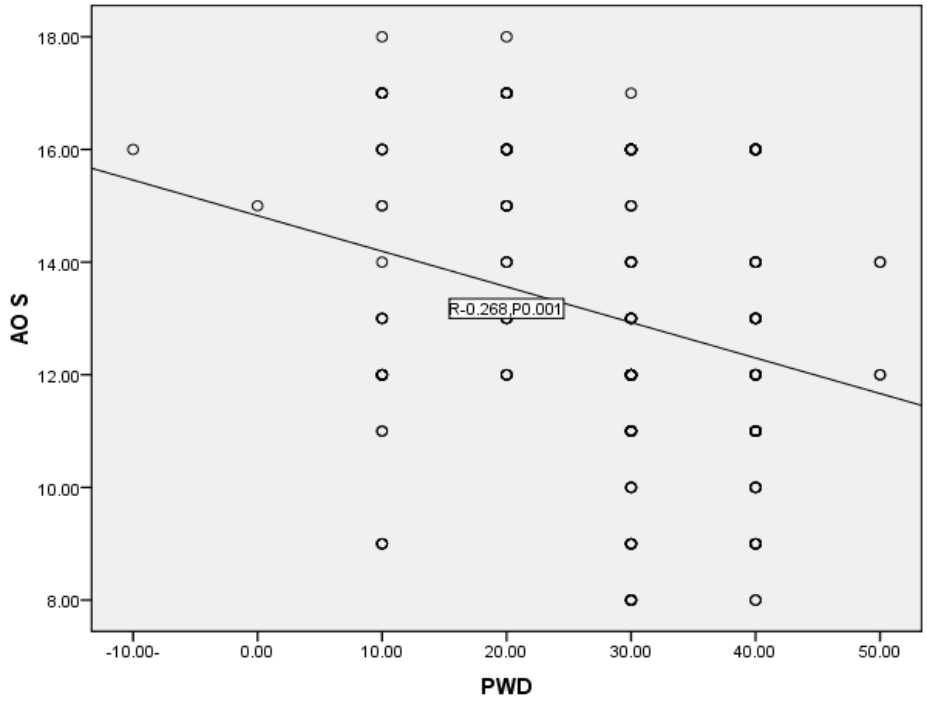

Figure (6): Correlation between AO_S and PWD **[AO_S**: aortic systolic wave, **PWD**: P wave dispersion**]**.

DISCUSSION

The main finding in our study was that AS patients have a higher aortic stiffness index SI compared to control this was concordant with **Ozen *et al.*** [25] who reported the same finding in a case-control study. **Biesbroek *et al.*** [26] concluded that compared to controls, AS patients showed increased arterial stiffness measured by higher aortic arch PWV. **Avram *et al.*** [27] reported that compared to healthy controls, AS patients had a significantly increased arterial stiffness as measured by aortic PWV. **Bodnar *et al.*** [28], reported higher arterial stiffness in people with AS's carotid femoral PWV. On the contrary, **Arida *et al.*** [29] and **Berg *et al.*** [30] found that arterial stiffness measured by PWV in the carotid and the femoral artery was not found in their studies.

Our AS population had higher systolic blood pressure when compared to the control this finding confirms the fact that arterial stiffness is a hypertension (HTN) precursor and a cardiovascular disease (CVD) risk factor [7].

Our AS population had lower aortic distensibility when compared to the control, this was concordant with **Moyssakis *et al.*** [31] who found that distensibility was significantly decreased in AS in comparison to the control.

The principle of using TDI to assess aortic wall movement described as aortic dilation causes the S wave to be produced when the heart contracts. Aortic retraction causes E and A waves to be produced as the heart relaxes. The stiffness will rise when the aorta's elasticity declines, reducing the distensibility and slowing the S wave, E wave, and A wave of the ascending aorta [32].

Up to our knowledge, the application of TDI in the aortic wall to assess arterial stiffness has been studied in other studies as premature coronary artery disease (CAD) [33], well-established CAD [34], and also hypertensive and ischemic patients [35], but in AS hasn't been investigated before.

Our study showed that AO_S velocity was lower in the AS population compared to the control, a finding indicating increased aortic stiffness, while other parameters of TDI on the aortic wall as AOE and AO_A were non-significant. **Eryol *et al.*** [34]**,** reported a significant decrease in AO_S in patients with CAD compared to those without CAD while non-significant AO_E, AO_A. **Güngör *et al.*** [33] found that by TDI on aortic wall AO_S, AO_A was non-significant between CAD cases and the control while E_{AO} was significantly decreased in CAD than the control. **Lu *et al.*** [35]**,** concluded that the S wave velocity of the anterior aortic wall was decreased progressively with increasing coronary severity in hypertensive ischemic patients.

Our study showed that AO_S by TDI and aortic SI by m-mode correlate negatively**. Eryol *et al.*** [34] reported negative correlation (r-0.28, P<0.01) but in CAD patients.

Actually, our study participants did not have a prior history of AF and were on sinus rhythm. To the best of our knowledge, in AS patients aortic stiffness has never been studied in relation to the PWD from routine ECGs as an AF risk.

We found that AS patients had a significantly wider duration of PWD in comparison to the control, the mechanism of PWD prolongation in AS is due to electrophysiological and structural alteration in the atrium [35].

Aksoy *et al.* [17] concluded that PWD was significantly prolonged in AS than control.

Our results showed that PWD correlates positively with SI, while correlating negatively with distensibility. **Celik *et al.*** [24] reported that in prehypertensive patients PWD correlates positively with SI, while correlate negatively with distinsibility). **Acar *et al.*** [16] found that SI and PWD correlate positively (r= 0.52; P= 0.005) in acute myocardial infarction (MI) patients.

LIMITATIONS

The relationship between aortic stiffness and AF was not directly addressed in this study; instead, PWD was employed as marker of.AF risk.

Despite the fact that PWD has been shown to be a sensitive and specific ECG predictor of AF in a number of clinical settings, no electro-physiologic study has been able to definitively identify a potential relationship between PWD and the dispersion in atrial conduction timings.

The method employed to determine PWD is not standardized. Ideally, a signal-averaging ECG system should be used for manual PWD measurement [39]. The gold standard for measuring arterial stiffness is aortic PWV, but this method is invasive and not available at our institute.

CONCLUSIONS AND RECOMMENDATIONS

Through detection of impaired Aortic elasticity parameters in patients with AS, Patients at early, subclinical risk for CVD could be identified. Lower AO_S velocity may indicate increased arterial stiffness in AS patients**.** In AS patients, the findings demonstrate an association between deteriorated aortic elasticity measures and prolonged PWD. The reported increase in PWD may lead to an increased risk of developing AF, through this study we could put a link between arterial stiffness and risk of AF occurrence in AS. So we recommend that further studies are needed to detect the long-term clinical follow up of these findings in AS.

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