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RELATION BETWEEN AORTIC STIFFNESS AND LEFT VENTRICULAR DISTOLIC FUNCTION IN PATIENTS WITH PROVEN CORONARY ARTERY DISEASE

R. Sakthi Abirami [1] R. Priya Dharshini [2] A. Sujhithra [3] Dr. M. Chokkalingam [4]

[1]Faculty of Allied Health Sciences, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education Kelambakkam 603 103, TamilNadu, India.
sabirami911@gmail.com;priya91194@gmail.com; sujhithra.1995@gmail.com
[2]Department of Cardiology, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam - 603 103, TamilNadu, India.
mchokkalingam2006@gmail.com

ABSTRACT

Background -The aorta losses its elastic property and becomes stiffen with the process of ageing and atherosclerosis. Aim and Objective - To evaluate aortic stiffness and its relation to left ventricular diastolic function in patients with proven coronary artery disease. Materials and Method –The cross-sectional study included 146 study subjects. Aortic strain and distensibility were calculated from the aortic diameters measured by echocardiography and blood pressure obtained by sphygmomanometer.Results were analyzed using SPSS version 2.1. Results -The aortic stiffness index is significantly increased in patients with proven coronary artery disease(mean ASI = 38.7) than control groups (mean ASI =21.9). High aortic stiffness index and presence of diastolic dysfunction is significantly correlated in patients with proven coronary artery disease .Conclusion - The aortic elasticity and left ventricular diastolic function are significantly impaired in the presence of coronary artery disease. Aortic stiffness index may be used as echocardiographic parameter to predict the atherosclerotic burden.

Keywords – Aortic stiffness index, AorticStrain, AorticDistensibility, LV diastolic dysfunction, coronary artery disease

INTRODUCTION

Coronary heart disease prevalence rates in India have been estimated over the past several decades and have ranged from 1.6% to 7.4% in rural populations and from 1% to 13.2% in urban populations(1). Coronary artery disease is almost always due to atheromatous narrowing,thickening of arterial walls and subsequent occlusion of the vessel (2). The annual number of deaths from CVD (cardiovascular disease) in India is projected to rise from 2.26 million in 1990 to 4.77 million in 2020 (3).

Arterial stiffening is a hallmark of the aging process and atherosclerosis, with a reduction in normal aortic compliance(6).A compliant aorta provides an important buffer for each ventricular contraction that maintains pulse pressure at low levels. Stiffening of the aortic wall and improper matching between aortic diameter and flow are associated with unfavorable alterations in pulsatile hemodynamics, including an increase in forward arterial pressure wave amplitude, which increases pulse pressure. Stiffening of the aortic wall also is associated with elevated pulse wave velocity (PWV) and premature wave reflection(5). Aortic stiffness has emerged as a good tool for further risk stratification because it has been linked to increased risk of atherosclerotic heart disease, myocardial infarction, heart failure, and stroke (6).

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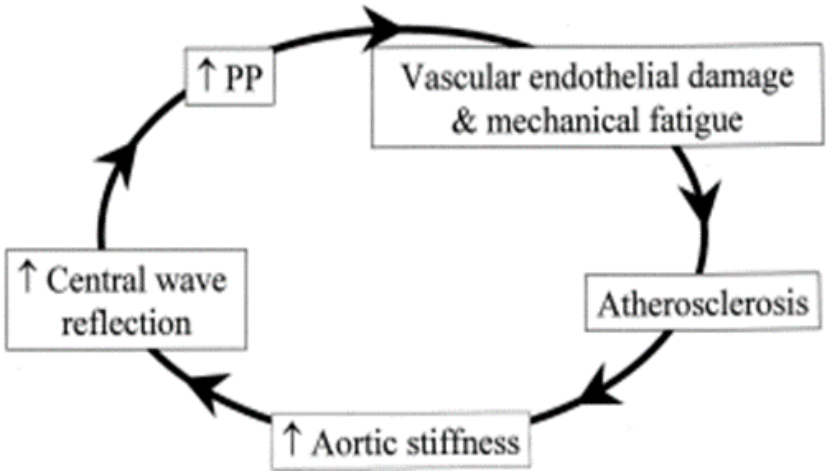

Figure -1: The destructive cycle of vascular damage, involving endothelial dysfunction, atherosclerosis and aortic stiffness (15).

The histological structure of the aorta varies immensely according to its site and functions as a reservoir and conductive system (Windkessel principle). For instance, the proximal aorta is rich in elastin that allows the support of each systolic impulse and accommodates the stroke volume. Thus, the thoracic aorta and its immediate branches show greater elasticity, whereas more distal vessels become progressively stiffer, given the predominance of collagen fibers (5,000 times the tensile modulus of elastin) (4).Stress (σ) is defined as the force applied/area to aparticular object (σ = F/A).It canbe applied in any direction: at radial, circumferential, and longitudinal components. Circumferential wall stress, defined by Laplace's law, is directly proportional to the vessel pressure and radius and inversely proportional to its thickness. Strain (ε) is the resulting deformation (percentage change in length) of an object/material subjectedto a stress force. It is dimensionless (no units) and is defined as:ε =(L- L0) ⁄L0where L is the final length and L0is the initial length.The elastic modulus (E), also known as young's modulus, is the stress/strain ratio. In most biologic materials, this relation is nonlinear, and the slope defines theintrinsic elastic properties ofthe wall material. E is ex-pressed by the formula: E = σ /C where C is the arterial compliance.Arterial compliance (C) is the absolute change in area (or change in diameter (ΔD) for a given pressure step (ΔP) at a fixed vessel length. It is the reciprocal of stiffness and is defined as C=Δ D/ ΔP distensibility, by contrast, is defined as the relative compliance or relative change in diameter/area/pressures step increase. It is the inverse of the elastic modulus (E).

AS = AOSD –AODD/AODD

AD = 2 X Aortic strain /PP

ASI = SBP/DBP/Aortic strain

(AS –Aortic strain, AD –Aortic distensibility, ASI –Aortic stiffness index, AOSD – Aortic systolic diameter, AODD – Aortic diastolic diameter, PP –pulse pressure, SBP – Systolic blood pressure,DBP –Diastolic blood pressure.).

Diastolic dysfunction refers to an increased stiffness and abnormal relaxation of the left ventricle leading to impaired filling during diastole. Myocardial ischemia plays a role in the pathophysiology of diastolic dysfunction, (2) it has been shown to alter the clinical course in CAD patients (7) abnormal arterial compliance may potentially contribute to the development of LV diastolic dysfunction through increased pulse pressure and LV afterload, which in turn promote LV hypertrophy and sub endocardialischemia.The present study aimed at determininghow aortic stiffness is affected in patients with proven coronary artery disease and also excludes hypertension as a criteria, and in evaluating the relation between aortic stiffness and left ventricular diastolic function.

METHODS AND MATERIALS

This is a cross-sectional study carried out at Chettinad Hospital and Research Institute Kelambakkam, Chennai. This study was approved by the Institutional Ethics Committee and a written informed consent was obtained from all study subjects.

A total of 146 study subjects in the age group of 20-80 years of both genders were included. These study subjects were categorized into two groups each comprising 73 (n=73) study subjects: Group 1- Healthy controls; Group 2- coronary artery disease.

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The subjects who were previously diagnosed to have coronary artery disease by coronary angiogram and patients with history of PTCA(percutaneous transluminal coronary angioplasty) or CABG(coronary artery bypass grafting) were taken in proven coronary artery disease group ,all these patients underwent transthoracic echocardiography during their routine follow ups to the cardiology outpatient department .Patients with Hypertension,aortic stenosis,diseases of aorta ,severe aortic regurgitation ,moderate to severe mitral stenosis, marfan syndrome, Bicuspid aortic valve were excluded from the study. Clinical details such as age, gender, medical history were obtained from by one-to-one interview and the hospital medical records.

Blood pressure was measured using sphygmomanometer Korotkoff phases I and V were used to determine the systolic and diastolic pressures, respectively.

ECHOCARDIOGRAPHIC MEASUREMENTS

2D transthoracic echocardiography was performed according to recommendation of current guidelines using commercially available equipment (vivid s5 –GE medical system,Esoate my lab).

In parasternal long axis window ascending aorta systolic and diastolic diameter were measured from the M-mode tracing at the level of 3cm above the aortic valve

The systolic diameter was measured at the maximum anterior motion of the aorta and the diastolic diameter was measured at the peak of the QRS complex on the simultaneously recorded ECG (Electrocardiogram)

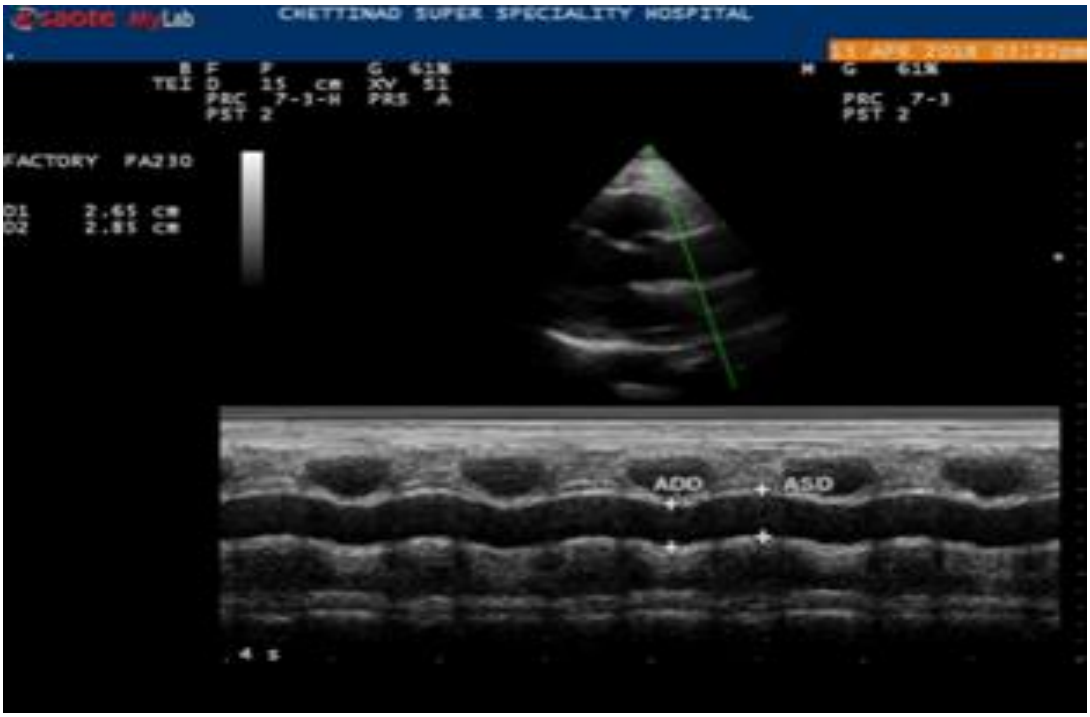

Figure 2 – M mode measurement of aortic diameter in systole and diastole.

Aortic stiffness parameters (Aortic strain,Aortic distensibility and Aortic stiffness index) were calculated by using the below formula (9),

Aortic strain (%) = aortic systolic diameter - diastolic diameter) / diastolic diameter

Distensibility (cm2 /dyn) = (2 x aortic strain) / (systolic pressure - diastolic pressure)

Aortic stiffness index = β=Ln (SBP/DBP)/ strain (Ln: natural logarithm).

LEFT VENTRICULAR DIASTOLIC FUNCTION PARAMETERS

The peak early transmitral filling velocity during early diastole (E), peak transmitral atrial filling velocity during late diastole (A), deceleration time (time elapsed between peak E velocity and the point where the extrapolated deceleration slope of the E velocity crosses the zero baseline), and isovolumetric relaxation time (time period between the end of mitral diastolic flow Doppler tracing and the beginning of aortic flow Doppler tracing) were used

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as left ventricular diastolic function parameters. The transmitral diastolic flow Doppler tracing was imaged in the apical four chamber view by using pulsed Doppler echocardiography with the sample volume sited at the tip of the mitral leaflets. The isovolumetric relaxation time was measured on Doppler tracings obtained in the apical five chamber view with the sample volume placed at the left ventricular outflow tract. The diastolic filling patterns of the study population were classified as normal, abnormal relaxation, pseudo normal, or restrictive pattern. (10).
Statistical analysis was performed using SPSS Version-21. Normally distributed continuous values were expressed as Mean, standard deviation, frequency, percentage. CHI square test was used for analysis of correlation between ASI and Diastolic function.The results with $p < 0.05$ were considered statistically significant.

RESULTS

A total 146 participants were enrolled for this study of which 108 were males and 28 were females. Mean ± SD value for Aortic stiffness and diastolic function measurements of the study subjects are shown in Table 1. Among this LV mass (182.86 v 162.96) and Aortic stiffness index(38.7 v 21.9) is significantly higher in CAD when compared to Control group. Aortic stiffness index of >21.9 is considered to be high. Aorticstrain (0.08 v 2.70) and distensibility (0.01 v 0.09) is significantly to low in CAD than control group.

Table 1 **- Aortic stiffness and diastolic function measurements**,

	Group						**Independent Samples t-test**	
	CAD			**Controls**				
	Mean	**SD**	**SEM**	**Mean**	**SD**	**SEM**	**t-Value**	**P - Value**
Age (yrs)	55.77	11.99	1.40	46.70	13.05	1.53	4.371	**.000**
LVD (cm)	4.60	.61	.07	4.31	.52	.06	3.123	**.002**
LVS (cm)	3.37	.71	.08	2.92	.53	.06	4.312	**.000**
SEPD (cm)	.98	.11	.01	.96	.12	.01	.632	.528
PWD (cm)	1.02	.14	.02	1.00	.11	.01	.972	.333
SEPS (cm)	1.23	.16	.02	1.29	.14	.02	-2.491	**.014**
PWS (cm)	1.29	.15	.02	1.35	.15	.02	-2.547	**.012**
LVMASS (g)	182.86	44.99	5.27	162.96	37.51	4.39	2.903	**.004**
EF (%)	50.00	10.13	1.19	61.81	2.50	.29	-9.673	**.000**
LAD (cm)	3.58	.33	.04	3.38	.27	.03	3.946	**.000**
AOR (cm)	2.78	.29	.03	2.85	.34	.04	-1.457	.147
BPS (mmHg)	111.14	19.40	2.27	117.40	10.41	1.22	-2.429	**.016**
BPD (mmHg)	70.27	7.81	.91	72.19	6.92	.81	-1.570	.119
PP (mmHg)	43.56	9.03	1.06	.00	.00	.00	41.207	**.000**
ASD (cm)	2.92	.31	.04	45.62	7.81	.91	-46.638	**.000**
ADD (cm)	2.74	.33	.04	2.95	.33	.04	-3.926	**.000**
AS (%)	.08	.07	.01	2.70	.32	.04	-68.612	**.000**
AD ($cm^2/dyn/10^3$)	.01	.06	.01	.09	.04	.00	-9.155	**.000**
ASI (β)	38.75	59.43	6.96	21.85	12.24	1.43	2.379	**.019**
E/A	.93	.50	.06	.96	.41	.05	-.359	.720
E/e’	9.36	2.93	.34	6.92	1.54	.18	6.277	**.000**
DT (ms)	195.23	41.77	4.89	212.89	43.18	5.05	-2.511	**.013**
E	.07	.02	.00	.09	.02	.00	-4.443	**.000**
A	.09	.02	.00	.10	.02	.00	-3.082	**.002**
S’	.07	.02	.00	.09	.02	.00	-4.741	**.000**
IVRT (ms)	89.22	13.70	1.60	94.79	17.21	2.01	-2.166	**.032**
IVCT (ms)	81.37	13.04	1.53	78.59	15.07	1.76	1.192	.235

(LVD- left ventricle in diastole, LVS- left ventricle in systole, SEPD- septum diastole, PWD- posterior diastole, SEPS- septum systole, PWD- posterior systole, EF- ejection fraction, LAD- left atrial diameter,AOR-aorta, BPS-blood pressure in systole, BPD-blood pressure in diastole, PP- pulse pressure, ASD- aorta systolic diameter, ADD-aorta diastolic diameter, AS- Aortic strain, AD- Aortic distensibiity, ASI- aortic stiffness index, E/A- early to late diastolic trans mitral flow velocity, E/e’- E to early diastolic mitral annular tissue velocity, DT- deceleration time, E- left ventricular relaxation in early diastole, A- flow in late diastole caused by atrial contraction, S’- Peak systolic annular velocityIVRT- isovolumetric relaxation time, IVCT- isovolumetric contraction time).

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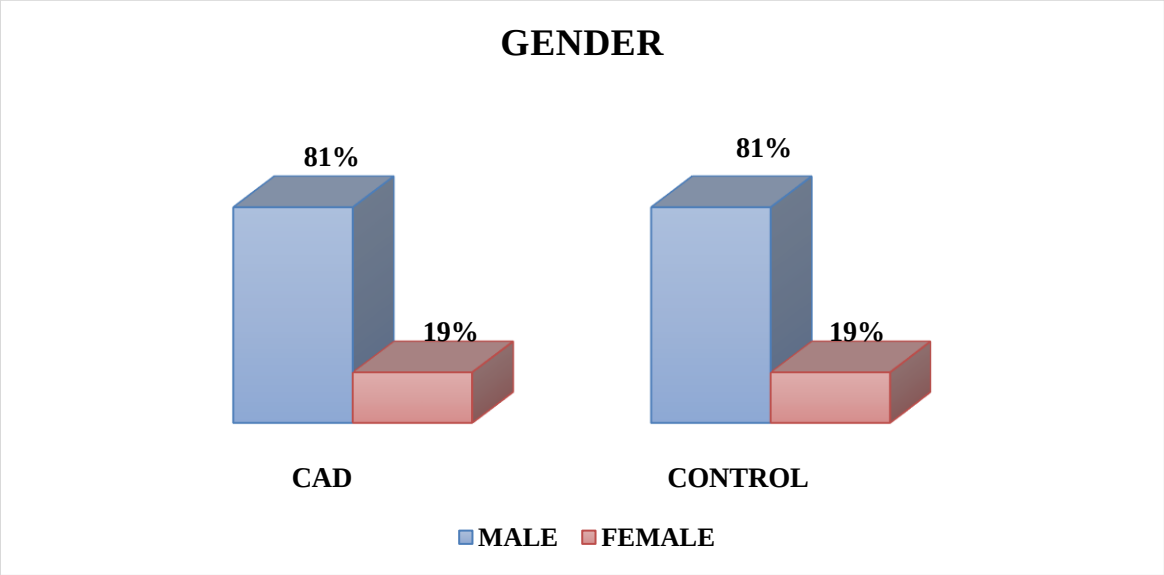

Figure 2 – Gender classification of CAD and Control group

Table 2 - COMPARISION OF ASI IN CAD AND CONTROL GROUP

ASI * CAD Crosstabulation				
ASI		CAD		Total
		CAD	Normal	
ASI ≤ 21.9	Count	22	51	73
	%	30.14	69.86	100.00
ASI > 21.9	Count	51	22	73
	%	69.86	30.14	100.00
Total	Count	73	73	146
	%	100.00	100.00	100.00

Chi-Square Tests		
	Value	Exact Sig. (2-sided)
Pearson Chi-Square	23.041	
Fisher's Exact Test		.000

From table 2 – ASI is significantly increased in patients with proven CAD than control group(significant value 0.000)

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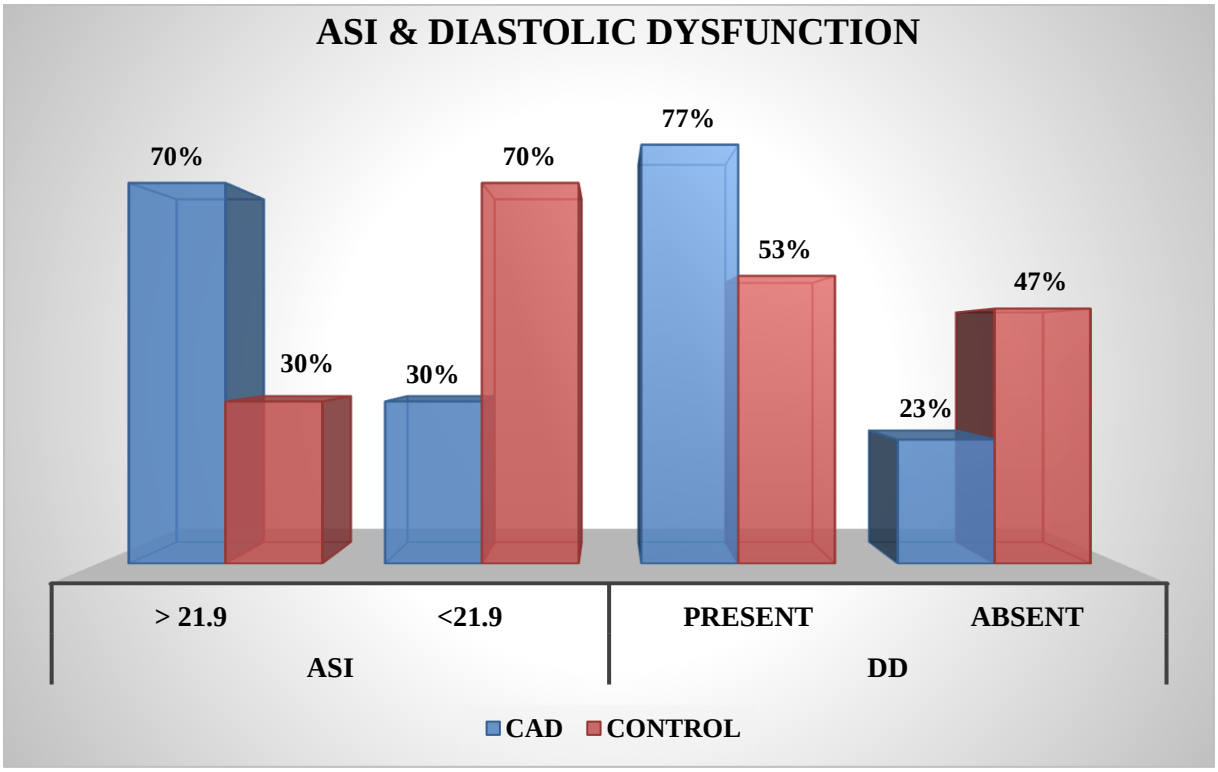

Figure 3 – Classification of ASI and Diastolic dysfunction in CAD and Control group

Table 3 - COMPARISION OF ASI AND DIASTOLIC DYSFUNCTION

CAD * ASI * DD Crosstabulation						
DD				ASI		Total
				ASI ≤ 21.9	ASI > 21.9	
Absent	CAD	CAD	Count	6	11	17
			Row %	35.29	64.71	100.00
			Col %	20.69	50.00	33.33
		Normal	Count	23	11	34
			Row %	67.65	32.35	100.00
			Col %	79.31	50.00	66.67
	Total		Count	29	22	51
			Row %	56.86	43.14	100.00
			Col %	100.00	100.00	100.00
Present	CAD	CAD	Count	16	40	56
			Row %	28.57	71.43	100.00
			Col %	36.36	78.43	58.95
		Normal	Count	28	11	39
			Row %	71.79	28.21	100.00
			Col %	63.64	21.57	41.05
	Total		Count	44	51	95
			Row %	46.32	53.68	100.00
			Col %	100.00	100.00	100.00
Total	CAD	CAD	Count	22	51	73
			Row %	30.14	69.86	100.00
			Col %	30.14	69.86	50.00

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		Normal	Count	51	22	73
			Row %	69.86	30.14	100.00
			Col %	69.86	30.14	50.00
	Total		Count	73	73	146
			Row %	50.00	50.00	100.00
			Col %	100.00	100.00	100.00

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Chi-Square Tests						
DD		Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Absent	Pearson Chi-Square	4.836	1	.028		
	Fisher's Exact Test				.038	.029
Present	Pearson Chi-Square	17.274	1	.000		
	Fisher's Exact Test				.000	.000
Total	Pearson Chi-Square	23.041	1	.000		
	Fisher's Exact Test				.000	.000

From table 3 , increased ASI and Diastolic Dysfunction are significantly correlated in proven CAD patients with the significant value of 0.000.

DISCUSSION

Atherosclerosis increases arterial wall thickness and the stiffness of theaorta. (11)
Aortic stiffness is associated with cardiovascular risk factors such as CAD,smoking, obesity hypertension, glucose tolerance, diabetes, and older age (11).
In our study Aortic strain and distensibiity was significantlylower in patients with CAD than control group and similar results was shown by Taner sen MD et.al(11).
Previous study suggested that aortic stiffness index is significantly increased in patient with CAD, butthe study had other comorbidities limitations such as hypertension, diabetesetc. (13).
Our study suggests that aortic stiffness index is significantly higher in patient with CAD even after excluding one such comorbidity (hypertension).
The study also suggests that there is significant correlation between increased aortic stiffness index and presence of diastolic dysfunction.
Study done by the Ömer ŞATIROĞLU et.al (14) statesthat increased extension of coronary atherosclerosis causes higher aortic stiffness, which differs from our study where increased ASI was notcorrelated with extent of CAD.
Noninvasive measurement of ASI by transthoracic echocardiography may be used as feasible method for the assumption of clinical CAD.

CONCLUSION

The aortic elasticity and left ventricular diastolic function are significantly impaired in the presence of CAD.
Aortic stiffness index may be used as echocardiographic parameter to predict the atherosclerotic burden.

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