Original Research Article

Correlation between impaired Aortic Distensibility and the severity of coronary artery disease and calcium scoring measured by cardiac CT

Abstract:

Background : Multi-Slice cardiac CT has evolved as a noninvasive imaging technique for evaluation of stenosis in the coronary arteries by what is called Coronary Computed Tomographic Angiography (CCTA), but it is also widely used in quantitative plaque assessments through Coronary Artery Calcium (CAC) scoring and plaque type identification (soft or Mixed VS calcific) . Evaluation of aortic distensibility and aortic stiffness can also be performed through Multi-Slice Computed Tomography (MSCT) by calculating Aortic Distensibility Index (ADI) and Pulse Wave Velocity (PWV).

Aim: To evaluate whether impaired Aortic Distensibility Index (ADI) and Aortic Stiffness measured by Cardiac CT is correlating with the severity of coronary artery disease and coronary calcium scoring in at-risk individuals (assessed by CCTA).

Patients and Methods: We included 180 patients. Patients were classified into four groups according to their CAC score and according to the degree of stenosis based on CCTA. All patients in this study have underwent full history taking, short clinical examination including B.P. and H.R. measurements, standard ECG, routine laboratory investigations, and Multi-Slice CT Coronary Angiography (MSCT-CA).

All patients underwent coronary artery calcium (CAC) scanning and CCTA, and their ADI and Aortic Stiffness were measured. Maximum systolic and maximum diastolic cross sectional-area (CSA) of ascending-aorta (AAo) was measured 15-mm above the left main coronary ostium. ADI was defined as: [(Systolic CSA –Diastolic CSA)/ (Diastolic CSA in X systemic-pulse-pressure) X 10^3]. Aortic stiffness was measured as PWV using **Bramwell-Hill equation**[1] [(3.57/ √distensibility)]

Results: There were strong correlation between Aortic distensibility and Aortic stiffness (PWV) with degree of stenosis and coronary artery calcium.

In patients stratified based on the degree of calcium scoring (CAC score), there was a statistically significant negative correlation between calcium scoring and the ADI (Pearson's r= -0.771, p< .001), and a statistically significant positive correlation between calcium scoring and PWV (Pearson's r=0.817, p< .001).

In patients stratified based on the degree of stenosis, there was a statistically significant negative correlation between ADI and the Degree of stenosis (Pearson's r=-0.707, p< .001), and there was a statistically significant positive correlation between PWV and the Degree of stenosis (Pearson's r=0.697, p< .001).

Conclusion: Impaired aortic distensibility strongly correlates with the severity of coronary atherosclerosis, degree of stenosis and coronary artery calcium. Addition of ADI to CAC and traditional risk factors provides incremental value to predict at-risk individuals.

Keywords: Aortic distensibility index, Aortic Stiffness, Pulse wave velocity Coronary computed tomographic angiography, Coronary artery calcium score.

Introduction:

"Recognized as a conduit for distributing blood, abnormalities of the functional properties of the aorta are increasingly realized as important contributors to cardiovascular (CV) disease. The aorta performs several important functions: First, the aorta transmits and distributes blood from the heart to medium-sized conduits that supply the periphery. Second, the aorta acts as an expandable reservoir that buffers the pulsatile force from left ventricular contraction"[2].

"Vascular dysfunction has been shown to be an independent predictor of adverse cardiovascular events"[3-5]

"Arterial stiffness is a hallmark of vascular aging[6], and studies have shown an association between arterial stiffness with factors such as coronary artery disease and arterial hypertension"[7].

"Arterial distensibility, a measure of vascular function, can serve as a marker of coronary heart disease risk in humans"[8,9], "In addition animal studies suggest that reduced arterial distensibility is an early sign of atherosclerotic change"[10]. "Previous studies revealed an inverse relationship between aortic distensibility and cardiovascular risk factors and may predict outcome"[11-13].

The study aimed to find correlation between aortic distensibility and aortic stiffness with the severity of coronary artery disease and coronary calcium scoring in at-risk individuals all measured by Cardiac CT.

Patients and methods:

Patients: This cross sectional study included all patients with suspected CAD (All patient with low to intermediate pretest probability based on age, sex, and symptoms according to "*2019 ESC Guideline on the diagnosis and management of Chronic Coronary Syndrome*") whom were referred for Non-Invasive Coronary Computed Tomography

Angiography (CCTA) during the period from April 2021 to March 2022 in Alazhar university hospitals.

Patients with history of allergy to contrast media; patients with renal insufficiency; Patients with history of open-heart surgery, CABG, history of coronary artery stenting (PCI), post valve replacement, pericardial effusion, and those with pacing leads; Patients with markedly irregular heart rhythm like AF and frequent Extra-systoles; Patients who have difficulties in performing CT, like inadequate breath holding and heart failure; Patients with recent myocardial infarction; and Patients with high probability CAD were excluded from the study.

During this study, there were 220 patients, but we excluded 40 patients due to some technical difficulties during measurements and only 180 **patients** were included.

The patients were classified into four groups according to their CAC score and according to the degree of stenosis to the following groups:

Table 1. Classification of patients according to the degree of stenosis

Groups	**Group 1**	**Group 2**	**Group 3**	**Group 4**
CTA-Diagnosed coronary artery disease **(Degree of Stenosis)**	Normal Coronaries	Mild Stenosis < 50 %	Moderate Stenosis 50 – 70 %	Severe Stenosis > 70%
No of Patients	107	30	18	25

Table 2. Classification of patients according to CAC score

Groups	**Group 1**	**Group 2**	**Group 3**	**Group 4**
Coronary artery calcium **CAC score**	0	1 - 99	100 - 400	> 400
No of Patients	102	37	31	10

Methods:

All patients were subjected to:

1. **Full history taking include the following data**: Age, Sex, Family history of premature CAD (first-degree relatives), Smoking, Hypertension, and Diabetes mellitus.
2. **Short clinical examination including** Blood pressure measurement, and Heart Rate.
3. **Standard ECG including the following data**: Rhythm, Rat, and Ischemic changes.
4. **Routine laboratory investigations including**: Hemoglobin (Hb), Serum creatinine, and Lipid profile which included the serum assay of: Total Cholesterol, Triglycerides (TG), LDL Cholesterol, and HDL Cholesterol.
5. **Coronary Computed Tomography Angiography (CCTA):**

a) **Imaging Technique**: All CT scans were performed on SIEMENS dual source 128- slice CT scanner (**SIEMENS SOMATOM Definition Flash**).

b) **Patient preparation and protocol:**

The following protocol was followed:

- All coronary arteries were evaluated at different phases of the cardiac cycle by acquisition of thin slice sections (0.5 mm).
- Heart rate of all patients was determined one hour before examination.
- If heart rate is > 75 BPM, the patient was given beta blocker agent orally (metoprolol 50 -100 mg) one hour before the study or postponed to another day with medication to control his heart rate.
- Five milligram sublingual dose of nitroglycerin was administered just before the scan.
- All scans were preceded by non-contrast enhanced scan for coronary calcium score.

c) **Topogram (similar to chest X ray)** taken from tracheal bifurcation to the diaphragm in a single breath-hold in the cranio-caudal direction which used to fix the acquisition limits of the study (define region of interest for imaging).

d) **Test bolus:** Injection of 10 ml Iopromide 370 mg/mL followed by 50 ml saline at a rate of **5 -5.5 ml/s** and then acquisition of sequence of images at the level of the Aorta and Pulmonary arteries every two seconds to calculate the actual delay time from start of injection till the maximum intensity of the dye in the ascending Aorta.

e) CT angiography:

After accurate calculation of delay time and checking the ECG trigger, images acquisition is done after injection of 70 ml Iopromide 370 at flow rate **5 -5.5 ml/s** followed by 50 ml saline at the same flow rate using power dual automatic injector.

f) Image reconstruction:

- The CT scanning was performed with ***retrospective ECG-gated acquisition spiral mode***. A 3D workstation was used to reconstruct axial images retrospectively at an optimal window. The image data sets were analyzed using Multi planar reformatted images (axial, coronal, and sagittal views), curved Multi-planar reformatted images (cMPR), thin-slab maximum- intensity projection images (thin MIP), and volume-rendered image (VRI).
- Two-dimensional reconstructions (curved Multi planar reformation) of the coronary arteries were performed on several planes to assess patency of the vessels. These 2-dimensional images show the vessel's wall and lumen and all the surrounding tissue. They are reconstructed on at least 2 orthogonal planes, and continuity of contrast material throughout the vessel serves as an indication of patency.
- All reconstruction were done by following workstations : Vitrea, Horos, and RadiAnt DICOM Viewer

g) Measurement of plaque burden and degree of coronary arteries stenosis and coronary arteries calcium score (CAC score) :

Coronary segments were visually scored for the presence of coronary plaque according to following scores: -

i. Segment-stenosis score (SSS):

"SSS was calculated as a measurement of total coronary plaque burden. Each segment was given a score from 0 to 3 according to the degree of lumen stenosis"[14]. [0] for normal, [1] for mild (<50%), [2] for moderate (50% to 69%), [3] for severe (≥70%).

ii. Coronary Artery Calcium Scoring (CAC) score:

In this test, which did not use X-ray contrast, pictures were taken of the heart to look for the presence of calcium deposits in the coronary arteries. The amount of calcium deposits was measured by **"agastone score** " as showed in **Table (3)**[15]

Table 3: Relationship between CT coronary calcium score, plaque burden and probability of significant CAD.

Ca Score	Presence of Plaque (Plaque burden)	Probability of significant CAD
0	No evidence of plaque	Very low (generally < 5% likelihood)
1-10	Minimal evidence of plaque	Very unlikely (generally < 5% likelihood)
11-100	Mild evidence of plaque	Mild or minimal coronary artery stenosis likely
101-400	Moderate evidence of plaque	Non-obstructive CAD highly likely, although obstructive disease possible
Over 400	Extensive evidence of plaque	High likelihood (> 90%) of at least one significant coronary stenosis

h) Measurement of Aortic Distensibility Index (ADI) and Aortic Stiffness

i. Aortic distensibility

Aortic distensibility is the degree to which the aorta can expand such that a stiff vessel has low distensibility. Distensibility can be expressed as follows[16]**:-**

$$Distensibility\left(\frac{1}{mmHg \times 10^3}\right) = \frac{(SA - DA)}{DA \times (SBP - DBP)} \times 10^3$$

Where **SA** is the maximal systolic area, **DA** is the minimal diastolic area, **SBP** is systolic blood pressure, and **DBP** is diastolic blood pressure**.**

True cross sectional area (CSA) and diameter of ascending aorta (AAo) was measured both manually and with the automated software.

The cross sectional area (CSA) and diameter of AAo were measured 15 mm above the ostium of left main coronary artery (LMCA) as shown in ***figure.1***

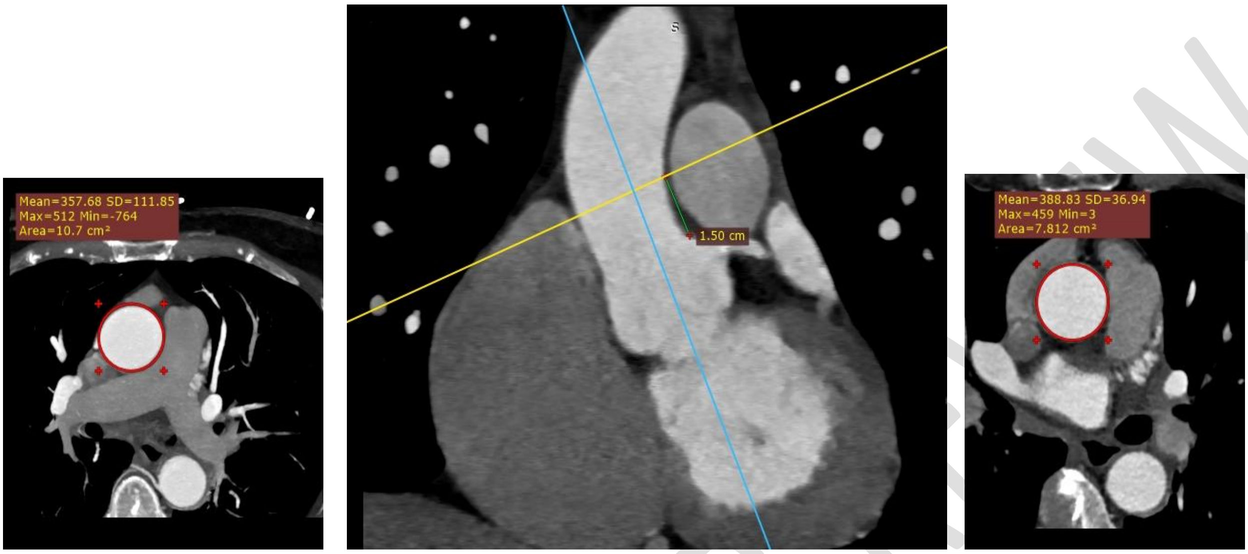


Figure 1. Measurement of area of the ascending aorta (AAo) at the maximum systole and diastole (as determined automatically by the machine) 15 mm above LM ostium using axial and coronal views.

Maximum AAo area and diameter were measured at both maximal systole (30 – 40 % of R–R interval) and maximum diastole (65 – 95% of R-R interval.

The determination of best (maximum) systole or diastole was done automatically by the machine.

The above equation for calculating the Distensibility was done through excel sheet by adding this equation in master sheet to be calculated automatically.

ii. Pulse wave velocity (PWV) and Aortic Stiffness

In this study, we measured **Aortic Stiffness** form Aortic distensibility by measuring **Pulse wave velocity (PWV**) as PWV and distensibility are inversely related to one another by the **Bramwell-Hill equation**[1]**:**

$$PWV = \frac{3.57}{\sqrt{Distensibility}}$$

The above equation for calculating the **Pulse wave velocity (PWV**) was done through excel sheet by adding this equation in master sheet to be calculated automatically.

Result

The demographics and clinical examination findings among included patients is shown below ***(Table 4)***

Table 4. Demographics and clinical examination findings (n= 180)

	N= 180
Sex	
Female	79 (43.9%)
Male	101 (56.1%)
Age	
Mean (SD)	53.3 (10.6)
Range	23.0 - 83.0
Diabetes Mellitus	
No	137 (76.1%)
Yes	43 (23.9%)
Hypertension	
No	104 (57.8%)
Yes	76 (42.2%)
Dyslipidemia	
No	77 (42.8%)
Yes	103 (57.2%)
Smoking	
No	125 (69.4%)
Yes	55 (30.6%)
Family History	
No	148 (82.2%)
Yes	32 (17.8%)
Systolic blood pressure (mmHg)	
Mean (SD)	119.7 (9.8)
Range	90.0 - 150.0
Diastolic blood pressure (mmHg)	
Mean (SD)	81.9 (10.0)
Range	60.0 - 110.0
Heart rate (bpm)	
Mean (SD)	60.1 (6.8)

Range	45.0 - 75.0
ECG Rhythm	
Atrial Fibrillation	1 (0.6%)
Normal sinus rhythm	178 (98.9%)
Premature ventricular complex	1 (0.6%)

The laboratory investigations among the included patients was as following ***(Table 5)***

Table 5. Laboratory Investigations among the included patients (n= 180)

	N= 180
Hemoglobin concentration (g/dl)	
Mean (SD)	14.0 (1.2)
Range	10.0 - 17.0
Serum Creatinine (mg/dl)	
Mean (SD)	1.0 (0.2)
Range	0.6 - 1.8
Total Cholesterol (mg/dl)	
Mean (SD)	187.8 (48.8)
Range	97.0 - 304.0
Triglyceride (mg/dl)	
Mean (SD)	179.8 (54.2)
Range	82.0 - 324.0
Low density Lipoprotein (mg/dl)	
Mean (SD)	109.3 (32.9)
Range	25.0 - 240.0
High density Lipoprotein (mg/dl)	
Mean (SD)	50.2 (9.3)
Range	27.0 - 70.0

The coronary plaque features of our included patients was as following ***(Table 6)***

Table 6. Coronary Plaque features among the included patients (n= 180)

Left Main Coronary Artery (LM)	
NO	170 (94.4%)
Calcific	6 (3.3%)
Mixed	4 (2.2%)
Left Anterior Descending Artery (LAD)	
Mixed	26 (14.4%)
No	98 (54.4%)
Calcific	42 (23.3%)
Soft	14 (7.8%)
Ramus Intermedius Artery	
Patients with no Ramus	151 (83.9%)
No	21 (11.7%)
Calcific	8 (4.4%)
Diagonal Artery (branch of LAD)	

No	164 (91.1%)
Calcific	8 (4.4%)
Mixed	5 (2.8%)
Soft	3 (1.7%)
Left Circumflex Artery (LCX)	
No	145 (80.6%)
Calcific	19 (10.6%)
Mixed	14 (7.8%)
Soft	2 (1.1%)
Obtuse Marginal Artery (branch of LCX)	
No	173 (96.1%)
Calcific	4 (2.2%)
Mixed	2 (1.1%)
Soft	1 (0.6%)
Right Coronary Artery (RCA)	
No	139 (77.2%)
Calcific	25 (13.9%)
Mixed	11 (6.1%)
Soft	5 (2.8%)

We assessed different degrees of coronary artery stenosis in the included patients and we found the following:

Twenty-five patients (13.9%) had significant coronary stenosis (> 70 %), 18 patients (10.0%) had moderate coronary stenosis, and 30 patients (16.7%) had mild coronary stenosis, while the rest 107 patients (59.4%) had no coronary stenosis. Left main coronary artery (LM) was found to be moderately stenosed in 1 patient (0.6%) and mildly stenosed in 5 patients (2.8%). Regarding the left anterior descending (LAD) artery, significant stenosis was found in 18 patients (10.0%), 17 patients (9.4%) had moderate coronary stenosis, and 29 patients (16.1%) had mild coronary stenosis, and 3 patients (1.7%) were non-evaluable cases. In Left Circumflex Artery (LCX), we found that 5 patients (2.8%) had significant stenosis, 6 patients (3.3%) had moderate stenosis, and 9 patients (5.0%) had mild stenosis. Right Coronary Artery (RCA) was found to be significantly stenosed in 7 patient (3.9%), moderately stenosed in 9 patients (5.0%), and mildly srenosed in 13 patients (7.2%).

Aortic distensibility index (ADI) was measured in all included patients. The mean systole of Ascending Aorta cross-sectional area was 9.9 (SD=1.8) with a range from 5.8 to 15.6, while the mean diastole of ascending aorta cross-sectional area was 7.3 (SD=1.4) with a range from 4.0 to 12.1. The mean aortic distensibility index and pulse wave velocity

(PWV) were 9.4 (SD= 1.3) [Min: 5.7 - Max: 12.1] and 1.2 (SD=0.1) [Min: 1.0 - Max: 1.5] respectively.

The overall mean aortic distensibility index was 9.4 (SD= 1.3). In the groups stratified based on CT CAC score, It was significantly higher among the normal group 10.2 (SD= 0.6) than patients with stenosis (P< 0.001). The overall mean pulse wave velocity was 1.4 (SD= 0.1). It was significantly higher among patients with severe stenosis 1.3 (SD= 0.1), (P< 0.001).

Table 7. Aortic Distensibility Index and Pulse Wave Velocity among the included patients stratified based on the CT coronary calcium score (n= 180)

	Group 1 (N=102)	**Group 2 (N=37)**	**Group 3 (N=31)**	**Group 4 (N=10)**	**Total (N=180)**	**p value**
Aortic Distensibility Index						**< 0.001[1]**
Mean (SD)	10.2 (0.6)	9.1 (0.8)	7.9 (0.7)	6.7 (1.3)	9.4 (1.3)	
Range	8.2 - 12.1	7.3 - 11.1	6.9 - 10.0	5.7 - 10.1	5.7 - 12.1	
Aortic Stiffness: Pulse Wave Velocity (PWV)						**< 0.001[1]**
Mean (SD)	1.1 (0.0)	1.2 (0.1)	1.3 (0.1)	1.4 (0.1)	1.2 (0.1)	
Range	1.0 - 1.2	1.1 - 1.3	1.1 - 1.4	1.1 - 1.5	1.0 - 1.5	

Group 1: CAC score= 0; group 2: CAC score= 1-99, group 3: CAC score= 100 – 400, and group 4: CAC score= > 400**.**

On the other hand, in the groups that stratified based on degree of coronary stenosis, The ADI was significantly higher among the normal group 10.2 (SD= 0.7) than patients with stenosis (P< 0.001). The overall mean pulse wave velocity was 1.2 (0.1). It was significantly higher among patients with severe stenosis 1.3 (SD= 0.1), (P< 0.001).

Table 8. Aortic Distensibility Index and Pulse Wave Velocity among the included patients stratified based on the degree of stenosis (n= 180)

	Normal Coronaries (N=107)	**Mild (Stenosis < 50 %) (N=30)**	**Moderate (Stenosis 50 – 70 %) (N=18)**	**Severe (Stenosis > 70%) (N=25)**	**Total (N=180)**	**p value**
Aortic Distensibility Index						< 0.001[1]
Mean (SD)	10.2 (0.7)	8.7 (1.3)	8.5 (0.8)	7.7 (1.2)	9.4 (1.3)	
Range	7.8 - 12.1	5.9 - 11.1	7.2 - 10.2	5.7 - 10.2	5.7 - 12.1	
Aortic Stiffness: Pulse Wave Velocity (PWV)						< 0.001[1]

Mean (SD)	1.1 (0.0)	1.2 (0.1)	1.2 (0.1)	1.3 (0.1)	1.2 (0.1)
Range	1.0 - 1.3	1.1 - 1.5	1.1 - 1.3	1.1 - 1.5	1.0 - 1.5

1. Linear Model ANOVA; 2. Pearson's Chi-squared test

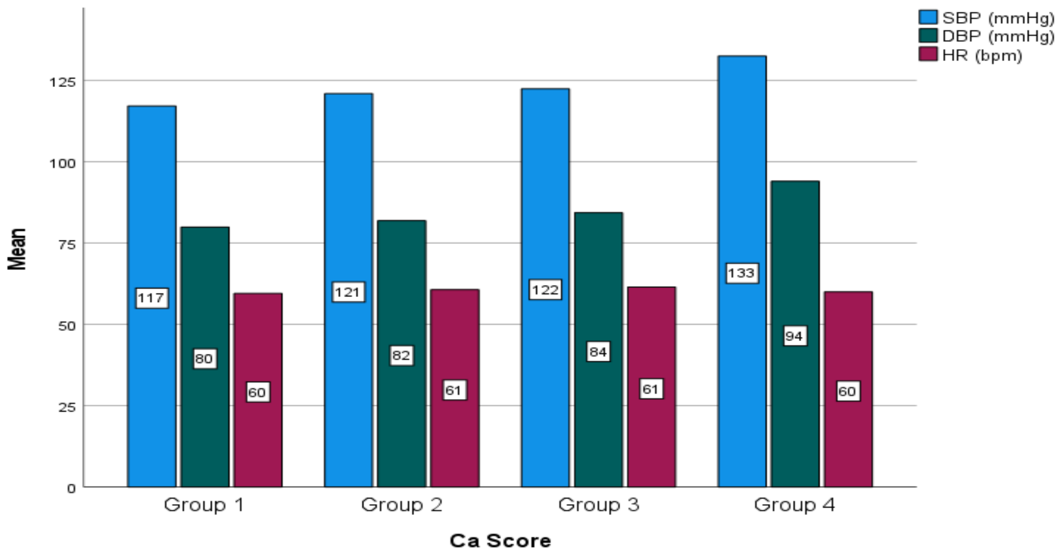
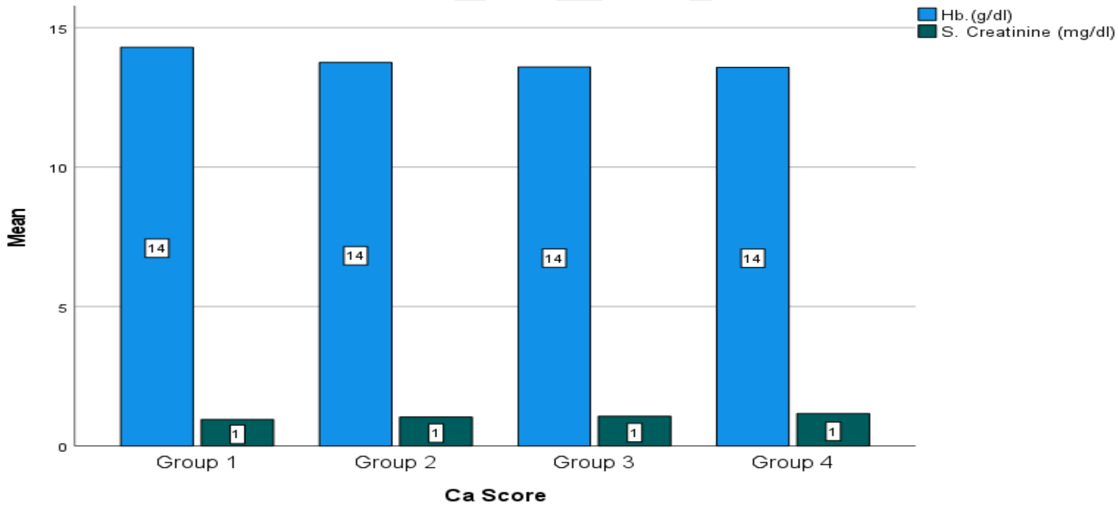


Figure 2. Clinical examination findings among the included patients stratified based on the CT coronary calcium score (n= 180)



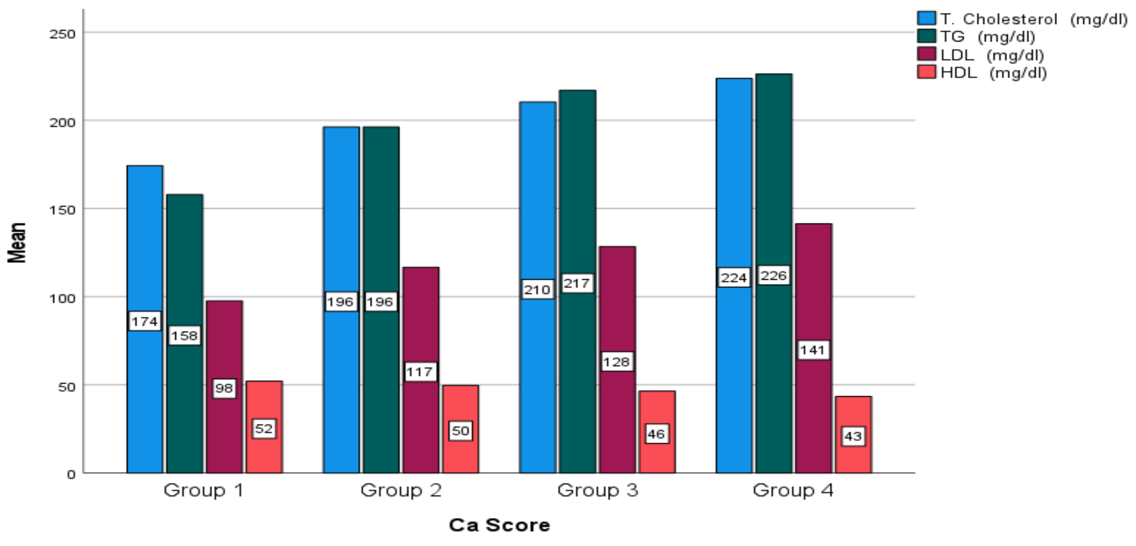


Figure 3. Laboratory Investigations among the included patients stratified based on the CT coronary calcium score (n= 180)

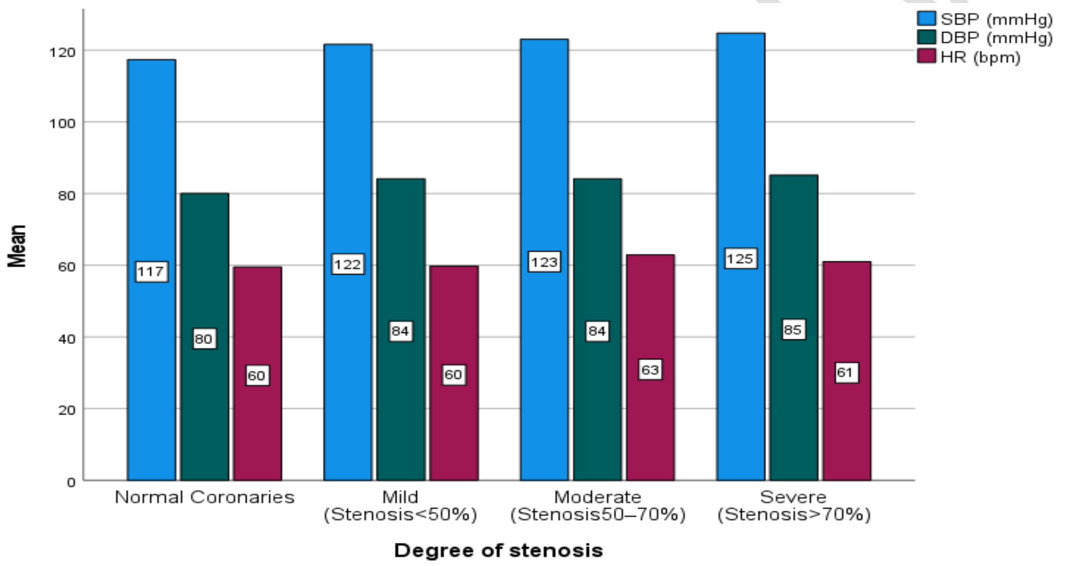
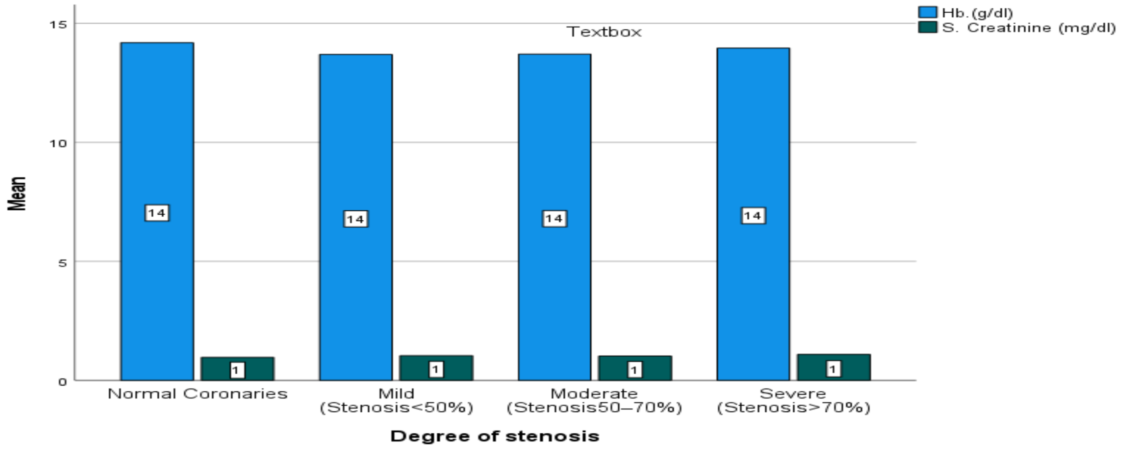


Figure 4. Clinical examination findings among the included patients stratified based on the degree of stenosis (n= 180)



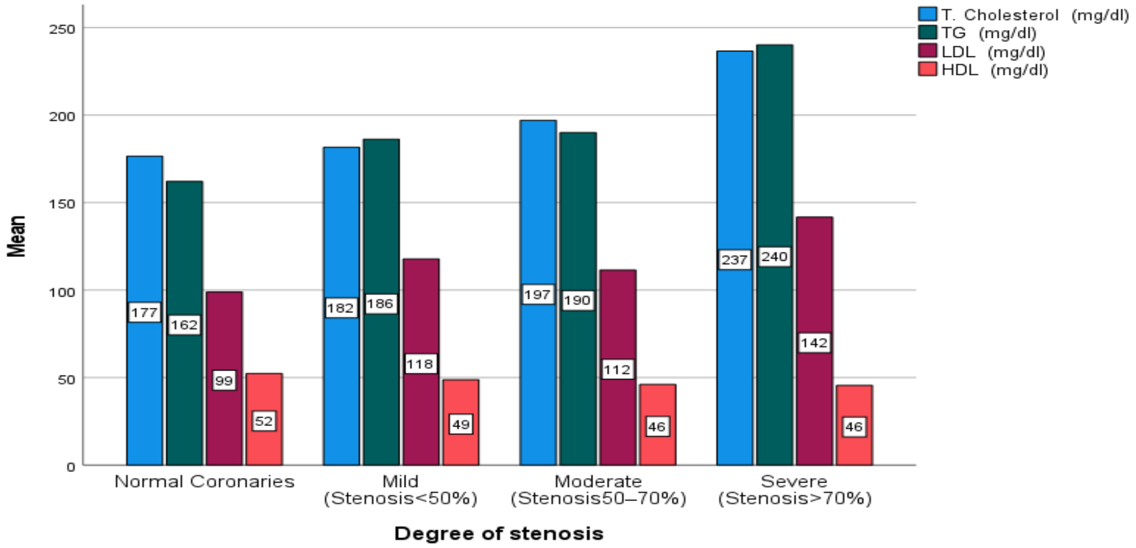


Figure 5. Laboratory Investigations among the included patients stratified based on the degree of stenosis (n= 180)

There was a statistically significant negative correlation between calcium scoring and the ADI (Pearson's r= -0.771, p< .001).

Table 9. The correlation between calcium scoring and ADI

		ADI
Ca Score	Pearson's r	-0.771
	p-value	< .001
	95% CI Upper	-0.705
	95% CI Lower	-0.825
	Spearman's rho	-0.793
	p-value	< .001
	N	180

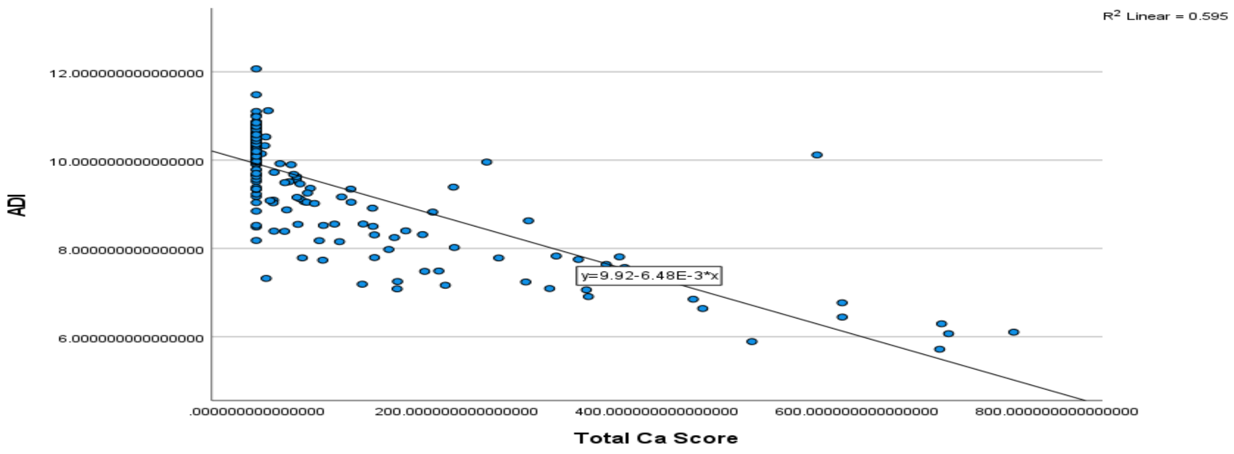


Figure 6. The correlation between calcium scoring and ADI

There was a statistically significant positive correlation between calcium scoring and PWV (Pearson's r=0.817, p< .001).

Table 10. The correlation between calcium scoring and PWV

		PWV
Ca Score	Pearson's r	0.817
	p-value	< .001
	95% CI Upper	0.861
	95% CI Lower	0.762
	Spearman's rho	0.793
	p-value	< .001
	N	180

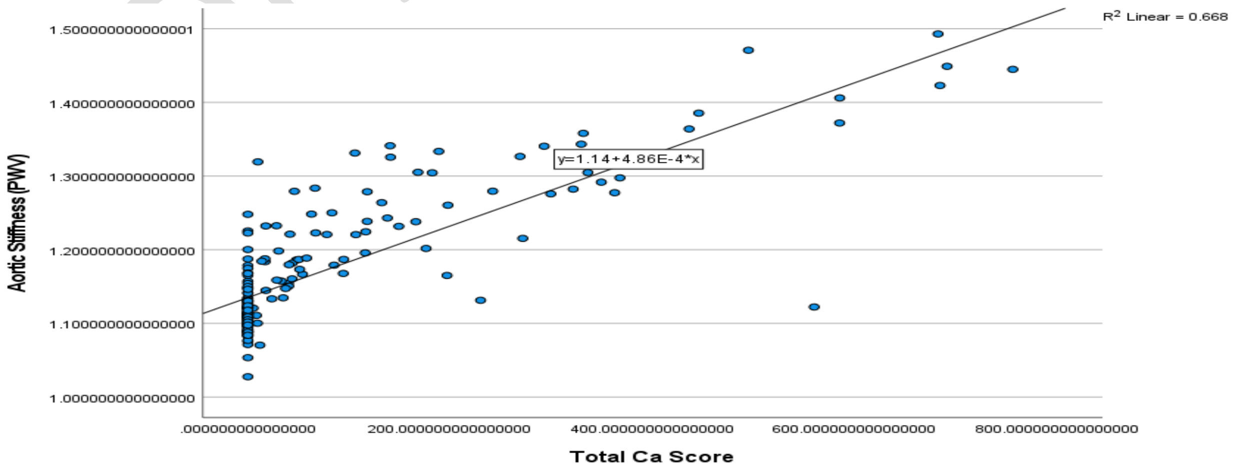


Figure 7. The correlation between calcium scoring and PWV

There was a statistically significant negative correlation between ADI and the Degree of stenosis (Pearson's r=-0.707, p< .001).

Table 11. The correlation between ADI and Degree of stenosis

		Degree of stenosis
ADI	Pearson's r	-0.707
	p-value	< .001
	95% CI Upper	-0.625
	95% CI Lower	-0.773
	Spearman's rho	-0.711
	p-value	< .001
	N	180

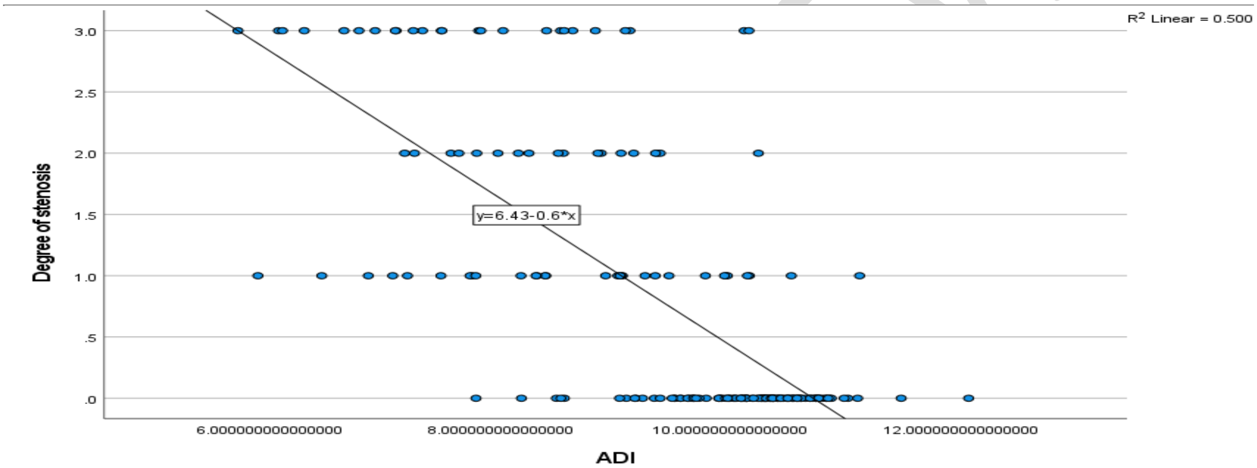


Figure 8. The correlation between ADI and Degree of stenosis

There was a statistically significant positive correlation between PWV and the Degree of stenosis (Pearson's r=0.697, p< .001).

Table 12. The correlation between PWV and the Degree of stenosis

		Degree of stenosis
PWV	Pearson's r	0.697
	p-value	< .001
	95% CI Upper	0.765
	95% CI Lower	0.613
	Spearman's rho	0.711

p-value	< .001
N	180

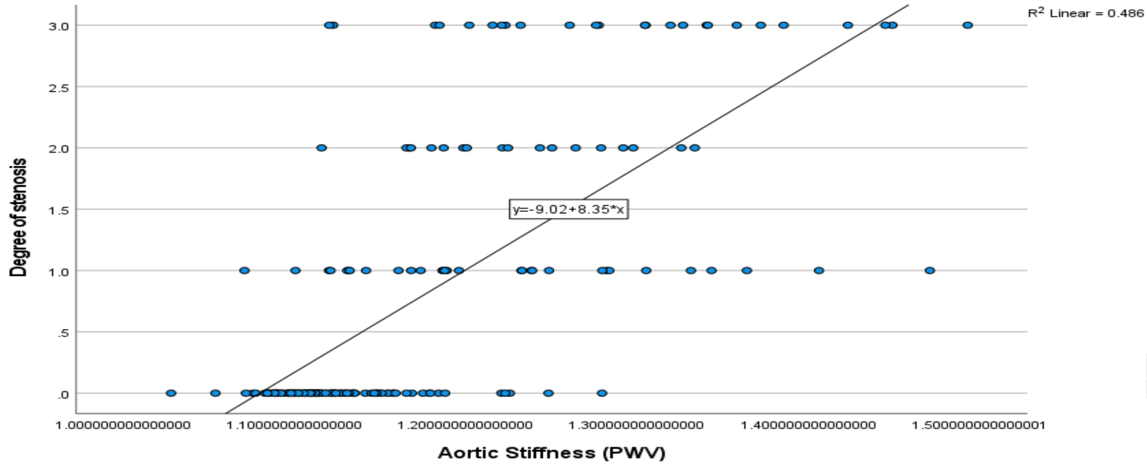


Figure 9. The correlation between PWV and the Degree of stenosis

Discussion

This current study demonstrates that: **1)** excellent correlation between ADI and PWV from one side and coronary artery diseases and CAC scoring from other side. **2)** CCTA measured ADI decreased proportionally with the severity of CAC and degree of stenosis of coronary arteries independent of other cardiovascular risk factor. **3)** PWV (aortic stiffness) calculated from Distensibility increased proportionally with the severity of CAC and degree of stenosis of coronary arteries independent of other cardiovascular risk factor. **4)** Addition of ADI and PWV to different scores that used to estimate the risk for coronary artery disease could provide incremental value to predict CAD.

In the current study, increased CACS was associated with increases in age, systolic and diastolic blood pressure, serum creatinine, total serum cholesterol, triglycerides, and LDL (P< 0.0011 for all). While increased CACS was associated with lower levels of Hb (P=0.0061) and HDL (P=0.0021).

“Similarly, LDL cholesterol was greater in the higher CAC score groups (P=0.002) in” (Serrano et al., 2019) study[17].

According to the present study, increased CACS was associated with higher incidences of diabetes, hypertension and dyslipidemia (P< 0.0012 for all).

“In agreement with our study, the presence of diabetes (P=0.002) and older age (P< 0.001) was more prevalent in the CAC >400 group in” (Serrano et al., 2019)[17] study.

However, (Serrano et al., 2019)[17] “results did not show any differences among the CAC groups regarding dyslipidemia”.

According to the current study, CACS was associated with higher incidences of smoking (P=0.0292).

This is in agreement with (Torngren et al., 2020)[18], “they reported that increased CACS was associated with increases in age, systolic blood pressure, and serum creatinine as well as showing higher prevalence in diabetics, and previous smokers”.

Aortic Distensibility Index (ADI) in this study was found to decrease with higher CACS (P< 0.0011). While aortic stiffness expressed by pulse wave velocity (PWV) was found to increase with higher CACS (P< 0.0011).

Coronary heart disease is depending on risk factors such as dyslipidemia, age, and gender (Mancia et al., 2013)[19]. In the current study, increased severity of stenosis was associated with increases in age (P< 0.001), systolic (P< 0.001) and diastolic blood pressure (P= 0.029), serum creatinine (P=0.010), total serum cholesterol (P< 0.001), triglycerides (P< 0.001), and LDL (P< 0.001). While increased severity of stenosis was associated with lower levels of HDL (P< 0.001).

“With aging, atherosclerotic changes occurs in the arteries resulting in increased stiffness. There is also an increase in wall thickness due to intimal thickening. Increased stiffness and an increase in wall thickness occur with age, also without atherosclerotic disease, due to depletion and fragmentation of elastin and the deposition of collagen in the media” (Bonarjee, 2018)[20]. In the current study, increased severity of stenosis was associated with older age (P< 0.001). In agreement with our finding, large-scale studies (AlGhatrif et al., 2013)[21]; (Meyer et al., 2016)[22] reinforced the observation that older age is independently related to an increase in pulse wave velocity.

According to the present study, increased severity of stenosis was associated with higher incidences of diabetes (P< 0.001), hypertension (P=0.005), dyslipidemia (P< 0.001), and smoking (P< 0.001).

In concordance with our study, (Larifla et al., 2014)[23] revealed that diabetes and hypertension were independent predictors of coronary artery disease severity for high risk lesions.

ADI in the present study was found to decrease with increased severity of stenosis (P< 0.0011). In concordance with our study, in (Shehata et al., 2015)[24] study, patients with significant obstructive CAD showed significantly lower ADI values.

While aortic stiffness expressed by PWV was found to increase with increased severity of stenosis (P< 0.0011).

"Increased plaque density contributes to higher CAC score and overall cardiovascular risk prediction, which is likely due to a strong association between CAC burden and CAD" (Arnson et al., 2017)[25]. "Calcium scoring in the current study was positively correlated with the degree of stenosis (r= 0.653, P< .001). Severe coronary calcification is known to be closely associated with significant coronary obstruction. For its simplicity, the novel approaches for calcium scoring have been attemped in the various opportunities to use CT scan, i.e. lung screening or attenuation correction" (Berman et al., 2017)[26].

In the current study, there was a significant negative correlation between calcium scoring and the ADI (r= -0.771, P< .001). Similarly, (Shehata et al., 2015)[24] found a significant inverse correlation between aortic distensibility measured using computed tomographic angiography and CAC scoring (r = –0.265, P= 0.042).

Calcium scoring was found to be positively correlated with the PWV in this study (r=0.817, P< .001). In concordance with our result, (Torngren et al., 2020)[18] found significant increases in arterial stiffness for groups of increasing CACS. Moreover, the aorta calcium score (ACS) in (Cho et al., 2015)[27] study was associated with mean brachial-ankle PWV (r=0.387, P=0.001), suggesting arterial stiffening with raised ACS.

Two groups have reported relations between aortic stiffness and CAC in community-dwelling adult cohorts (Kullo et al., 2006)[28]; (van Popele et al., 2006)[29]. "These studies showed that greater carotid-femoral pulse wave velocity (CFPWV) was associated with the presence and extent of CAC. Extending these investigations", (Tsao et al., 2014)[30] examined "the relations of other measures of pressure pulsatility and wave reflection with CAC and found that CFPWV had the strongest association with CAC".

ADI in the present study was inversely correlated with the degree of stenosis (r=-0.707, P< .001). In agreement with our finding, (Shehata et al., 2015)[24] found a significant inverse correlation between aortic distensibility measured using computed tomographic angiography and severity of coronary artery disease (percent luminal stenosis) r = –0.244, P = 0.045).

According to the present study, PWV was positively correlated with the degree of stenosis (r=0.697, P< .001). Similarly, (Vallée et al., 2019)[31] reported that measurements of aortic PWV positively correlated with the severity of coronary heart disease (p = 0.003). Moreover, aortic PWV index in (Yannoutsos et al., 2018)[32] was positively correlated with the severity of coronary heart disease judged on the 3 degrees of coronary arterial changes evaluated as less than 20%, presence of non-obstructive lesions, and presence of obstructive lesions (P=0.001).

In this study, there was a significant negative correlation between number of involved vessels and ADI (r=-0.771, P< .001). Similarly, (Razik et al., 2021)[33] found "decreased aortic distensibility (AD) was correlated with the complexity of CAD. They also found AD to be a good predictor of CV events similar to ejection fraction and may therefore be an early sign of CAD". Moreover, (Shehata et al., 2015)[24] found "a negative correlation between number of diseased coronary arteries and ADI. Yet, the correlation was not significant (r = –0.067, P = 0.578)". Furthermore, (Ahmadi et al., 2011)[34] showed that "aortic distensibility inversely correlates with the severity of coronary atherosclerosis (assessed using CAC and degree of coronary luminal stenosis using CTA)".

According to the present study, PWV inversely correlated with ADI among diabetic patients (r=-0.992, P< .001), hypertensive patients (r=-0.991, p< .001), patients with dyslipidemia (r= -0.991, p< .001), and smokers (r= -0.993, p< .001). In line with our finding, (Salvi et al., 2022)[35] found a significant inverse correlation between carotid distensibility and carotid–femoral PWV (r = −0.75; p < 0.001).

"Finally, recent studies have shown that functional changes in arteries precede the development of structural changes and also reverse more quickly in response to therapies"[36-39].

Current findings revealed that CTA provides an accurate measure for vascular function rather than just anatomical studies ; Furthermore, in this study aortic distensibility decreased substantially with the severity of coronary atherosclerosis in both genders irrespective of other risk factors like D.M, HTN, smoking, and dyslipidemia.

Conclusion

Impaired aortic distensibility and Aortic stiffness are well correlating with the severity of coronary artery disease and coronary calcium scoring independent of age, gender, and cardiovascular risk factors. Non-invasive ADI assessment is a feasible procedure to predict atherosclerotic CAD. A low ADI value is associated with significant obstructive CAD, high CAC score, and increased number of involved vessels. Furthermore, addition of ADI to traditional risk factors and CAC score provides the largest contribution to detect significant coronary atherosclerosis, and highlights the diagnostic utility of ADI in the early detection and monitoring of patients with atherosclerotic cardiovascular disease by a single noninvasive diagnostic study.

Ethical approval and consent:

Informed consent was taken from all patients and the ethics committees in Alazhar Faculty of Medicine and Alazhar Cardiology Department approved the study.

References

1. **Bramwell JC, Hill AV.** The velocity of the pulse wave in man. Proc R Soc Lond B Biol Sci 1922; 93:298–306.
2. **Nichols WW. McDonald's** Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles. 6th edition. London, England: Hodder Arnold, 2011.
3. **Epstein, F.H., Fuster, V., Badimon, L., Badimon, J.J., Chesebro, J.H., 1992.** The Pathogenesis of Coronary Artery Disease and the Acute Coronary Syndromes. N. Engl. J. Med. https://doi.org/10.1056/nejm199201303260506
4. **Epstein, F.H., Vane, J.R., Änggård, E.E., Botting, R.M., 1990.** Regulatory Functions of the Vascular Endothelium. N. Engl. J. Med. https://doi.org/10.1056/nejm199007053230106
5. **Griendling, K.K., Ushio-Fukai, M., Lassègue, B., Alexander, R.W., 1997.** Angiotensin II signaling in vascular smooth muscle: New concepts. Hypertension. https://doi.org/10.1161/01.hyp.29.1.366
6. **Nilsson, P.M., 2008.** Early vascular aging (EVA): consequences and prevention. Vasc. Health Risk Manag. https://doi.org/10.2147/vhrm.s1094
7. **Liao, J., Farmer, J., 2014.** Arterial stiffness as a risk factor for coronary artery disease. Curr. Atheroscler. Rep. https://doi.org/10.1007/s11883-013-0387-8
8. **Bank, A.J., Wang, H., Holte, J.E., Mullen, K., Shammas, R., Kubo, S.H., 1996.** Contribution of collagen, elastin, and smooth muscle to in vivo human brachial artery wall stress and elastic modulus. Circulation. https://doi.org/10.1161/01.CIR.94.12.3263
9. **Sudhir, K., Mullen, W.L., Hausmann, D., Fitzgerald, P.J., Chou, T.M., Yock, P.G., Chatterjee, K., 1995.** Contribution of endothelium-derived nitric oxide to coronary arterial distensibility: An in vivo two-dimensional intravascular ultrasound study. Am. Heart J. https://doi.org/10.1016/0002-8703(95)90322-4

10. **Hironaka, K., Yano, M., Kohno, M., Tanigawa, T., Obayashi, M., Konishi, M., Umemoto, S., Matsuzaki, M., 1997.** In vivo aortic wall characteristics at the early stage of atherosclerosis in rabbits. Am. J. Physiol. - Hear. Circ. Physiol. https://doi.org/10.1152/ajpheart.1997.273.3.h1142
11. **Cruickshank, K., Riste, L., Anderson, S.G., Wright, J.S., Dunn, G., Gosling, R.G., 2002.** Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: An integrated index of vascular function? Circulation. https://doi.org/10.1161/01.CIR.0000033824.02722.F7
12. **Kingwell, B.A., Waddell, T.K., Medley, T.L., Cameron, J.D., Dart, A.M., 2002.** Large artery stiffness predicts ischemic threshold in patients with coronary artery disease. J. Am. Coll. Cardiol. https://doi.org/10.1016/S0735-1097(02)02009-0
13. **Tentolouris, N., Liatis, S., Moyssakis, I., Tsapogas, P., Psallas, M., Diakoumopoulou, E., Voteas, V., Katsilambros, N., 2003.** Aortic distensibility is reduced in subjects with type 2 diabetes and cardiac autonomic neuropathy. Eur. J. Clin. Invest. https://doi.org/10.1111/j.1365-2362.2003.01279.x
14. **Min J, Shaw L, Devereux R, et al.** Prognostic value of multidetector coronary computed tomographic angiography for prediction of all-cause mortality. J Am Coll Cardiol 2007; 50:1161–1170.
15. **Wexler L, Brundage B, Crouse J, et al.** Coronary artery calcification: pathophysiology, epidemiology, imaging methods, and clinical implications. A statement for health professionals from the American Heart Association. Circulation. 1996; 94:1175–1192.
16. **Ganten M, Boese JM, Leitermann D, Semmler W.** Quantification of aortic elasticity: development and experimental validation of a method using computed tomography. Eur Radiol 2005; 15:2506–12.
17. **Serrano, C. V., De Mattos, F. R., Pitta, F. G., Nomura, C. H., De Lemos, J., Ramires, J. A. F., & Kalil-Filho, R. (2019**). Association between neutrophil-lymphocyte and platelet-lymphocyte ratios and coronary artery calcification score among asymptomatic patients: data from a cross-sectional study. Mediators of inflammation, 2019**.**
18. **Torngren, K., Rylance, R., Björk, J., Engström, G., Frantz, S., Marko-Varga, G., Melander, O., Nihlen, U., Olsson, H., & Planck, M. (2020).** Association of coronary calcium score with endothelial dysfunction and arterial stiffness. Atherosclerosis, 313, 70-75.
19. **Mancia, G., Fagard, R., Narkiewicz, K., Redón, J., Zanchetti, A., Böhm, M., Christiaens, T., Cifkova, R., De Backer, G., & Dominiczak, A. (2013).** Task Force Members. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J hypertens, 31(7), 1281-1357.
20. **Bonarjee, V. V. (2018).** Arterial stiffness: a prognostic marker in coronary heart disease. available methods and clinical application. Frontiers in Cardiovascular Medicine, 5, 64.
21. **AlGhatrif, M., Strait, J. B., Morrell, C. H., Canepa, M., Wright, J., Elango, P., Scuteri, A., Najjar, S. S., Ferrucci, L., & Lakatta, E. G. (2013).** Longitudinal trajectories of arterial stiffness and the role of blood pressure: the Baltimore Longitudinal Study of Aging. Hypertension, 62(5), 934-941.
22. **Meyer, M. L., Tanaka, H., Palta, P., Cheng, S., Gouskova, N., Aguilar, D., & Heiss, G. (2016).** Correlates of segmental pulse wave velocity in older adults: the Atherosclerosis Risk in Communities (ARIC) Study. American journal of hypertension, 29(1), 114-122.

23. **Larifla, L., Armand, C., Velayoudom-Cephise, F.-L., Weladji, G., Michel, C. T., Blanchet-Deverly, A., Deloumeaux, J., & Foucan, L. (2014).** Distribution of coronary artery disease severity and risk factors in Afro-Caribbeans. Archives of cardiovascular diseases, 107(4), 212-218.
24. **Shehata, M., Elsayegh, A., Gomaa, Y., & Gamal, M. (2015).** Using aortic distensibility index to detect coronary stenosis. Acta cardiologica, 70(4), 465-472.
25. **Arnson, Y., Rozanski, A., Gransar, H., Friedman, J. D., Hayes, S. W., Thomson, L. E., Tamarappoo, B., Slomka, P., Wang, F., & Germano, G. (2017).** Comparison of the coronary artery calcium score and number of calcified coronary plaques for predicting patient mortality risk. The American Journal of Cardiology, 120(12), 2154-2159.
26. **Berman, D. S., Arnson, Y., & Rozanski, A. (2017).** Assessment of coronary calcium density on noncontrast computed tomography. In (Vol. 10, pp. 855-857): American College of Cardiology Foundation Washington, DC.
27. **Cho, I.-J., Chang, H.-J., Park, H.-B., Heo, R., Shin, S., Shim, C. Y., Hong, G.-R., & Chung, N. (2015).** Aortic calcification is associated with arterial stiffening, left ventricular hypertrophy, and diastolic dysfunction in elderly male patients with hypertension. Journal of hypertension, 33(8), 1633-1641.
28. **Kullo, I. J., Bielak, L. F., Turner, S. T., Sheedy, P. F., & Peyser, P. A. (2006).** Aortic pulse wave velocity is associated with the presence and quantity of coronary artery calcium: a community-based study. Hypertension, 47(2), 174-179.
29. **van Popele, N. M., Mattace-Raso, F. U., Vliegenthart, R., Grobbee, D. E., Asmar, R., van der Kuip, D. A., Hofman, A., de Feijter, P. J., Oudkerk, M., & Witteman, J. C. (2006).** Aortic stiffness is associated with atherosclerosis of the coronary arteries in older adults: the Rotterdam Study. Journal of hypertension, 24(12), 2371-2376.
30. **Tsao, C. W., Pencina, K. M., Massaro, J. M., Benjamin, E. J., Levy, D., Vasan, R. S., Hoffmann, U., O'Donnell, C. J., & Mitchell, G. F. (2014).** Cross-sectional relations of arterial stiffness, pressure pulsatility, wave reflection, and arterial calcification. Arteriosclerosis, thrombosis, and vascular biology, 34(11), 2495-2500.
31. **Vallée, A., Zhang, Y., Protogerou, A., Safar, M. E., & Blacher, J. (2019).** Added value of aortic pulse wave velocity index for the detection of coronary heart disease by elective coronary angiography. Blood Pressure, 28(6), 375-384.
32. **Yannoutsos, A., Ahouah, M., Dreyfuss Tubiana, C., Topouchian, J., Safar, M. E., & Blacher, J. (2018).** Aortic stiffness improves the prediction of both diagnosis and severity of coronary artery disease. Hypertension Research, 41(2), 118-125
33. **Razik, N. A., Kishk, Y., Essa, M., & Ghany, M. A. (2021).** Aortic distensibility can predict events in patients with premature Coronary Artery Disease: A Cardiac Magnetic Resonance study. Angiology, 72(4), 332-338.
34. **Ahmadi, N., Nabavi, V., Hajsadeghi, F., Flores, F., Azmoon, S., Ismaeel, H., Shavelle, D., Mao, S. S., Ebrahimi, R., & Budoff, M. J. (2011**). Impaired aortic distensibility measured by computed tomography is associated with the severity of coronary artery disease. The international journal of cardiovascular imaging, 27(3), 459-469.
35. **Salvi, P., Valbusa, F., Kearney-Schwartz, A., Labat, C., Grillo, A., Parati, G., & Benetos, A. (2022).** Non-Invasive Assessment of Arterial Stiffness: Pulse Wave Velocity, Pulse Wave Analysis and Carotid Cross-Sectional Distensibility: Comparison between Methods. Journal of Clinical Medicine, 11(8), 2225.

36. **Warnholtz A, Wild P, Ostad MA, Elsner V, Stieber F, Schinzel R, Walter U, Peetz D, Lackner K, Blankenberg S, Munzel T (2008)** Effects of oral niacin on endothelial dysfunction in patients with coronary artery disease: results of the randomized, double-blind, placebo-controlled INEF study. Atherosclerosis.
37. **Shechter M, Issachar A, Marai I, Koren-Morag N, Freinark D, Shahar Y, Shechter A, Feinberg MS (2009)** Long-term association of brachial artery flow-mediated vasodilation and cardiovascular events in middle-aged subjects with no apparent heart disease. Int J Cardiol 134(1):52–58.
38. **Papathanassiou K, Naka KK, Kazakos N, Kanioglou C, Makriyiannis D, Pappas K, Katsouras CS, Liveris K, Kolettis T, Tsatsoulis A, Michalis LK (2009)** Pioglitazone vs glimepiride: differential effects on vascular endothelial function in patients with type 2 diabetes. Atherosclerosis 205(1):221–226.
39. Ostad MA, Eggeling S, Tschentscher P, Schwedhelm E, Boger R, Wenzel P, Meinertz T, Munzel T, Warnholtz A (2009) Flow-mediated dilation in patients with coronary artery disease is enhanced by high dose atorvastatin compared to combined low dose atorvastatin and ezetimibe: results of the CEZAR study. Atherosclerosis 205(1):227–232.