Original Articles

Increased Arterial Stiffness Correlates with the Severity of Coronary Artery Disease in Patients with acute ST Elevation MI

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Keywords:
Pulse wave analysis (PWA), Augmentation index (AIx), Arterial stiffness, STEMI, IHD

Abstract

Background: *The aim of this study was to evaluate the association between arterial stiffness determined noninvasively by pulse wave analysis (PWA) and the severity of coronary artery disease in patients with acute ST elevation myocardial infarction (STEMI).*

Methods: *This cross sectional study was conducted in the National Institute of Cardiovascular Disease, Dhaka over a period of ten months starting from July 2011 to April 2012. Patients were purposively selected from those who were admitted in NICVD with acute STEMI myocardial infarction agreed to do coronary angiography. Total 99 patients (male: 81, female: 18) were included in this study. Assessment of arterial stiffness was performed noninvasively with the commercially available SphygmoCor system using applanation tonometry with a high-fidelity micromanometer. Augmentation index (AIx), Augmentation pressure (AP) and Augmentation index corrected for heart rate 75beats/min (AIx@75) were derived from this with the technique of PWA. Coronary angiography was performed in those patients during the same hospital stay and severity was assessed by vessel score, Friesinger score and Leaman score.*

Results: *It was found that 9 (9.1%) patients had score 0, 42 (42.4%) had score 1, 23 (23.2%) had score 2 and 25 (25.3%) had score 3. However higher the number of vessels is involved, the greater is the AIx @75. Mean score in single, double and triple vessel disease was 24.50, 33.57 and 34.60 respectively. The mean level of AIx @75 was observed 23.97±11.47 and 31.76±11.26 in insignificant and significant CAD respectively using Friesinger score. The difference was statistically significant (p<0.05). Spearman correlation analysis demonstrated a positive correlation between the AIx@75 and the severity of coronary artery disease (p= <0.05, r=0.40).*

Conclusion: *In conclusion, the results presented herein indicate that augmentation pressure (AP), augmentation index (AIx), and augmentation index corrected for heart rate 75/minute (AIx@75), measures closely related to wave reflections and arterial stiffness, are predictors of severity of CAD. It may be considered as a recommended test for the evaluation of CV risk in addition to other routine investigations.*

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Introduction:

Coronary heart disease (CHD) is a major cause of mortality globally and this health problem is reaching pandemic in both developed, as well as in developing countries.[1]Despite numerous improvements in risk scoring, there still remain patients identified as being low risk who experience CHD events, as well as patients deemed high risk who remain free of CHD events. This has led to a search for additional emerging risk variables that may aid in further risk discrimination. Various barriers exist, however, to the use of these emerging variables, limiting there more widespread use. In some cases, the tests are not universally available (apolipoprotein B) or are relatively expensive (lipoprotein-associated phospholipase A2). In other cases, the tests harbor potential risk (radiation with myocardial perfusion imaging or cardiac CT) or require specialized laboratories for testing (brachial flow mediated dilation and genetic testing).[2]

Blacher et al.[3] found that increased arterial stiffness has been shown to correlate with coronary risk factors. In addition, measures of arterial stiffness correlate with the presence of angiographic coronary artery disease (CAD).[4] Arterial stiffness determined invasively, has

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been shown to predict a higher risk of coronary atherosclerosis. However, invasive techniques are of limited value for screening and risk stratification in larger patient groups. Noninvasive detection of coronary artery disease is a prime goal for diagnostics in clinical cardiology. Pulse pressure, reflecting the pulsatile component of blood pressure and thus to some extent arterial stiffness is a well-known risk factor for myocardial infarction, particularly in men.[5,6]

The central aortic pressure wave is composed of a forward-traveling wave generated by left ventricular ejection and a later-arriving reflected wave from the periphery.[7] As aortic and arterial stiffness increase, transmission velocity of both forward and reflected waves increase, which causes the reflected wave to arrive earlier in the central aorta and augment pressure in late systole. Therefore, augmentation of the central aortic pressure wave is a manifestation of early wave reflection and is the boost of pressure from the first systolic shoulder to the systolic pressure peak. It can be expressed in absolute terms (augmented pressure [AP]) or as a percentage of pulse pressure (augmentation index [AIx]). AIx, determined noninvasively. They have been shown to be predictive for coronary artery disease (CAD) [4]. There were several studies from developed countries on the severity of CAD and arterial stiffness of AMI patients at all ages. But there were not enough data from Bangladesh addressing pulse wave analysis as an independent risk assessment tool for detecting severity of CAD. As a noninvasive approach clearly would be of value for the examination of larger populations, this observational study was designed to demonstrate in detail the association between CAD and aortic AIx, assessed by noninvasive pulse waveform analysis (PWA).

Materials and methods:

This cross sectional study was conducted in the National Institute of Cardiovascular Disease, Dhaka over a period of ten months starting from July 2011 to April 2012. Patients were purposively selected from those who were admitted in NICVD with acute STEMI myocardial infarction agreed to do coronary angiography. Total 99 patients (male: 81, female: 18) were included in this study. Assessment of arterial stiffness was performed noninvasively with the commercially available SphygmoCor system (The SphygmoCor Vx pulse wave Analysis system Model SCOR-Mx_DCN: 100521 P/N:1-00418, Rev:9.0/0-0m, SphygmoCor Software Version: 8, AtCor Medical Private Ltd) using applanation tonometry with a high-fidelity micromanometer (Millar Instruments). Patients with valvular, congenital heart disease and cardiomyopathy, suspected myocarditis or pericarditis, major non cardiovascular disorder such as severe renal impairment, uncontrolled hypertension (systolic blood pressure >160mmHg), prior PCI or CABG were excluded from the study. Informed consent was obtained in accordance with the study protocol approved by the local ethical committee.

Noninvasive assessment of arterial stiffness by PWA:[8]

In brief, peripheral pressure waveforms were recorded from the radial artery at the wrist, using applanation tonometry with a high-fidelity micromanometer (Millar Instruments). After 20 sequential waveforms were acquired, a validated generalized transfer function was used to generate the corresponding central aortic pressure waveform. AIx and AP were derived from this with the technique of PWA. The merging point of the incident and the reflected wave (the inflection point) was identified on the generated aortic pressure waveform. AP was the maximum systolic pressure minus pressure at the inflection point. The AIx was defined as the AP divided by pulse pressure and expressed as a percentage. Larger values of AIx will indicate increased wave reflection from the periphery or earlier return of the reflected wave as a result of increased pulse wave velocity (attributable to increased arterial stiffness) and vice versa. In addition, because AIx was influenced by heart rate, an index normalized for heart rate of 75 bpm (AIx@75) was used.[9] Only high-quality recordings, defined as an in-device quality index e”80% (derived from an algorithm including average pulse height, pulse height variation, diastolic variation, and the maximum rate of rise of the peripheral waveform) and acceptable curves on visual inspection by 1 investigator was included in the analysis. All PWA measurements was taken in the sitting position in a quiet, temperature-controlled room (22±1°C) after a brief period (at least 5 minutes) of rest, most often on the day before cardiac catheterization by a doctor not involved in performance or interpretation of the angiograms.

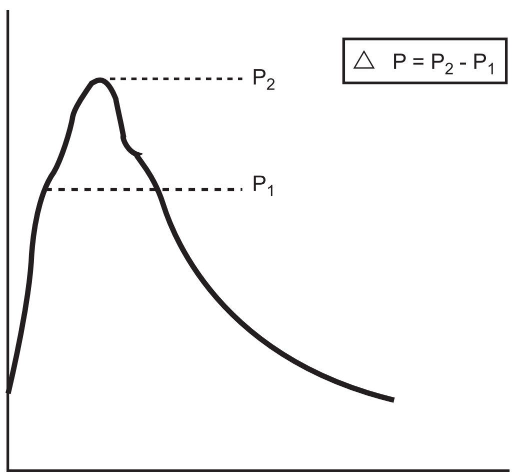

Fig.-1: *Augmentation pressure*

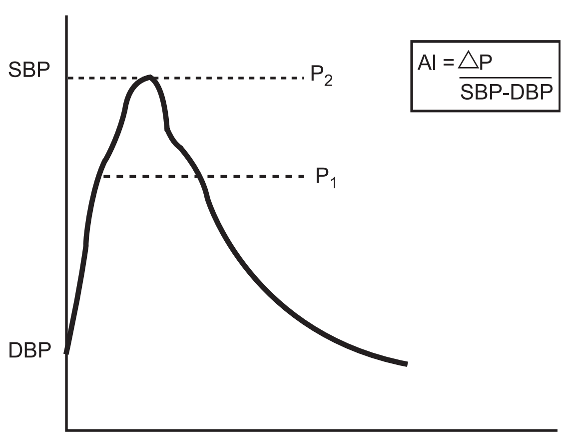

Fig.-2: *Augmentation index(AIx), SBP-systolic blood pressure, DBP- diastolic blood pressure*

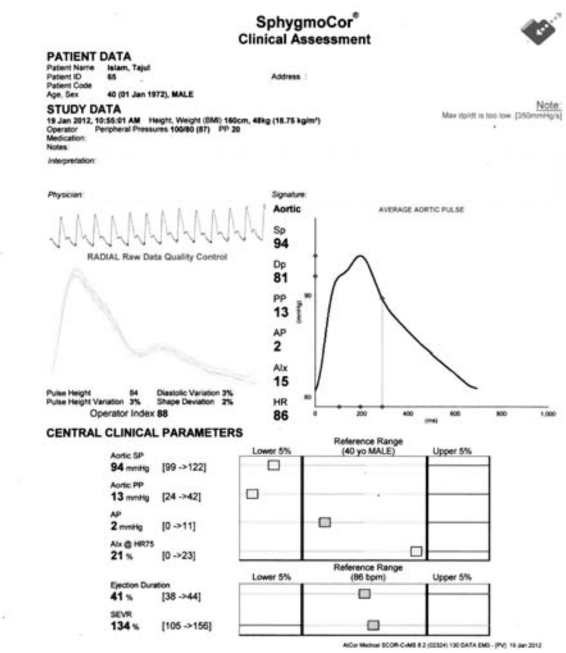

Fig.-3: *Patient with normal AIx@75*

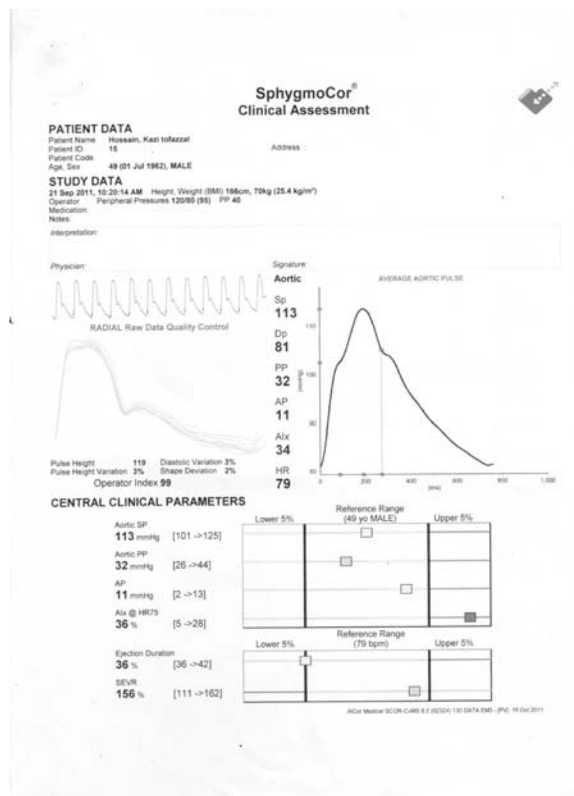

Fig.-4: *Patient with increased AIx@75*

Angiographic pattern and severity of coronary artery disease:

Coronary angiography was performed by percutaneous femoral approach using standard angiographic techniques. Interpretation of coronary angiogram was done by visual estimation by two cardiologists to assess the severity of coronary artery disease. Severity of coronary stenosis was graded according to the number of major epicardial vessel with significant stenosis (vessel score), Friesinger score and Leaman score.

A. Vessel score: [10]

This was the number of vessels with a significant stenosis (for left main coronary artery 50% or greater and for others 70% or greater reduction in luminal diameter).[11] Score ranged from 0 to 3, depending on the number of vessel involved. Left main coronary artery was scored as single vessel disease.[12]

Score 0 = no vessel involvement.

Score 1 = single vessel involvement.

Score 2 = double vessel involvement.

Score 3 = triple vessel involvement.

B. Friesinger score:[10]

The Friesinger index was a score ranges from 0 to 15. Each of the three main coronary arteries was scored separately from 0 to 5.

Score 0 : No arteriographic abnormality

Score 1: Trivial irregularities (lesion from 1-29%)

Score 2: Localized 30-68% luminal narrowing

Score 3: Multiple 30-68% luminal narrowing of same vessel;

Score 4: 69-100% luminal narrowing without 100% occlusion of proximal segments

Score 5: Total obstruction of a proximal segment of a vessel.

C. The Leaman score: [13]

It is a coronary scoring system to determine the severity of the underlying CAD. The 'Leaman score' is based on the severity of luminal diameter narrowing and weighed according to the usual blood flow to the left ventricle in each vessel or vessel segment.

Statistical Methods:

The numerical data obtained from the study was analyzed and significance of differences was estimated by using statistical methods. Data were presented as frequency and percents for categorical variables and as mean with standard deviation for quantitative variables. Categorical variables were analyzed by chi-square test. Quantitative variables were analyzed by t-test or ANOVA. Correlation between AIx @75 and angiographic severity was measured by Spearman's correlation test. P<0.05 was considered as significant. Statistical analyses were performed with SPSS, version 16.0 (SPSS Inc).

Results:

Out of 99 patients 81(82%) were male & 18 (18%) were female having a male and female ratio 4.5:1. The mean age of the study population was 50.6±9.4 ranging from 21 to 80 years. 76.8% patients were smoker, 36.4% were hypertensives, 38.4% were diabetic, 27.2% patients were dyslipidaemic and 23.2% having family history of IHD.

Table I

Age distribution of the study patients (n=99)

Age in years	Number	Percentage (%)
d" 40	15	15.2
41 – 50	37	37.4
51 – 60	40	40.4
> 60	7	7.1
Mean ± SDRange (min – max)		50.6±9.4(21 – 80)

Table I shows the age distribution of the study patients. Majority of the study patients belonged to 41-50 and 51-60 years age in both groups, which were 37 (37.4%) and 40 (40.4%) respectively. The mean age was found 50.6±9.4 years.

Table-II

Distribution of the study patients according to risk factors (n=99)

Risk factors	Numbers	Percent(%)
Smoking	76	76.8
Hypertension	36	36.4
Diabetes mellitus	38	38.4
Dyslipidemia	27	27.2
Family H/OCAD	23	23.2

Table II. Shows the risk factors among the population under study. Smoking habit was found in 76 (76.8%). Chewing tobacco was observed in 32 (32.3%). Hypertension was found in 36 (36.4%). Diabetes mellitus was found in 38 (38.4%). Dyslipidemia was found in 6 (6.1%). Family history of CAD was found 23 (23.2%).

In this study, angiographic severity was assessed by vessel score, Friesinger's score and Leaman score.

It was found that among the patients, highest percentage had one vessel score 42.4% followed by three vessels score 25.3%, two vessel score 23.2% and 0 score 9.1%.

Table-III

Distribution of the study patients according to vessel score (n=99)

Vessel Score	Number	Percent(%)
Score – 0	9	9.1
Score – 1	42	42.4
Score – 2	23	23.2
Score – 3	25	25.3

Table III shows the vessel score of the study patients. It was found that 9 (9.1%) patient had score 0, 42 (42.4%) patient had score 1. However 23 (23.2%) and 25 (25.3%) patient had score 2 and 3 respectively.

Table-IV

Association between AIx @75 and number of vessels involved (n=99)

No. of vessel involved	AIx @75		P value
	Mean	SD	
Single (n=42)	24.50	11.6	0.001^{s}
Double (n=23)	33.57	10.4	
Triple (n=25)	34.60	11.2	

Table IV shows that higher the number of vessels involved, the greater is the AIx @75 with mean score in single, double and triple vessel disease being 24.50, 33.57 and 34.60 respectively. There was significant association between AIx@75 and vessel involvement of the study patients.

Spearman's correlation showed a positive correlation with the AIx@75 and increasing number of vessel involvement (r=0.38, p<0.05).

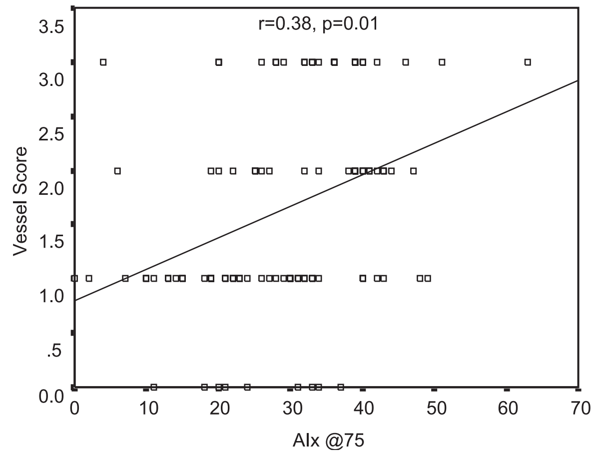

Fig.-5: *Spearman's Correlation between AIx@75 and vessel score*

Figure 1 shows that there is a positive correlation between AIx@75 and coronary artery disease severity in terms of vessel score (r=0.38). It was observed that correlation was statistically significant (p=0.01) by Spearman's Rank correlation test.

The score in Fresinger index ranges from 0 to 14 (Ringqvist, et al. 1983). In this study Friesinger score 1–4 was found 27.3%, score 5-10 was found 42.4% and Friesinger score 11-14 was found in 25.3% patients. Spearman's Rank correlation rest also showed positive correlation (0.40, p= <0.05).

Table-V

Mean status of AIx @75 of the study patients according to significant coronary artery disease defined by Friesinger score (n=99)

AIx @	Insignificant 75 bpm(%) score 0-4) C2AD	Significant (Friesinger score ≥5) CAD	P value\ (Friesinger
Mean ± SD	23.97±11.47	31.76±11.26	0.002^{s}
Mean ± SD	23.97±11.47	31.76±11.26	0.002^{s}

The mean level of AIx @75 was observed 23.97±11.47 and 31.76±11.26 in insignificant and significant CAD respectively (p<0.05). Significant CAD was significantly higher in patients with increased status of AIx @75 bpm. This study provided the evidence that increased AIx@75 was signiûcantly associated with the presence and severity of CAD in acute STEMI. This association showed a positive linear relation between

AIx@75 and vessel score, Friensinger score and Leaman score.

Multiple regression analysis considering arterial stiffness (AIx@75) as dependant variable showed that after adjusting smoking, diabetes mellitus, hypertension and dyslipidaemia arterial stiffness (AIx@75) remained significantly associated with severe CAD.

Table-VI

Multiple regression analysis considering AIx@75 as dependant variable

Variables of interest	Multiple regression analysis		
	Standardized (β) coefficient	95% Confidence Interval for B	p value
Constant		-28.020-14.477	0.528
Smoking	0.158	-0.746-9.594	0.093
Diabetes mellitus	0.072	-2.766-6.294	0.443
Hypertension	-0.102	-8.234-2.464	0.287
Dyslipidemia	0.245	2.908-23.440	0.012 s
Vessel score	0.357	2.124-6.577	0.001s

Table VI demonstrates the multiple regression analysis of standard coefficient (â) for characteristics of the subjects likely to be associated with arterial stiffness (AIx@75). Of the 5 variables AIx@75 bpm were found to be significantly associated with dyslipidaemia (standardized coefficient (â) 0.245, 95% confidence interval 2.908-23.440, $p < 0.05$) and vessel score (standardized coefficient (â) 0.357, 95% confidence interval 2.124-6.577, $p < 0.001$). The above table showed negative standardized coefficient (â) for hypertension and this was due to antihypertensive therapy. Thus after adjusting smoking, diabetes mellitus, hypertension and dyslipidaemia arterial stiffness remained significantly associated with severe CAD.

Discussion:

This study was carried out with an aim to find out the association between the arterial stiffness and the angiographic severity of coronary artery disease in patients with acute ST elevation myocardial infarction. A total 99 patients with acute STEMI who were agreed to undergo coronary angiography were included in the study.

The mean age of the patients was 50.6±9.4 years. Maximum frequency was found in the age group of 51-60 years. Weber et al.[8] had also shown mean age was significantly higher in CAD group (63.8+_10.3 years) than with no CAD group (53.7+_11.70 years). Another major factor influencing wave reflections, and thus AIx, AP, and AIx@75, is gender. Male female ratio was 4.5:1.The mean level of AIx @75 was observed 27.6±12.2% in male and 36.26.5% in female. The AIx @75 is significantly higher in female than male. Gatzka et al.[14] had shown AIx was higher in women. Weber et al.[15] had also shown higher AIx@75 was associated with female gender.

It was found that among the patients, highest percentage had one vessel score 42.4% followed by three vessels score 25.3%, two vessel score 23.2% and 0 score 9.1%. There was a positive correlation with the AIx@75 and increasing number of vessel involvement (Spearman's correlation coefficient). Park et al.[16] and Weber et al.[8] found that arterial stiffness index increased significantly with the increasing number of stenotic coronary vessels.

The score in Fresinger index ranges from 0 to 14 [10]. In this study Friesinger score 1–4 was found 27.3%, score 5-10 was found 42.4% and Friesinger score 11-14 was found in 25.3% patients. spearman's Rank correlation rest also showed positive correlation.

The study of Nürnberger et al.[17] however, complements the findings of the present study; they found a strong positive correlation between AIx and the risk of developing CAD, as assessed by the European Society of Cardiology Risk Score, in 144 asymptomatic patients without a previous history of CAD or atherosclerotic disease. Weber et al.[8] also found that AIx was significantly increased in CAD group compared with the control group.

Hlimonenko et al.[18] found that aortic pulse wave velocity was significantly increased in the coronary artery disease group and also showed the strong association of aortic stiffness and atherosclerosis. In the Rotterdam study, Van Popele et al.[19] reported that arterial stiffness was strongly associated with atherosclerosis at a variety of sites on the vascular tree.

Covic et al.[20] had shown patient with normal angiograms had significantly less arterial stiffness (as reflected by both a lower PWV=8.42±1.53 m/s and a lower AIx= 17.9±5.55%) compared with 35 subjects with evidence of obstructive CAD (PWV=9.21±1.15 m/s and AIx =23.4±5.4%, P<0.05 for both). Moreover as more coronary vessels were affected, PWV and AIx increased proportionately. There was a statistically significant linear relationship between the atherosclerotic burden and both measures of arterial stiffness.

Multiple regression analysis considering arterial stiffness (AIx@75) as dependant variable showed that after adjusting smoking, diabetes mellitus, hypertension and dyslipidaemia arterial stiffness (AIx@75) remained significantly associated with severe CAD.

Conclusion:

In conclusion, the results presented herein indicate that augmentation pressure (AP), augmentation index (AIx), and augmentation index corrected for heart rate 75 bpm (AIx@75), measures closely related to wave reflections and arterial stiffness, are predictors of severity of CAD in younger and middle aged patients. It may be considered as recommended test for the evaluation of CV risk in addition to other routine investigation.

Study limitation:

Although the result of this study support the hypothesis, there are some fact to be considered which might affect the result

1. A single center study with a relatively small number of patients. Thus, further studies in larger populations, ideally in a multicenter design, may add additional information.
2. Because of the well-known effects of severe systolic dysfunction on AIx (i.e. reduction of AIx due to the incapability of the failing ventricle to generate a pressure boost to fully compensate the reflected pressure wave, we excluded patients with an ejection fraction 35% [21]. Therefore, the prognostic value of AIx@75 in these patients remains unknown. This is also true for patients with valvular heart disease and for those with atrial fibrillation.
3. However angiography was evaluated by visual estimation, so there was chance of inter observer and intra observer variation of interpretation of the severity of the CAD.

Conflict of Interest - None.

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