Impact of Aortic Stiffness on Exercise Tolerance and Left Ventricular Filling Pressure after Percutaneous Coronary Intervention for Patients with Chronic Stable Coronary Artery Disease

**Abstract**

**Background and Aim:** In patients with stable coronary artery disease aortic rigidity may contribute to exercise intolerance and impaired left ventricular (LV) function after coronary intervention. However, this relationship has not yet been investigated. We aimed to assess the impact of aortic stiffness on both exercise tolerance and left ventricular diastolic filling pressure after percutaneous coronary intervention (PCI).

**Methods:** A percutaneous coronary intervention and stenting was performed in 98 consecutive patients with stable coronary artery disease (CAD) and positive exercise ECG. Before and after PCI, echocardiographic study, exercise stress test and aortic stiffness indices were calculated.

**Results:** Aortic stiffness index was significantly higher in patients with CAD (19.5 ± 4.9 vs 5.6 ± 2.1; P<0.0001), and still elevated even after successful PCI (11.5 ± 2.7; P<0.002). METs was significantly correlated with Aortic beta index (r = 0.64, P< 0.001), LAVI (r = 0.49, P<0.001) and E/E′ (r = 0.53, P < 0.001). ASI of <15 and <16.5 were the best cut-off values for prediction of improved exercise tolerance and LV filling pressure after PCI. The AUROC was calculated as 0.93 and 0.94 respectively (P<0.001).

**Conclusion:** In patients with stable coronary artery disease, increase in aortic rigidity, as assessed by aortic beta index, was independently correlated with reduced exercise tolerance and increased LV filling pressures, after PCI. ASI<15 and <16.5 were powerful predictors for improved exercise tolerance and decreased LV filling pressures after PCI.

**Keywords:** Aortic stiffness; Exercise tolerance; Left ventricular filling; Coronary stenting

**Abbreviations:** ASI: Aortic Stiffness Index; PCI: Percutaneous Coronary Intervention; CAD: Coronary Artery Disease; E/E: Ratio of Early Mitral Flow Velocity Wave (E) to the Early Mitral Anular Velocity Wave (E′); LAD: Left Anterior Descending Artery; RCA: Right Coronary Artery; LCX: Circumflex Artery; LAV: Left Atria Volumes; BSA: Body Surface Area; AOST: Aortic Strain

**Introduction**

Aortic stiffness is associated with cardiovascular risk factors and atherosclerosis [1-3]. It has been shown that aortic stiffness is a powerful predictor of future cardiovascular events and cardiovascular mortality. [4]. Several studies investigated the negative impact of aortic stiffness on coronary circulation. relationship between aortic stiffness and coronary circulation [5,6]. Kingwell et al. [7] demonstrated that aortic stiffness decreases the chest pain in patients with CAD. Fukuda et al. [5] showed that pulse wave velocity (PWV) increased and was significantly correlated with the number of diseased vessels. Noninvasive evaluation is an important clinical issue for patients with suspected CAD. Despite the presence of various diagnostic tools, diagnosis of significant CAD may be a difficult clinical challenge. The prognostic role of aortic stiffness measurement in cardiovascular disease was demonstrated in previous studies [8-11].

Considering the association between a stiff aorta and the rate percutaneous coronary intervention (PCI), the significance of aortic stiffness in prediction of exercise tolerance and left ventricular function after PCI is not well studied. We therefore sought to examine the impact of aortic stiffness on exercise tolerance and left ventricular filling after PCI for patients with stable angina pectoris.

**Methods**

**Patient population**

Ninty-eight patients with stable angina pectoris and 70 healthy subjects were included in the study, from Jan 2012 to September 2012 in zagazig university hospital. Inclusion criteria included patients presented with typical angina pectoris and had positive exercise stress test and with documented significant coronary
Aortic stiffness measurement

The following aortic stiffness indices were calculated as previously described [15, 16]:

- Aortic strain (AOST) = systolic diameter (SD) - diastolic diameter (DD)/diastolic diameter (DD) × 100.
- Aortic distensibility = (2 \ aortic strain)/Pulse pressure (pure number); and elastic modulus E(p) = PP/strain.
- Aortic stiffness index (beta) was calculated according to the following formula: [β] Index = ln (systolic blood pressure/diastolic blood pressure)/AOST.

Exercise test

Modified Bruce protocol utilizing Marquette T-2000 treadmill was applied for all patients. Electrocardiograms and blood pressure recordings were monitored throughout. Total exercise time, stage, maximum workload (metabolic equivalents, or METs), peak exercise, and resting heart rate were recorded.

Follow-up assessment

All patients underwent clinical follow-up as well as complete echo-Doppler study including ASI assessment and exercise stress test 3 months after the PCI.

Statistical analysis

SPSS 18.0 for Windows (SPSS Inc., Chicago, IL, USA) was used to analyse our results. Student’s t-test was used for comparison. Stepwise multiple linear regression analyses were performed. To calculate optimal cut off values the receiver operating characteristic (ROC) Analysis was performed. Sensitivity, specificity, predictive values, and accuracy were calculated using typical formulas. The multivariate enter logistic regression was performed to identify the independent predictors of METs and E/E’ after PCI. Reproducibility of aortic stiffness index (ASI) was assessed in seven subjects. Biological variability (over 10 cardiac cycles) and inter observer variability (two observers selecting 10 cardiac cycles for analysis) had <8%.

Results

PCI was successful in all patients with a TIMI flow 3 was achieved. There were no major complications occur in hospital period and during the 3 months of follow-up. PCI was performed to Left Anterior Descending artery (LAD) in 45 patients, Circumflex artery (LCX) in 16 patients, Right Coronary Artery (RCA) in 24 patients and for both LAD and RCA in 13 patients.

Baseline characteristics of the study groups are shown in (Table 1). The two groups were comparable with respect to age, body mass index, systolic and diastolic blood pressures, and heart rate. The mean ASI was 5.6 ± 2.1 in the controls versus 19.5 ± 4.9 in patients with CAD (p<0.001). Following successful PCI the mean ASI decreased significantly by 34.3% to 11.5 ± 2.7 (p<0.002). However, the post procedural ASI values were still significantly higher in patients than those in the control group (Table 2 and Figure 1).

Thirteen patients had positive stress test and a significantly elevated LAVI (P<0.03) and significantly elevated LV filling pressure (P<0.01). ASI was significantly higher in those with positive than in patients with negative exercise test after PCI (AOST %: 7.9 ± 2.5 vs 11.6 ± 3.7 (P<0.001), Distensibility, mmHg.1103: 2.9 ± 1.5 vs 4.8 ± 1.2 (P <0.01); Elastic modulus N/m2: 8.3 ± 1.5 vs 5.8 ± 1.7 (P<0.001) and ASI: 23.9± 2.8 vs 13.5±1.1 (P <0.001) (Table 3).

Correlation analysis before and after PCI, showed that METs was inversely correlated with age (r= -0.31, P<0.05; r= -0.28, P <0.05), peak S (P <0.02), E’ mean (P <0.01 &<0.03), LAVI (P<0.01 &<0.001), E/E’ ratio (r = 0.55 & 0.53, P <0.001), and ASI (r = 0.61& 0.64, P <0.001) (Table 4). On the other hand E/E’ was significantly correlated with LAVI ml/m2 (r =0.58& 0.62; P<0.001), and aortic index (r =0.61& 0.64, P <0.001), (Table 5).

Receiver operating characteristic curve analysis showed that ASI<15 was the best cut off value for the prediction of improved exercise tolerance (increased METs), with a sensitivity, specificity, positive predictive value and negative predictive value of (95%, 64%, 94% and 70% respectively). The area under the curve was 0.93 (0.873-0.985) (Figure 4). While the best cut-off value in predicting decreased LV filling pressure (significantly decreased E/E’) was <1.65, with a sensitivity, specificity, positive predictive value and negative predictive value of (96%, 63%, 95% and 68% respectively). The AUROC was calculated as 0.94 (0.872-0.992) (Figure 5).
Impact of Aortic Stiffness on Exercise Tolerance and Left Ventricular Filling Pressure after Percutaneous Coronary Intervention for Patients with Chronic Stable Coronary Artery Disease

Figure 1: Aortic stiffness Index before and after PCI in patients with stable CAD [before PCI (IIa) & after PCI (IIb) versus control subjects (I). (*) the difference patients before PCI (IIa) and control subjects (I). While**: the difference patients after PCI (IIb) and control subjects (I)].

Figure 2: Linear regression analysis and Pearson correlation coefficient for the relationship between exercise capacity (METs) and aortic beta index.

Figure 3: Linear regression analysis and Pearson correlation coefficient for the relationship between E/E' and aortic beta index.

Figure 4: ROC analysis showing that ASI <15 is the best cut-off value in predicting improved exercise tolerance after PCI (AUC: 0.93 and P<0.001).

Figure 5: ROC analysis showing that ASI <16.5 is the best cut-off value in predicting decreased E/E' after PCI (AUC: 0.94 and P<0.001).

Discussion

We demonstrated that aortic stiffness was inversely correlated with exercise tolerance and directly correlated with LV filling pressure (E/E') in subjects with stable ischemic heart disease before and after PCI. Moreover the decrease in ASI significantly correlated with improved exercise tolerance and LV diastolic function after PCI for subjects with patients with chronic CAD. We have been demonstrated that ASI of <15 and <16.5 were the best cut-off values for prediction of improved exercise tolerance and decreased LV filling pressure (E/E') after PCI. Compared to healthy subjects, we found that patients with significant coronary lesions had significantly higher ASI values, even after successful PCI. We observed that ASI values significantly decreased after PCI. The exact mechanism for the decrease in ASI after PCI is uncertain. Successful PCI have been associated with hemodynamic and biochemical effects in the early term, especially improvements in left ventricular function and neurohumoral activation.[17-18] These changes after PCI may be responsible for ASI changes after PCI.

Citation: Ragab A, Mahfouz, Amr A, Ateah, Elawady W, et al. (2015) Impact of Aortic Stiffness on Exercise Tolerance and Left Ventricular Filling Pressure after Percutaneous Coronary Intervention for Patients with Chronic Stable Coronary Artery Disease. J Cardiol Curr Res 4(2): 00137. DOI: 10.15406/jccr.2015.04.00137
Table 1: Demographic and echocardiographic characteristics of patients versus control subjects.

| Variables                  | Patients (n = 98) | Controls (n = 70) | p     |
|----------------------------|------------------|------------------|-------|
| Age (years)                | 56.9 ± 5.2       | 54.6 ± 6.4       | >0.05 |
| Gender (males %)           | -70%             | -65%             | >0.05 |
| Body mass index (kg/m²)    | 25.8±3           | 24.7±5           | >0.05 |
| DM                         | 39 (38.7%)       | 0 (0%)           |       |
| Hypertension               | 48 (49%)         | 0 (0%)           |       |
| Smoking                    | 35 (36%)         | 0 (0%)           |       |
| SBP                        | 139 ± 11.5       | 136.5 ± 9.3      | >0.05 |
| DBP                        | 83.5 ± 4.5       | 84.2 ± 3.9       | >0.05 |
| EF%                        | 65.3 ± 6.4       | 67.2 ± 5.7       | 0.26  |
| FS%                        | 34.3 ± 3.2       | 35.25 ± 4.1      | 0.34  |
| LAVI mL/m²                 | 37.6 ± 5.4       | 21.5 ± 4.2       | <0.001|
| E                          | 68.1 ± 12.1      | 76.3 ± 6         | >0.05 |
| A                          | 58.9 ± 9.1       | 56.5 ± 3.3       | >0.05 |
| E/A                        | 1.14 ± 0.41      | 1.24 ± 0.2       | >0.05 |
| E′ mean (m/s)              | 6.1 ± 1.4        | 11.3 ± 1.7       | <0.05 |
| E/E′                       | 14.3±0.11        | 6.1±0.11         | <0.001|
| S mean (cm/s)              | 0.08±0.02        | 0.14±0.03        | >0.05 |
| AOST %                     | 8.7 ± 2.3        | 14.8 ± 2.8       | <0.001|
| Distensibility, mm Hg1.103 | 3.3 ± 1.3        | 4.9 ± 1.5        | <0.01 |
| Elastic modulus N/m²       | 6.9 ± 2.8        | 4.1 ± 1.7        | <0.01 |
| Aortic Stiffness Index     | 19.5±4.9         | 5.6              | <0.001|

DM: Diabetes Mellitus; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LVEF: Left Ventricular Ejection Fraction; FS: Fractional Shortening; LAVI: Left Atrial Volume Index; E: E-Wave Velocity; A: A-Wave Velocity; AOST: Aortic Strain.

Table 2: Exercise and echocardiographic parameters before PCI and 3 months after PCI.

| Variables                  | Before PCI     | 3 Months After PCI | P     |
|----------------------------|----------------|--------------------|-------|
| Stress test                |                |                    |       |
| - Negative                 | 0              | 85 (86.7%)         | <0.001|
| - Positive                 | 98             | 13 (13.3%)         |       |
| Duration of exercise (minutes) | 7.85±1.02     | 12.16±1.53         | < 0.001|
| METs                       | 7.87 ± 1.75    | 10.65 ± 1.6        | < 0.001|
| LVEDD                      | 47.25 ± 5.7    | 48.30 ± 5.2        | 0.07  |
| LVESD                      | 31.4 ± 4.2     | 31.1 ± 7.4         | 0.76  |
| EF                         | 65.2 ± 6.3     | 66.4 ± 7.1         | 0.06  |
| E/A                        | 1.05 ± 0.4     | 1.28 ± 0.3         | < 0.001|
| LAVI mL/m²                 | 37.6 ± 5.4     | 29.5±3.2           | < 0.01 |
| E/ E′ mean                 | 14.3±0.11      | 8.6±0.09           | < 0.01 |
| S mean, m/s                | 0.08±0.02      | 0.11±0.04          | > 0.05 |
| ASI                        | 19.5±4.9       | 11.5±2.7           | < 0.001|

METs: Metabolic Equivalent; LAVI: Left Atrial Volume Index; LVEDD: Left Ventricular End-Diastolic Dimension; LVESD: Left Ventricular End-Systolic Dimension; EF%: Ejection Fraction; E/E′: Ratio of Early Mitral Flow Velocity to Myocardial Early Velocity; ASI: Aortic Stiffness Index.
Impact of Aortic Stiffness on Exercise Tolerance and Left Ventricular Filling Pressure after Percutaneous Coronary Intervention for Patients with Chronic Stable Coronary Artery Disease

Table 3: Echocardiographic indices of patients with negative Stress test versus those with positive Stress test after PCI.

|                        | Patients with Negative Stress Test after PCI (n=85) | Patients with Positive Stress Test after PCI (n=13) | P-Value |
|------------------------|----------------------------------------------------|-----------------------------------------------------|---------|
| LVEF, %                | 63 ± 6                                             | 62 ± 6                                              | >0.05   |
| LAVI mL/m²             | 26.1 ± 2.7                                         | 33.5 ± 3.4                                          | <0.03   |
| E/A                    | 1.29 ± 0.04                                        | 1.21 ± 0.03                                         | >0.05   |
| S mean, m/s            | 0.12 ± 0.02                                        | 0.10 ± 0.02                                         | >0.05   |
| E'/E'' mean            | 5.98 ± 1.9                                         | 10.83 ± 2.1                                         | <0.01   |
| Aortic stiffness Indices |                                             |                                                     |         |
| AOST %                 | 11.6 ± 3.7                                         | 7.9 ± 2.5                                           | <0.001  |
| Distensibility (mmHg 1.103) | 4.8 ± 1.2                                         | 2.9 ± 1.5                                           | <0.01   |
| Elastic modulus (N/m²) | 5.8 ± 1.7                                          | 8.3 ± 1.5                                           | <0.01   |
| Aortic stiffness index (β)| 13.5 ± 1.1                                        | 23.9 ± 2.8                                         | <0.001  |

LVEF: Left Ventricular Ejection Fraction; FS: Fractional Shortening; LAVI: Left Atrial Volume Index; AOST: Aortic Strain.

Table 4: Linear Regression Analysis (Univariate Analysis) for prediction of METs before and after percutaneous coronary intervention.

| Variable   | Before PCI | P-value | After PCI | P-value |
|------------|------------|---------|-----------|---------|
| Age, y     | -0.31      | <0.04   | -0.28     | <0.05   |
| BMI        | -0.22      | >0.05   | -0.19     | >0.05   |
| LVEF, %    | 0.26       | >0.05   | 0.21      | >0.05   |
| LAVI mL/m² | -0.45      | <0.01   | -0.49     | <0.001  |
| S mean m/s | 0.43       | <0.02   | 0.42      | <0.01   |
| E/A ratio  | -0.21      | >0.05   | -0.23     | >0.05   |
| E'/E'' mean| -0.44      | <0.02   | -0.41     | <0.03   |
| E/E'       | -0.55      | <0.001  | -0.53     | <0.001  |
| ASI        | -0.61      | <0.0001 | -0.64     | <0.0001 |

BMI: Body Mass Index; LVEF: Left ventricular ejection fraction; LAVI: Left atrial volume index; ASI: Aortic stiffness index.

Table 5: Linear Regression Analysis (Univariate Analysis) for prediction of E/E’ before and after percutaneous coronary intervention.

| Variable   | Before PCI | P-value | After PCI | P-value |
|------------|------------|---------|-----------|---------|
| Age, y     | -0.31      | <0.04   | -0.28     | <0.05   |
| BMI        | -0.22      | >0.05   | -0.19     | >0.05   |
| LVEF, %    | 0.26       | >0.05   | 0.21      | >0.05   |
| LAVI mL/m² | -0.45      | <0.01   | -0.49     | <0.001  |
| S mean m/s | 0.43       | <0.02   | 0.42      | <0.01   |
| E/A ratio  | -0.21      | >0.05   | -0.23     | >0.05   |
| E'/E'' mean| -0.44      | <0.02   | -0.41     | <0.03   |
| E/E'       | -0.55      | <0.001  | -0.53     | <0.001  |
| ASI        | -0.61      | <0.0001 | -0.64     | <0.0001 |

BMI: Body Mass Index; LVEF: Left Ventricular Ejection Fraction; LAVI: Left Atrial Volume Index; ASI: Aortic Stiffness Index.

Citation: Ragab A, Mahfouz, Amr A, Ateah, Elawady W, et al. (2015) Impact of Aortic Stiffness on Exercise Tolerance and Left Ventricular Filling Pressure after Percutaneous Coronary Intervention for Patients with Chronic Stable Coronary Artery Disease. J Cardiol Curr Res 4(2): 00137. DOI: 10.15406/jccr.2015.04.00137
Table 6: Multivariate logistic regression analysis for prediction of improved exercise tolerance.

| Variable              | OR    | 95% CI       | P value |
|-----------------------|-------|--------------|---------|
| Age (year)            | 1.8   | 0.5-4.8      | >0.05   |
| Body mass index (kg/m²)| 1.5   | 0.3-4.1      | >0.05   |
| SBP (mmHg)            | 2.7   | 1.1-6.9      | <0.05   |
| DBP (mmHg)            | 1.6   | 0.4-4.3      | >0.05   |
| LAVI (mL/m²)          | 3.7   | 1.3-8.8      | <0.01   |
| LV EF%                | 1.9   | 0.5-4.5      | >0.05   |
| ASI                   | 6.5   | 2.5-13.5     | <0.001  |

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LAVI: Left Atrial Volume Index; EF%: Ejection Fraction; ASI: Aortic Stiffness Index.

Table 7: Multivariate logistic regression analysis for prediction of decreased LV filling pressure.

| Variable              | OR    | 95% CI       | P value |
|-----------------------|-------|--------------|---------|
| Age (year)            | 1.65  | 0.48-4.50    | >0.05   |
| Body mass index (kg/m²)| 1.59  | 0.36-4.31    | >0.05   |
| SBP (mmHg)            | 3.2   | 1.82-7.46    | <0.05   |
| DBP (mmHg)            | 1.9   | 0.55-4.35    | >0.05   |
| LAVI (mL/m²)          | 4.3   | 1.75-9.22    | <0.02   |
| LV EF%                | 1.82  | 0.52-4.33    | >0.05   |
| ASI                   | 7.35  | 2.5-14.8     | <0.001  |

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LAVI: Left Atrial Volume Index; EF%: Ejection Fraction; ASI: Aortic Stiffness Index.

Significant correlations have been found between ASI and parameters of left ventricular diastolic and systolic functions [16-20]. These changes after PCI may be responsible for PWV changes in the early term.

Enko K et al. [21] had demonstrated that, patients with high PWV had lower exercise capacity than patients with low PWV. A low myocardial ischemia threshold, as well as an enhancement of the ventilatory response to exercise, was also found in patients with high PWV. The peripheral arteries are less stiffening than ascensin aorta and consequently don't reflect the exact load imposed by vascular system on left ventricle [22,23]. In addition stiffness in ascending aorta can be assessed easily and noninvasively with more accuracy than peripheral arteries [24].

Stiffer central vessels may affect Vo2, influencing LV relaxation. The association between a higher PWV and a more restrictive mitral filling pattern is consistent with this. The association between a higher PWV and a more restrictive mitral filling pattern is consistent with this. A link between greater aortic stiffness and a restrictive mitral filling pattern could occur as a result of cardiac hypertrophy, changing the properties of both the myocytes and the interstitium, which is known to be a factor that influences LV diastolic filling [25,26].

Clinical Implication

Changes in ASI may be a clinically important parameter in predicting exercise response and may become an additional target for therapeutic interventions that aim to improve quality of life and ventricular burden of subjects with CAD.

Conclusion

The current study demonstrated that aortic stiffness is an independent predictor exercise tolerance and left ventricular filling pressures before and after PCI. Our data provided that an ASI < 15 and < 16.5 were the best cut-off values for prediction of improved exercise tolerance and reduced LV filling pressure respectively after successful PCI.

References

1. Mitchell GF, Parise H, Benjamin EJ, Larson MG, Keyes MJ, et al. (2004) Changes in arterial stiffness and wave reflection with advancing age in healthy men and women: the Framingham Heart Study. Hypertension 43(6): 1239-1245.
2. Tedesco MA, Natale F, Di Salvo G, Caputo S, Capasso M, et al. (2004) Effects of coexisting hypertension and type II diabetes mellitus on arterial stiffness. J Hum Hypertens 18(7): 469-473.
3. Sharman JE, McEniery CM, Dhakam ZR, Coombes JS, Wilkinson IB, et al. (2007) Pulse pressure amplification during exercise is significantly reduced with age and hypercholesterolemia. J Hypertens 25(6): 1249-1254.
4. Vlachopoulos C, Azmaouridis K, Stefanadis C (2010) Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol 55(13): 1318-1327.
5. Fukuda D, Yoshiyama M, Shimada K, Yamashita H, Ebara S, et al. (2006) Relation between aortic stiffness and coronary flow reserve in patients with coronary artery disease. Heart 92(6): 759-762.
6. Nemes A, Forster T, Gruber N, Csanady M (2004) Coronary flow
velocity reserve and indices describing aortic distensibility in patients after coronary angiography. Int J Cardiol 96(1): 29-33.

7. Kingwell BA, Waddell TK, Medley TL, Cammann JD, Dart AM (2002) Large artery stiffness predicts ischemic threshold in patients with coronary artery disease. J Am Coll Cardiol 40(4): 773-779.

8. Mattace-Raso FU, van der Cammen TJ, Hofman A, van Popele NM, Bos ML, et al. (2006) Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study. Circulation 113(5): 657-663.

9. Sutton-Tyrrell K, Najjar SS, Boudreau RM, Venkitachalam L, Kupelian V, et al. (2005) Elevated aortic pulse wave velocity, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults. Circulation 111(25): 3384-3390.

10. Willems-Hansen T, Staessen JA, Torp-Pedersen C, Rasmussen S, Thijs L, et al. (2006) Prognostic value of aortic pulse wave velocity as index of arterial stiffness in the general population. Circulation 113(5): 664-670.

11. Mahfouz RA, Abdulmoneim A, Abduo M, Elawady W (2013) The relation of aortic stiffness and in-stent restenosis in patients undergoing percutaneous coronary stenting. Echocardiography 30(5): 582-587.

12. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, et al. (2005) Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 18(12): 1440-1463.

13. Ommeren SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, et al. (2000) Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: A comparative simultaneous Doppler-catheterization study. Circulation 102(15): 1786-1793.

14. Abhayaratna WP, Seward JB, Appleton CP, Douglas PS, Oh JK, et al. (2006) Left atrial size: physiologic determinants and clinical applications. J Am Coll Cardiol 47(12): 2357-2363.

15. Lacombe F, Dart A, Dewar E, Jennings G, Cameron J, et al. (1992) Arterial elastic properties in man: a comparison of echo-Doppler indices of aortic stiffness. Eur Heart J 13(8): 1040-1045.

16. O'Rourke MF1, Staessen JA, Vlachopoulos C, Duprez D, Plante GE (2002) Clinical applications of arterial stiffness; definitions and references values. Am J Hypertens 15(5): 426-444.

17. Lang TW, Corday E, Gold H, Meerbaum S, Rubins S, et al. (1974) Consequences of reperfusion after coronary occlusion. Effects on hemodynamic and regional myocardial metabolic function. Am J Cardiol 33(1): 69-81.

18. Remmelink M, Sjauw KD, Henriques JP, Vis MM, van der Schaaf RJ, et al. (2009) Acute left ventricular dynamic effects of primary percutaneous coronary intervention from occlusion to reperfusion. J Am Coll Cardiol 53(17): 1498-502.

19. Katayama T, Nakashima H, Yonekura T, Honda Y, Suzuki S, et al. (2003) Clinical significance of acute-phase brain natriuretic peptide in acute myocardial infarction treated with direct coronary angioplasty. J Cardiol 42(5): 195-200.

20. Tavil Y, Kanbay A, Sen N, Ulukavak Ciftci T, Abaee A, et al. (2007) The relationship between aortic stiffness and cardiac function in patients with obstructive sleep apnea, independently from systemic hypertension. J Am Soc Echocardiogr 20(4): 366-372.

21. Enko K, Sakuragi S, Kakishita M, Okawa K, Nagase S, et al. (2008) Arterial Stiffening is Associated with Exercise Intolerance and Hyperventilatory Response in Patients with Coronary Artery Disease. Clinical Medicine Insights: Cardiology 2: 41-48.

22. van der Heijden-Spek JJ, Staessen JA, Fagard RH, Hoeks AP, Boudier HA, et al. (2000) Effect of age on brachial artery wall properties differs from the aorta and is gender dependent: a population study. Hypertension 35(2): 637-642.

23. Nelson AJ, Worthey SG, Cameron JD, Willoughby SR, Plantaditi C, et al. (2009) Cardiovascular magnetic resonance-derived arterial distensibility: validation and observed regional differences in the elderly. J Hypertens 27(3): 535-542.

24. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, et al. (2006) Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J 27(21): 2588-2605.

25. Weber KT, Brilla GC (1991) Pathological hypertrophy and cardiac interstitium: fibrosis and renin-angiotensin-aldosterone system. Circulation 83(6): 1849-1865.

26. Pearson AC, Gudpitt C, Nagelhout D, Sear J, Cohen JD, et al. (1991) Echocardiographic evaluation of cardiac structure and function in elderly subjects with isolated systolic hypertension. J Am Coll Cardiol 17(2): 422-430.