CORONARY ARTERY DISEASE AND SEGMENTAL ISOVOLUMIC RELAXATION PATTERNS- WHAT IS THE RELATION?
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ABSTRACT
Background: Some segments relax with the early diastolic peak velocity lying in the isovolumic relaxation period. Its significance for prediction of coronary artery disease has not been fully elucidated. So we aimed to elucidate if the presence of abnormal isovolumic relaxation velocities can add a value to predict presence of significant coronary artery disease.
Methods: This study included 100 consecutive subjects; 60 subjects with coronary artery disease (CAD), 40 normal subjects as a control group. Echocardiographic evaluation of: wall motion abnormalities, transmitral; E and A-velocities & E/A ratio. Tissue-Doppler study of the isovolumic relaxation velocities detected in the four basal segments. Patients with CAD were divided into; group I with significant CAD, group II with non significant CAD, the control group represents group III.
Collected data underwent statistical analysis.
Result: post systolic shortening (PSS) was more frequent in the ischemic myocardium; with high specificity (92.5%) and good positive predictive value (86.6%) in detecting segments with significant coronary stenosis. The incidence of occurrence of peak early diastolic velocity (PVIVR) is more in patients with non significant CAD; it has good specificity (86.2%) for detection of any degree of coronary stenosis.
Conclusion: The presence of abnormal isovolumic relaxation velocities could be considered as a good positive test for prediction of CAD.
Key wards: Isovolumic relaxation velocity, Post systolic shortening (PSS), peak early diastolic velocity (PVIVR).

INTRODUCTION
Despite a decline in mortality attributed to coronary artery disease (CAD), the burden of CAD remains high and is the leading cause of death and heart failure worldwide. This emphasizes the need for early detection of CAD in order to prevent heart failure and further reduce mortality due to CAD.
Analysis of the regional myocardial systolic and diastolic performance could be more sensitive methods than the assessment of global systolic left ventricular in CAD.
The normal early segmental diastolic velocity pattern has been described as a high diastolic velocity corresponding to the rapid filling phase and low uniphasic or biphasic velocities in the isovolumic relaxation (IVR) period, that can be disturbed by persistent contraction after the aortic valve closure in ischemic myocardium; termed as post systolic shortening (PSS). In clinical practice some segments relax with the early diastolic peak velocity lying in the IVR period (PVIVR) instead of the rapid filling phase.
The Pulsed-wave Doppler Tissue Imaging (TDI) techniques offer a simple noninvasive method to analyze regional systolic and diastolic left ventricular motion.

AIM OF THE WORK
We aimed in this work to elucidate if the presence of abnormal isovolumic relaxation velocities (detected by the resting TDI) can add a value to predict presence of significant CAD and consequently rapid intervention.

SUBJECTS AND METHODS
The study include 100 subjects (56 males and 44 females) with mean age of 53±9.75 years; including 60 consecutive subjects with coronary artery disease (CAD); diagnosed from history of typical ischemic chest pain or by the noninvasive diagnostic modalities as electrocardiography (ECG) -either resting or exercise ECG- who were referred for diagnostic coronary angiography and 40 age matched healthy subjects as a control group.
Patients with recent myocardial infarction, more than mild valvular heart disease, bundle branch block, cardiomyopathy, or patients, who had undergone percutaneous coronary intervention (PCI) or coronary artery bypass grafts (CABG) before, were excluded from the study.
Approval was obtained for performing the study from the IRP in the faculty of medicine, Zagazig University, Egypt.
After giving an informed consent, all participants were subjected to the following:
1) Full history taking including (age, gender, history of hypertension, diabetes mellitus, smoking, family history of CAD, history of previous PCI or CABG) and thorough clinical examination (mainly for blood pressure and heart rate).
2) Complete 12-leads ECG for signs of ischemia (ST-T wave changes).
3) Conventional echocardiographic and Doppler studies were performed on each subject using a
Hewlett Pakard (SONOS 5500) echo-set using a 2.5 MHz transducer. The echo, were obtained at rest with the subjects in the left lateral decubitus position, with simultaneous ECG. The following studies were done:

1- 2-Dimensonal echocardiography (2-D Echo) to evaluate the wall motion abnormalities (WMA) in the four basal segments by an independent blinded observer, with 1 = normal motion, 2 = hypokinesia, 3 = akinesia and 4 = dyskinesia.

2- Pulsed wave Doppler (PW) study of the mitral flow for the following:

I: The E-wave, A-wave and E/A ratio, taken from the apical 4-5 chamber views.

II: The isovolumic relaxation time (IVRT); defined as the time interval between the time points when the aortic valve closed (the end of systolic output flow) and the mitral valve opened (the onset of transmitral E flow) was measured.

3- Tissue-Doppler imaging (TDI) was done to assess the following (strain rate imaging had been not performed):

I- Early diastolic peak velocity (Ve) and peak velocity during atrial contraction (Va) of the 4 basal segments (the basal septal, basal lateral, basal anterior and basal inferior) from the apical 4- and apical 2-chamber views. We selected the basal segments as TDI is angle dependent, so that it is difficult and inaccurate to measure myocardial velocity in mid-apical region.

II- The segmental early diastolic velocity pattern, during the IVRT. These were classified into three categories: (1) early diastolic peak velocity lying in the IVR period (PVIVR), (2) post systolic shortening (PSS), characterized by a persistent systolic velocity after aortic valve closure and (3) normal pattern (Non-PVIVR Non-PSS), characterized by a lower diastolic velocity in the IVRT than in the rapid filling phase or slight biphasic velocity deflections in the IVRT.

4) Coronary angiography: Coronary angiography was performed to all patients using Judkins technique. The coronary artery narrowing was visually estimated and expressed as percentage of luminal diameter stenosis. Patients with ≥ 70% narrowing in left anterior descending (LAD) artery, circumflex artery (LCx) or right coronary artery (RCA) or their major branches were classified as having significant angiographic CAD.

The lesion was considered as proximal lesion if affecting LAD artery before the origin of the first diagonal artery, affecting the LCx artery before the origin of the first obtuse marginal artery or affecting the proximal third of the RCA. Myocardial blush of the basal segments were estimated to prove that these segments suffer from ischemia secondary to this proximal lesion (myocardial blush grade (MBG) developed by van’t Hof et al. A grade of 0 = no blush and a grade of 3 = normal blush. An MBG grade 1 or 2 represents diminished intensity in the myocardium).

Accordingly we divided patients with CAD into 2 groups:

Group I: 40 patients with proximal significant CAD (＞70% stenosis with MBG <3) and group II: 20 patients with proximal non-significant (NS) CAD (＜70% stenosis with MBG <3). While Group III did not undergo coronary angiography (40 healthy subjects) acting as a control group.

Two independent observers estimated intra-and inter-observer variability of the measurements of TDI parameters and the detection of PSS and PVIVR. Both were blinded to the patient data, and so of each other readings.

Statistical analysis: Data were collected and analyzed using SPSS (Statistical Package for the Social Sciences) version 15. Continuous variables were expressed as mean ± SD and categorical variables are expressed as percentages. Differences among the study groups were analyzed by ANOVA test. Sensitivity, specificity and predictive values were estimated. A p value < 0.05 was regarded as being statistically significant.

RESULTS

We enrolled 100 subjects in this study, among them 40 healthy subjects, 40 subjects with significant CAD and 20 subjects with non-significant CAD. Basal characteristics of groups were shown in Table 1.

Mitral valve E-wave velocity was significantly lower in patients with significant CAD compared to control group, A-wave was significantly higher in patients with significant CAD than in control subjects and E/A ratio was significantly lower in patients with significant CAD than in control subjects and patients with non-significant CAD.

The IVRT was significantly longer in CAD groups than control group.

- The value of WMA, PSS and PVIVR in detecting segments with any degree of CAD as in Table 2: Sensitivity of WMA was 62%, specificity was 85.4%, positive predictive value was 69.8%, negative predictive value was 84.7%, and overall accuracy was 80.8%.

Sensitivity of PSS was 7.5%, specificity was 96.2%, positive predictive value was 50%, negative
predictive value was 67.5%, and overall accuracy was 66.6%.
Sensitivity of PVIVR was 47.5%, specificity was 86.2%, positive predictive value was 63.3%, negative predictive value was 76.6%, and overall accuracy was 73.3%.
- The value of WMA, PSS and PVIVR in detecting segments with significant CAD as in table 3:
  - Sensitivity of WMA was 68.4%, specificity was 88.8%, positive predictive value was 72.2%, negative predictive value was 83%, and overall accuracy was 79.3%.
  - Sensitivity of PSS was 24.3%, specificity was 92.2%, positive predictive value was 86.6%, negative predictive value was 56% and overall accuracy was 60.3%.
  - Sensitivity of PVIVR was 25.6%, specificity was 86.2%, positive predictive value was 65%, negative predictive value was 53.6%, and overall accuracy was 55.9%.

* We had 60 patients with proximal CAD in our study (40 with proximal significant CAD and 20 with non-significant CAD). We examined 4 basal segments for every patient with TDI, so we examined 240 segments in patients with CAD. Among these segments, 36 segments showed PVIVR, 35 segments showed PSS, and 169 segments showed neither PVIVR nor PSS, as in table 4:
  - Segments with PVIVR showed significantly more incidence of non significant stenosis of supplying coronary artery (21 segments; 58.3%) than in PSS segments (3 segments; 8.6%) and in normal segments (3 segments; 1.8%), p < 0.01.
  - Segments with PSS showed significantly more incidence of significant stenosis of supplying coronary artery (25 segments; 71.4%) than in PVIVR segments (9 segments; 25%) and in normal segments (45 segments; 26.6%), p < 0.01.

**Table 1: Basal characteristics of groups:**

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 40)</th>
<th>Significant CAD (n = 40)</th>
<th>Non-Sign CAD (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (ys)</td>
<td>51.48±12.08</td>
<td>55.8±6.6</td>
<td>52±7.4</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>18/22</td>
<td>28/12</td>
<td>10/10</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0</td>
<td>18(**)</td>
<td>10(**)</td>
</tr>
<tr>
<td>DM</td>
<td>0</td>
<td>5(**)</td>
<td>3(**)</td>
</tr>
<tr>
<td>Smoking</td>
<td>0</td>
<td>14(**)</td>
<td>6(**)</td>
</tr>
<tr>
<td>Family History</td>
<td>0</td>
<td>4(**)</td>
<td>3(**)</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>77±11.2</td>
<td>80.1±17.8</td>
<td>86±7.8</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>117±12.4</td>
<td>122±16.9</td>
<td>125±13.3</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>79±9.5</td>
<td>80±10.3</td>
<td>82±8.9</td>
</tr>
<tr>
<td>E-wave (cm/s)</td>
<td>81.9±24.6</td>
<td>69.3±22.1 (*)</td>
<td>74.3±22.1</td>
</tr>
<tr>
<td>A-wave (cm/s)</td>
<td>62.2±1.2</td>
<td>72.75±20.5(*)</td>
<td>61.1±15.6</td>
</tr>
<tr>
<td>E/A Ratio</td>
<td>1.29±0.36</td>
<td>0.9±0.11 (*)</td>
<td>1.21±0.34 ($)</td>
</tr>
<tr>
<td>IVRT (ms)</td>
<td>57.95±1.08</td>
<td>83.5±0.825 (*)</td>
<td>81±1.25 (**)</td>
</tr>
<tr>
<td>WMA</td>
<td>1±0</td>
<td>1.34±0.19 (**)</td>
<td>1±0 (**)</td>
</tr>
<tr>
<td>Lateral segments: Ve (cm/s)</td>
<td>14.2±4.5</td>
<td>11.4±3.6 (*)</td>
<td>11.7±3.8 (*)</td>
</tr>
<tr>
<td>Va (cm/s)</td>
<td>10.2±4.6</td>
<td>10.8±4</td>
<td>14.2±2.9 (*)</td>
</tr>
<tr>
<td>Ve/Va</td>
<td>1.6±0.3</td>
<td>1.2±0.5 (*)</td>
<td>0.8±0.7 (*)</td>
</tr>
<tr>
<td>PSS</td>
<td>1 (2.5%)</td>
<td>8 (20%) (*)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>PVIVR</td>
<td>4 (10%)</td>
<td>6 (15%) (*)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Septal segments: Ve (cm/s)</td>
<td>11.5±4.1</td>
<td>9.7±3.2 (*)</td>
<td>10.4±3.3</td>
</tr>
<tr>
<td>Va (cm/s)</td>
<td>10.6±4.2</td>
<td>11.5±5</td>
<td>12.5±3.3</td>
</tr>
<tr>
<td>Ve/Va</td>
<td>1.2±0.7</td>
<td>0.9±0.3 (*)</td>
<td>0.9±0.4 (*)</td>
</tr>
</tbody>
</table>
Coronary artery disease and

PSS 2 (5 %) 6 (15 %) 2 (10 %)
PVI 2 (5 %) 5 (12.5 %) 5 (25 %)

Anterior segments:
Ve (cm/s) 13.3±3.6 10.3±3.5 (*) 10.3±3.5 (*)
Va (cm/s) 10.6±4.4 12.6±4.7 (*) 13.8±2.6 (*)
Ve/Va 1.4±0.6 0.8±0.3 (*) 0.9±0.4 (*)
PSS 3 (7.5 %) 8 (20 %) 0 (*$)
PVI 1 (2.5 %) 4 (10 %) 4 (20 %)

Inferior segments:
Ve (cm/s) 13.1±4.7 10.6±3.3 11.2±3.3
Va (cm/s) 10.6±4.2 11.6±3.9 14.2±1.9 ($)$
Ve/Va 1.4±0.7 1±0.8 0.8±0.3 (*)
PSS 0 7 (17.5 %) 2 (10 %)
PVI 1 (2.5 %) 7 (17.5 %) (*) 2 (10 %)

HR; heart rate, SBP; systolic blood pressure, DBP; diastolic blood pressure, DM: diabetes mellitus, A: peak late diastolic flow; E: peak early diastolic flow; IVRT: the Isovolumic Relaxation Time. WMA; Wall motion abnormalities. Va: peak myocardial velocity during left atrial contraction; Ve: peak myocardial velocity during early diastole; PSS; post systolic shortening. PVI; peak velocity lying in the IVR period. Values are mean ± SD. * = p < 0.05 vs control, ** = p < 0.001 vs control, $ = p < 0.05 vs sig, CAD, $$ = p < 0.01 vs sig, CAD.

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>WMA</td>
<td>62 %</td>
<td>85.4 %</td>
<td>69.8 %</td>
<td>84.7 %</td>
</tr>
<tr>
<td>PSS</td>
<td>7.5 %</td>
<td>96.2 %</td>
<td>50 %</td>
<td>67.5 %</td>
</tr>
<tr>
<td>PVI</td>
<td>47.5 %</td>
<td>86.2 %</td>
<td>63.3 %</td>
<td>76.6 %</td>
</tr>
</tbody>
</table>

PPV = positive predictive value, NPV = negative predictive value.

Table 3: Value of WMA, PSS, and PVI in detecting segments with significant CAD.

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>WMA</td>
<td>68.4 %</td>
<td>88.8 %</td>
<td>72.2 %</td>
<td>83 %</td>
</tr>
<tr>
<td>PSS</td>
<td>24.3 %</td>
<td>92.2 %</td>
<td>86.6 %</td>
<td>56 %</td>
</tr>
<tr>
<td>PVI</td>
<td>25.6 %</td>
<td>86.2 %</td>
<td>65 %</td>
<td>53.6 %</td>
</tr>
</tbody>
</table>

Table 4: Comparison between PVI, PSS, and normal segments in CAD patients.

<table>
<thead>
<tr>
<th></th>
<th>PVI (n = 36)</th>
<th>PSS (n = 35)</th>
<th>Normal segments (n = 169)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Significant CAD</td>
<td>21 (58.3 %)</td>
<td>3 (8.6 %) (**)</td>
<td>3 (1.8 %) (**$)</td>
</tr>
<tr>
<td>Significant CAD</td>
<td>9 (25 %)</td>
<td>25 (71.4 %) (**)</td>
<td>45 (26.6 %) (****$)</td>
</tr>
</tbody>
</table>

* = p < 0.05 vs PVI, ** = p < 0.01 vs PVI, $ = p < 0.05 vs PSS, $ = p < 0.01 vs PSS.

DISCUSSION

In the present study, we used the resting tissue Doppler imaging for prediction of significant coronary artery lesion depending on the presence of abnormal velocities in the IVR period. Previous studies were done on open hearts of dogs, dobutamine stress tissue Doppler imaging or using strain rate imaging. In agreement with Edvardsen et al. we detected that the IVRT was longer in patients with sig. CAD.

We found that WMA increased in sig. CAD patients, Nakajima et al. stated that WMA has sensitivity (68%), but lower specificity (70%) in detecting non-obstructive CAD in the resting echocardiogram this may be due to...
detection of the relation between presence of the PSS or the PVIVR in the IVR period by resting tissue Doppler imaging and the presence of significant CAD. This limits the generalizability of our findings, because patients with these characteristics represent a substantial number of those referred for further evaluation because of suspected CAD in every day practice.

We advice to use the strain rate imaging and speckle tracking imaging to study the 16 myocardial segments to evaluate patients with distal significant CAD.

**Authors’ contribution:** Drafting article, Critical revision of article and Data collection by Tarek Abd El-Aziz and Ibtesam I El-Dosouky. Statistics and concept / design were by Tarek Abd El-Aziz and Mohammad M Al-Daydamony. All authors contribute in Data analysis/interpretation and article approval.

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**REFERENCE**


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