Background
Coronary artery disease (CAD) risk factors

- Hypertension
- Insulin resistance/diabetes
- Dyslipidemia
- Smoking/Obesity
- Male gender/Old age

Atherosclerosis

Arterial stiffness precedes atherosclerosis development

Arterial stiffness as a surrogate end point for CAD

Framingham Heart Study
Artery stiffness estimated by 2D speckle tracking technique

**Current clinical issue**

- Development of accurate, simple and non invasive method
- Early diagnosis of arteriosclerosis in individuals without symptoms of overt atherosclerotic disease

< 2D speckle tracking technique as a new diagnostic method>

- Estimate vascular tissue motion and deformation
- Strain and strain rate to be a useful parameter of arterial stiffness

### Arterial stiffness by 2D speckle tracking technique

- Simple
- Non invasive
- Angle independent
- In expensive
- Pressure dependent
Beta stiffness index (BSI) as a pressure independent arterial stiffness parameter

**Beta stiffness index**
- Correction for the ratio of systolic and diastolic pressures
- Changes in arterial diameter during the cardiac cycle
- Good correlation with arterial stiffness


**Arterial distensibility derived BSI**
\[
\text{BSI} = \ln \left( \frac{\text{SBP} - \text{DBP}}{\frac{\text{Ds} - \text{Dd}}{\text{Ds}}} \right)
\]

SBP: systolic blood pressure
DBP: diastolic blood pressure
Ds: systolic diameter of CCA
Dd: diastolic diameter of CCA

**Strain derived BSI**
\[
\text{BSI} = \ln \left( \frac{\text{SBP}}{\text{DBP}} \right)
\]

- Peak strain(%)

Aim of study

• To explore usefulness of common carotid artery (CCA) strain derived \textit{beta stiffness index} for the prediction of concurrent coronary artery disease in comparison with stiffness index derived from CCA distensibility, and conventional arterial stiffness parameters such as pulse wave velocity (PWV) and carotid intima-media thickness (IMT).
Method
Total n=101 (age = 59±10yrs)
Coronary angiography in Inha university hospital

Obstructive coronary artery disease (CAD) -> stenosis of more than 50% in at least one major epicardial coronary artery

- 9 patients were excluded: 7pts due to ABI<0.9
- 2 pts due to poor echo window

CAD (N=46)

non-CAD (N=46)

Exclusion criteria:
- Previous PCI, STEMI & Non-STEMI
- Atrial fibrillation, Poor window for 2DE of CCA
- ABI <0.9
Echocardiographic baseline data

**Systolic function**
- LVEF
- LV end systolic volume
- LV end diastolic volume
  - *by biplane simpson’s method*

**Diastolic function**
- Left atrium size
  - *AP diameter on parasternal short axis view*
- E/A ratio
  - *by dividing mitral flow early diastolic velocity with mitral flow late diastolic velocity*
- E/E’ ratio
  - *by dividing mitral flow early diastolic velocity with mitral septal annular peak diastolic tissue velocity*

*Vivid 7, GE Vingmed Ultrasound*
Brachial-ankle pulse wave velocity & Carotid intima-media thickness

**Brachial-ankle pulse wave velocity**
- Automated waveform analyzer
- PWV = Distance / Transit time
- Mean baPWV

**Carotid intima-media thickness (IMT)**
- 13 MHz probe
- Longitudinal axis image of Lt. CCA
- Semi-automated technique
- Far wall of Lt. CCA at 1.5cm from carotid bulb

**VP 1000, Colin Waveform analyzer**

**Vivid 7, GE Vingmed Ultrasound**
Stiffness Index Beta 1 (BSI 1) as distensibility parameter of common carotid artery

**Vivid 7, GE Vingmed Ultrasound**

**CCA distensibility by M-mode**
- 2D longitudinal axis cine loop of Lt. CCA
- Peak systolic & diastolic inner diameter
- Brachial artery systolic and diastolic pressure

**B stiffness index 1 (BSI 1)**

\[
BSI\ 1 = \frac{\ln(SBP) - \ln(DBP)}{Ds-Dd} / Ds
\]

SBP: systolic blood pressure
DBP: diastolic blood pressure
Ds: systolic diameter of CCA
Dd: diastolic diameter of CCA
Measurement of strain & strain rate of common carotid artery by 2D speckle tracking technique

**Vivid 7, GE Vingmed Ultrasound, Echopac 7.0.0 software**

### Measurements of strain and strain rate
- 2D short axis cine loops of Lt. CCA with a 13MHz linear transducer
- At least three consecutive heartbeats with average frame rate of 76 frames/second
- Offline analysis using 2D strain software
- Region of interest (ROI) on cross-sectional area of the CCA wall
- Global & posterior wall (far wall)

### Circumferential strain & strain rate
- Global
- Posterior (far wall)

### Radial strain & strain rate
- Posterior (far wall)
Stiffness Index Beta 2 (BSI 2)
estimated by strain variables of common carotid artery

\[
\text{BSI 2} = \ln \left( \frac{\text{SBP}}{\text{DBP}} \right) \frac{\text{Peak strain(\%)} - 100}{100}
\]

SBP: systolic blood pressure
DBP: diastolic blood pressure

**BSI 2 calculated by**
- Global circumferential strain
- Posterior circumferential strain
- Posterior radial strain

**Inter & intra-observer variability**
- By analysis of 20 random patients
- Using a coefficients of variation (CV)
Result
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>CAD (n=46)</th>
<th>Non-CAD (n=46)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yr)</strong></td>
<td>61.9 (10.8)</td>
<td>56.3 (8.6)</td>
<td>p=0.007</td>
</tr>
<tr>
<td><strong>DM n(%)</strong></td>
<td>16 (34)</td>
<td>5 (10)</td>
<td>p=0.006</td>
</tr>
<tr>
<td><strong>Hypertension n(%)</strong></td>
<td>29 (63)</td>
<td>28 (60)</td>
<td>p=0.83</td>
</tr>
<tr>
<td><strong>Hyperlipidemia n(%)</strong></td>
<td>15 (32)</td>
<td>5 (10)</td>
<td>p=0.01</td>
</tr>
<tr>
<td><strong>Stroke n(%)</strong></td>
<td>4 (8)</td>
<td>0 (0)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td><strong>Smoking n(%)</strong></td>
<td>17 (37)</td>
<td>9 (20)</td>
<td>0.064</td>
</tr>
<tr>
<td><strong>BMI (kg/m^2)</strong></td>
<td>24.5 (2.7)</td>
<td>25.4 (2.9)</td>
<td>p=0.129</td>
</tr>
<tr>
<td><strong>EF(%)</strong></td>
<td>62 (5.5)</td>
<td>67 (4.7)</td>
<td>p=0.16</td>
</tr>
<tr>
<td><strong>LVEDV (ml)</strong></td>
<td>103 (20)</td>
<td>104 (19)</td>
<td>p=0.8</td>
</tr>
<tr>
<td><strong>LVESV (ml)</strong></td>
<td>38 (9.05)</td>
<td>36 (8.4)</td>
<td>p=0.053</td>
</tr>
<tr>
<td><strong>LA dimension (mm)</strong></td>
<td>3.6 (0.46)</td>
<td>3.6 (0.38)</td>
<td>p=0.8</td>
</tr>
<tr>
<td><strong>E/A</strong></td>
<td>1.2 (0.4)</td>
<td>1.4 (0.5)</td>
<td>p=0.6</td>
</tr>
<tr>
<td><strong>E/E’</strong></td>
<td>10 (3.26)</td>
<td>9.6 (2.4)</td>
<td>p=0.19</td>
</tr>
</tbody>
</table>

CAD, coronary artery disease; DM, diabetes mellitus; BMI, body mass index; TG, triglyceride; LDL, low density lipoprotein; HDL, high density lipoprotein; EF, ejection fraction; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end systolic volume; E/E’, the ratio of mitral flow peak early diastolic velocity (E) and mitral annular early diastolic tissue velocity (E’).
Strain & strain rate variables of common carotid artery between two groups

<table>
<thead>
<tr>
<th>Measured variables</th>
<th>CAD (n=46)</th>
<th>Non- CAD (n=46)</th>
<th>p- value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Circumferential variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global strain (%)</td>
<td>3.11 (1.26)</td>
<td>3.56 (1.13)</td>
<td>p=0.074</td>
</tr>
<tr>
<td>Global early strain rate (1/s)</td>
<td>0.44 (0.17)</td>
<td>0.47 (0.27)</td>
<td>p=0.52</td>
</tr>
<tr>
<td>Global late strain rate (1/s)</td>
<td>-0.18 (0.07)</td>
<td>-0.02 (0.17)</td>
<td>p=0.34</td>
</tr>
<tr>
<td>Posterior strain (%)</td>
<td>6.47 (2.91)</td>
<td>8.83 (3.22)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Posterior early strain rate (1/s)</td>
<td>0.77 (0.30)</td>
<td>1.04 (0.39)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Posterior late strain rate (1/s)</td>
<td>-0.78 (0.24)</td>
<td>-1.02 (0.78)</td>
<td>p=0.45</td>
</tr>
<tr>
<td><strong>Radial variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior strain (%)</td>
<td>-3.43 (3.22)</td>
<td>-5.76 (5.30)</td>
<td>p=0.012</td>
</tr>
<tr>
<td>Posterior early strain rate (1/s)</td>
<td>-0.78 (0.64)</td>
<td>-1.02 (0.78)</td>
<td>p=0.11</td>
</tr>
<tr>
<td>Posterior late strain rate (1/s)</td>
<td>0.62 (0.34)</td>
<td>0.76 (0.39)</td>
<td>p=0.084</td>
</tr>
</tbody>
</table>

All values as mean with SD; CCA, common carotid artery; CAD, coronary artery disease
The intra and inter observer variability for the measurement of strain and strain rate variables of common carotid artery

<table>
<thead>
<tr>
<th>Measured variables</th>
<th>Intra observer CV(%)</th>
<th>Inter-observer CV(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Circumferential variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global peak strain (%)</td>
<td>12.8</td>
<td>14.2</td>
</tr>
<tr>
<td>Global early strain rate (1/s)</td>
<td>10.4</td>
<td>11.6</td>
</tr>
<tr>
<td>Global late strain rate (1/s)</td>
<td>12.2</td>
<td>13.8</td>
</tr>
<tr>
<td>Posterior peak strain (%)</td>
<td>6.4</td>
<td>8.8</td>
</tr>
<tr>
<td>Posterior early strain rate (1/s)</td>
<td>5.8</td>
<td>6.2</td>
</tr>
<tr>
<td>Posterior late strain rate (1/s)</td>
<td>14.8</td>
<td>17.2</td>
</tr>
<tr>
<td><strong>Radial variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior peak strain (%)</td>
<td>28.5</td>
<td>32.1</td>
</tr>
<tr>
<td>Posterior early strain rate (1/s)</td>
<td>70.8</td>
<td>85.6</td>
</tr>
<tr>
<td>Posterior late strain rate (1/s)</td>
<td>148.5</td>
<td>195.4</td>
</tr>
</tbody>
</table>

CV, coefficient of variation
Carotid IMT, PWV, BSI1 and three kinds of strain derived BSI 2s between two groups

All values as mean with SD; IMT, intima-media thickness; PWV, pulse wave velocity; BSI, beta stiffness index; G cir, global circumferential strain; P cir, posterior circumferential strain; P rad, posterior radial strain
Uni and multivariate regression analysis of IMT, PWV, BSI1 and BSI2s in predicting concurrent CAD

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Carotid IMT</td>
<td>1.65 (1.21-2.24)</td>
<td>0.001</td>
</tr>
<tr>
<td>ba PWV</td>
<td>1.002 (1.001-1.004)</td>
<td>0.006</td>
</tr>
<tr>
<td>BSI 1</td>
<td>1.56 (1.14-2.15)</td>
<td>0.005</td>
</tr>
<tr>
<td>BSI 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global circumferential strain</td>
<td>1.065 (1.002-1.13)</td>
<td>0.04</td>
</tr>
<tr>
<td>Posterior circumferential strain</td>
<td>1.18 (1.05-1.33)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

CI, confidence interval; IMT, intima-media thickness; ba PWV, brachio-ankle pulse wave velocity; BSI, beta stiffness index
Correlations of posterior circumferential strain derived BSI 2 with BSI 1, PWV and IMT

- $r=0.40, p=0.001$
- $r=0.36, p=0.001$
- $r=0.49, p<0.001$
Receiver operating characteristic curves of posterior circumferential strain derived BSI2, BSI 1, PWV and IMT in predicting concurrent CAD

<table>
<thead>
<tr>
<th>Parameters</th>
<th>AUC (95%CI)</th>
<th>Cut off value</th>
<th>Sensitivity(%)</th>
<th>Specificity(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSI 1</td>
<td>0.661 (0.55-0.79)</td>
<td>5.4</td>
<td>65</td>
<td>60</td>
</tr>
<tr>
<td>BSI 2 by posterior circumferential strain</td>
<td>0.70 (0.56-0.81)</td>
<td>7.25</td>
<td>74</td>
<td>61</td>
</tr>
<tr>
<td>ba PWV (m/s)</td>
<td>0.677 (0.56-0.81)</td>
<td>1.51</td>
<td>74</td>
<td>63</td>
</tr>
<tr>
<td>Carotid IMT (mm)</td>
<td>0.73 (0.63-0.83)</td>
<td>0.64</td>
<td>73</td>
<td>60</td>
</tr>
</tbody>
</table>
Among CCA strain derived stiffness indices, only posterior circumferential strain derived stiffness index, BSI 2 was found to be independent determinant of concurrent CAD by multivariate analysis adjusted with age, DM, stroke, hyperlipidemia.

Posterior circumferential strain derived BSI 2 showed significant association with CCA distensibility derived BSI 1 as well as carotid IMT and baPWV.

With ROC curve analysis, area under the curve (AUC) of BSI 2 was found to be comparable to those of BSI 1, carotid IMT and baPWV in predicting concurrent coronary artery disease.
Conclusions

- Posterior circumferential strain derived BSI2 of CCA was found to be comparable to other conventional parameters for arterial stiffness in predicting concurrent coronary artery disease.
Study limitations

- Cross sectional study
- Small population
- Selection bias
Thank you
## Atherosclerosis Vs Arteriosclerosis

<table>
<thead>
<tr>
<th></th>
<th>Atherosclerosis</th>
<th>Arteriosclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anatomic location</strong></td>
<td>focal</td>
<td>diffuse</td>
</tr>
<tr>
<td><strong>Vascular physiology</strong></td>
<td>artheroma</td>
<td>elasticity, stiffness</td>
</tr>
<tr>
<td><strong>Vascular location</strong></td>
<td>Intima</td>
<td>media</td>
</tr>
<tr>
<td><strong>Parameter</strong></td>
<td>carotid IMT</td>
<td>PWV, central BP, augmentation index</td>
</tr>
</tbody>
</table>

*Nichols WW, O’Rourke MF. McDonald’s Blood flow in Arteries*
Novel indicators of arterial stiffness and atherosclerosis

**Pulse wave velocity (PWV)**
- Non-invasive, simple and robust
- Pressure dependent
- Inaccurate results in patients with metabolic syndrome, obesity and peripheral artery disease

**Arterial distensibility**
- Non-invasive, direct measurement of arterial stiffness
- Angle dependent
- Limited precision of diameter measurement

**Carotid intima-media thickness (IMT)**
- Non-invasive, simple
- Depending on the focal atherosclerosis

*Stephane Laurent, Expert consensus document on arterial stiffness, European Heart Journal 2006*