YOUNG INVESTIGATOR AWARD SESSION

Thursday 8 December 2011, 12:45–13:45
Location: Pecs

180 Noninvasive ultrasound molecular imaging of the effect of atorvastatin on vascular inflammation
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Purpose: Non-invasive assessment of changes in vascular inflammatory activity may be of use in managing medical therapy in patients with atherosclerotic disease and for developing new candidate therapies. We hypothesized that molecular imaging of vascular cell adhesion molecule-1 (VCAM-1) expression with contrast enhanced ultrasound (CEU) could be used to assess the effects of HMG-CoA reductase inhibitors on vascular inflammation.

Methods: Mice deficient for the LDL receptor and ApoB-100 editing protein that develop atherosclerosis in a time-dependent fashion were studied. Beginning at 12 weeks of age, mice received 8 weeks of either regular chow (n=10) or chow containing atorvastatin (0.01% wt/wt; n=12). At 20 weeks of age, CEU molecular imaging of the ascending aorta was performed after i.v. injection of VCAM-1-targeted (MBV) and control microbubbles (MBC). High frequency transcranial ultrasound imaging (40MHz) was used for noninvasive assessment of plaque burden by measuring aortic wall thickness. Plasma levels of total cholesterol and LDL-VLDL cholesterol were measured. Histology with Movat’s pentachrome was used to quantify plaque burden. Fluorescence immunohistology and Western blot was used to localize and quantify VCAM-1 expression in the aortic wall.

Results: Atorvastatin treatment lowered plasma LDL+VLDL cholesterol levels by 20% in statin-treated animals vs control animals (189.1mg/dl vs 233 mg/dl, p=0.03). On histology, plaque burden was reduced by 61% in statin treated animals (3.7% of luminal area vs 9.2%, p<0.005). Aortic VCAM-1 expression on Western blot was reduced by 41% (p=0.01) by atorvastatin, which corresponded to less endothelial expression of VCAM-1 on immunohistology. High frequency ultrasound was unable to detect differences in aortic wall thickness between the two animal groups. In contrast, CEU molecular imaging demonstrated selective signal enhancement for MBV in control animals (MBV 2.2 ± 1.1 vs MBC 0.7 ± 0.8, P<0.01), but not in statin-treated animals (MBV 0.8 ± 0.5 vs MBC 1.0 ± 0.6, p=ns; p<0.01 for the effect of statin treatment on MBV signal).

Conclusions: Non-invasive CEU molecular imaging can detect changes in vascular inflammatory phenotype in response to antiatherogenic treatments at a point in time when non-invasive morphologic imaging is unable to detect differences in plaque burden. This technique may be useful in the assessment of treatment effects both in preclinical research as well as in patients.

181 Quantitative assessment of myocardial stiffness using shear wave imaging in normal and hypertrophic isolated rat hearts
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Purpose: Shear wave Imaging (SWI) is a novel ultrasound-based technique for quantitative, local and non-invasive mapping of soft tissues elastic properties. Myocardial stiffness can be measured in real time over the cardiac cycle using SWI, allowing quantification of stiffness variation between systole and diastole. In a recent study on normal isolated rat hearts, we have shown that SWI can be used to provide an index of myocardial contractility [pennot et al. JACC 58, 1 2011:65–72]. The goal of the present study is to evaluate the performance of SWI on hypertrophied isolated rat hearts.

Methods: SWI was performed in normal and hypertrophic Langendorff perfused isolated rat hearts (Heart/body weight ratio: 3.7 ± 0.2 mg/g in sham and 6.1 ± 0.9 mg/g in hypertrophy, n=6 each). Left ventricular hypertrophy was induced at 3 weeks of age (body weight <60 g): the thorax was opened and a stainless steel hemoclip of 0.6 mm ID was placed on the ascending aorta. Age-matched control animals (sham-operated) underwent the same procedure without placement of the clip. Studies were performed 4 months after the surgery. Shear wave was generated and imaged in the anterior wall of the left ventricle using a conventional ultrasonic probe connected to an ultrastar scanner (12,000 frames/s). The local myocardial stiffness was derived from the shear wave velocity every 7.5 ms during one single cardiac cycle.

Results: Myocardial stiffness was measured in all hearts with a good reproducibility all over the cardiac cycle (r<0.05). In normal hearts, the average myocardial stiffness was 2.1 ± 0.8 kPa in diastole and 9.2 ± 1.5 kPa in systole. In hypertrophic hearts, myocardium was found significantly stiffer in diastole (3.8 ± 0.9 kPa, p<0.01, n=6) but not in systole (10.7 ± 2.0 kPa, p=0.17, n=6). Myocardial stiffness was also measured during administration of isoproterenol (10-9, 10-8 and 10-7 M, 5 min each). Systolic myocardial stiffness was found to increase strongly up to 23.4 ± 3.4 kPa in normal hearts whereas no significant change was found for hypertrophic hearts. In contrast, diastolic stiffness did not change in both normal and hypertrophic hearts during isoproterenol stimulation.

Conclusions: Passive and active elastic properties of the myocardium can be investigated locally and quantitatively using SWI. The application of SWI to an hypertrophied heart exhibits a strong increase of stiffness in diastole, which can be interpreted as reflecting underlying fibrosis within the myocardium. The failure of hypertrophied heart to increase its contractility under an isotropic stimulation is also highlighted by SWI when performed in systole.

182 Accuracy of real-time single and multi beat 3D speckle tracking echocardiography in vitro
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Aim: To test the agreement between strain measurements with 3D echocardiography and sonomicrometer in an in vitro setup using a left ventricular phantom.

Methods: A polyvinyl alcohol phantom of the left ventricle was connected to a stepping motor controlled volume pump and submerged in a water container. Using a Vivid E9 scanner and a 4V probe (GE Vingmed Ultrasound, Horten, Norway), 3D ultrasound recordings were acquired at 15 different stroke volumes (10 to 150 ml), all at a heart rate of 100 beats per minute. The phantom was exposed to different levels of mechanical strain: ischemia, systolic, and diastolic. The strain was measured using 3D speckle tracking echocardiography and compared to the reference strain values obtained from the sonomicrometer. Statistical analysis was performed using intraclass correlation coefficients (ICC) and Bland-Altman plots to assess the agreement between the two methods.

3D speckle tracking strain versus sonomicrometer

<table>
<thead>
<tr>
<th>Direction</th>
<th>Mode</th>
<th>FPS</th>
<th>R</th>
<th>Mean Error (%)</th>
<th>1.96 SD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longitudinal</td>
<td>Single</td>
<td>15</td>
<td>0.791</td>
<td>2.16</td>
<td>7.28</td>
</tr>
<tr>
<td></td>
<td>Multi</td>
<td>30</td>
<td>0.978</td>
<td>–0.02</td>
<td>2.45</td>
</tr>
<tr>
<td></td>
<td>Multi</td>
<td>36.6</td>
<td>0.990</td>
<td>0.83</td>
<td>1.54</td>
</tr>
<tr>
<td></td>
<td>Multi</td>
<td>52.3</td>
<td>0.954</td>
<td>2.92</td>
<td>3.86</td>
</tr>
<tr>
<td>Circumferential</td>
<td>Single</td>
<td>13.9</td>
<td>0.169</td>
<td>6.04</td>
<td>11.83</td>
</tr>
<tr>
<td></td>
<td>Multi</td>
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<td>0.965</td>
<td>–1.95</td>
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<tr>
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<td>0.963</td>
<td>–0.78</td>
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<tr>
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<td>Multi</td>
<td>52.3</td>
<td>0.804</td>
<td>3.99</td>
<td>7.43</td>
</tr>
</tbody>
</table>

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rate of 60 beats/min. As a reference method, 8 sonomicrometer crystals were implanted into the phantom, monitoring changes in longitudinal, circumferential and radial lengths. For each situation, single beat as well as several multi beat recordings of 6 cycles were acquired at several frame rates (FR). 3D strain curves were generated using EchoPac BT11 (GE Vingmed Ultrasound). Peak strain values were compared with sonomicrometry to evaluate the accuracy of 3D speckle tracking strain values for different FR and volumes, using correlation coefficients and Bland-Altman analysis.

**Results:** The table shows the comparison of longitudinal and circumferential strain at different frame rates. Sonomicrometry values, spanning from -1.86 % to -22.15 % in the circumferential direction, correlated well to stroke volume ($r = -0.99$). Multi beat acquisition improved accuracy. Best correlation and smallest limits of agreement ($\pm 1.96SD$) were obtained with a FR of 36.6 frames/sec (FPS).

**Conclusions:** Multi beat gave excellent agreement with sonomicrometer, best agreement were obtained at 36.6 FPS, indicating a possible optimal FR for 3D strain measurement lower than for corresponding 2D strain.