Cardiac CT and MR Techniques to Identify the Vulnerable Patient

Are we out of the Gate yet?

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Serologic Markers of Vulnerability
(Reflecting Metabolic and Immune Disorders)

- Lipids (high LDL, low HDL, abnormal LDL and HDL size density, lipoprotein (a), Lp-PLA)
- Insulin resistance syndrome (e.g. diabetes, hyper triglyceridemia)
- Inflammation (e.g. hsCRP, CD40L, ICAM-1, VCAM-1, P-selectin, etc)
- Markers of lipid-peroxidation (e.g. ox-LDL and ox-HDL)
- Homocysteine
- Pregnancy-associated plasma protein A (PAPP-A)
- Circulating apoptosis marker(s) (e.g., Fas/Fas ligand, not specific to plaque)
- Asymmetric dimethylarginine (ADMA) / dimethylarginine dimethylaminohydrolase (DDAH)
- Circulating nonesterified fatty acids (e.g. NEFA)

Blood Markers of Vulnerability
(Reflecting Hypercoagulability)

- Markers of blood hypercoagulability (e.g., fibrinogen, D-dimer, and factor V Leiden)
- Increased platelet activation and aggregation (e.g., gene polymorphisms of platelet glycoproteins IIb/IIIa, Ia/IIa, and IIb/IX)
  - Increased coagulation factors (e.g., clotting of factors V, VII, VIII, von Willebrand factor, XIII)
- Decreased anticoagulation factors (e.g., proteins S, C, thrombomodulin, and antithrombin III)
- Decreased endogenous fibrinolysis activity (e.g., reduced t-PA, increased PAI-1, certain PAI-1 polymorphisms)
- Other thrombogenic factors (e.g., anticardiolipin antibodies, thrombocytosis, sickle cell disease, polycythemia, diabetes mellitus, hypercholesterolemia, hyperhomocysteinemia)
  - Increased viscosity

Schematic of vulnerable plaque

Coronary Computed Tomography Angiography
Plaque Characterization

Prognostic Value of CTA

Pundziute G et al, JACC 2007; 49:62-70

Duke Prognostic CAD Index

Min JK et al., JACC 2007; 50:1161-1170
Coronary Artery Disease: Perspectives on Imaging

Results of ACIC 2011: Villines T et al. JACC 2011;58:2533-40

Figure 2: Relationship Between Stress Test Results and CCTA

Figure 5: Major Adverse Events Stratified by CAC Score and Stenosis

Villines T et al. JACC 2011;58:2533-40
Cardiac Magnetic Resonance
Perfusion and Angiography

Integrative Computed Tomography Imaging of Ischemic Heart Disease.
Ruzsics, Balazs; MD, PhD
DOI: 10.1097/RTI.0b013e3181dc2a1f

FIGURE 4. Forty-five-year-old male patient with known CAD. SPECT examination as standard functional imaging modality at stress (A) and rest (B) revealed the presence of stress-induced reversible ischemia in the anterolateral wall. First-pass contrast-enhanced MR perfusion images show at stress (C) and rest (D) the reversible ischemia in the anterolateral territory (black arrows) along with a small mainly subendocardial reversible ischemia of the inferior myocardial region (white arrowhead). Adenosine stress second generation DECT using adenosine stress test (E) also delineates a reversible perfusion defect of the corresponding anterolateral (black arrows) and inferior wall (white arrowhead). DECT shows normal perfusion at rest (D, F).
101 symptomatic patients with suspected CAD (62 ± 8.0 years, 67% males) and intermediate/high pre-test probability underwent MDCT, CMR and invasive coronary angiography. Functionally significant CAD was defined by the presence of occlusive/subocclusive stenoses or FFR measurements ≤0.80 in vessels >2mm.

On a patient-based model, the MDCT-IP had a sensitivity, specificity, positive and negative predictive values of 89%, 83%, 80% and 90%, respectively (global accuracy 85%). These results were closely related with those achieved by CMR-Perf: 89%, 88%, 85% and 91%, respectively (global accuracy 88%). When comparing test accuracies using noninferiority analysis, differences greater than 11% in favour of CMR-Perf can be confidently excluded.

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RESULTS In our study, 1,229 consecutive patients were enrolled. The mean follow-up period was 4.2 ± 2.1 years. During this time, 88 primary endpoints occurred. In patients with reversible perfusion deficits, significantly more cardiac deaths (p < 0.0001) and nonfatal myocardial infarctions (p = 0.001) were observed than in the control group. On multivariate analysis, reversible perfusion deficit was the strongest independent predictor for an event, with a 3-fold increased risk. Moreover, the absence of a perfusion deficit was shown to exhibit high negative predictive value.
Images in a 81-Year-Old Male Patient With Multiple Risk Factors
(A) Thin-slab maximum intensity projection image and (B) conventional angiogram show significant stenosis (red arrow) in the proximal portion of the left anterior descending artery.

Images in a 84-Year-Old Male Patient With Chest Pain on Effort
(A) Thin-slab maximum intensity projection image and (B) conventional angiogram show significant stenosis (red arrow) in the proximal portion of the left circumflex artery.
Prognostic Value of Coronary Magnetic Resonance Angiography for Prediction of Cardiac Events in Patients With Suspected Coronary Artery Disease


Kaplan-Meier Event-Free Survival Curves
Curves for (A) severe cardiac events and (B) all cardiac events.

The VP Pyramid

Screening >> Diagnosis >> Treatment

A lot of techniques
A lot of expertise
A lot to remember 😊
Imaging Plaque “Activity”

- FDG for macrophages
- $^{99m}$Tc labeled Annexin 5 for apoptosis
- $^{99m}$Tc labeled MCP-1 for monocytes
- $^{111}$In oxyquinolone for monocytes

### Table 1: Clinical Variables Stratified by Quantiles of SUV

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>1st Quartile (x = 54)</th>
<th>2nd Quartile (x = 54)</th>
<th>3rd Quartile (x = 54)</th>
<th>4th Quartile (x = 54)</th>
<th>p Value</th>
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<tbody>
<tr>
<td>Lipid profile, mg/dl</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Total cholesterol</td>
<td>220 ± 95</td>
<td>209 ± 94</td>
<td>214 ± 90</td>
<td>216 ± 42</td>
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<td>LDL cholesterol</td>
<td>131 ± 29</td>
<td>124 ± 29</td>
<td>127 ± 20</td>
<td>139 ± 19</td>
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<td>HDL cholesterol</td>
<td>64 ± 10</td>
<td>56 ± 13</td>
<td>52 ± 12</td>
<td>48 ± 13</td>
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<td>Triglycerides</td>
<td>108 ± 6</td>
<td>123 ± 7</td>
<td>132 ± 8</td>
<td>192 ± 8</td>
<td>0.141</td>
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<tr>
<td>FPG, mg/dl</td>
<td>109 ± 6</td>
<td>109 ± 6</td>
<td>109 ± 6</td>
<td>109 ± 6</td>
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<td>glucose, mg/dl</td>
<td>1.20 (0.36)</td>
<td>1.30 (0.36)</td>
<td>1.32 (0.36)</td>
<td>1.36 (0.36)</td>
<td>0.005</td>
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<tr>
<td>HbA1c, %</td>
<td>5.4 ± 0.4</td>
<td>5.6 ± 0.3</td>
<td>5.7 ± 0.3</td>
<td>5.8 ± 0.6</td>
<td>0.023</td>
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<td>UACR, mg/mmol</td>
<td>60 ± 25</td>
<td>80 ± 20</td>
<td>84 ± 20</td>
<td>76 ± 24</td>
<td>0.262</td>
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<td>Urine creatinine, mg/dl</td>
<td>5.8 ± 2.3</td>
<td>5.8 ± 2.6</td>
<td>6.0 ± 2.9</td>
<td>6.8 ± 2.6</td>
<td>0.005</td>
</tr>
<tr>
<td>creatinine, mg/dl</td>
<td>0.64 ± 0.03</td>
<td>0.60 ± 0.03</td>
<td>0.60 ± 0.03</td>
<td>0.60 ± 0.03</td>
<td>0.30</td>
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<td>Medications, n (%)</td>
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<tr>
<td>Hypertension</td>
<td>11 (24)</td>
<td>19 (37)</td>
<td>22 (41)</td>
<td>37 (68)</td>
<td>0.001</td>
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<td>Diabetes mellitus</td>
<td>8 (9)</td>
<td>6 (11)</td>
<td>6 (11)</td>
<td>9 (16)</td>
<td>0.097</td>
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<td>Angiography</td>
<td>4 (7)</td>
<td>3 (6)</td>
<td>3 (6)</td>
<td>5 (9)</td>
<td>0.186</td>
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<tr>
<td>Renal</td>
<td>6 (11)</td>
<td>5 (9)</td>
<td>5 (9)</td>
<td>7 (12)</td>
<td>0.086</td>
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<td>Medical history, n (%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cardiovascular disease</td>
<td>4</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td>0.278</td>
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<tr>
<td>Cardiovascular disease</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>0.275</td>
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</table>
PET/CT Imaging of Plaque Inflammation

A

Simvastatin

Diet

PET

Baseline

Post-treatment

Simvastatin

PET

PET/CT

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Conditions and Markers Associated with Myocardial Vulnerability

With atherosclerosis-derived myocardial ischemia as shown by:

**ECG abnormalities:**
- During rest
- During stress test
- Silent ischemia (e.g. ST changes on Holter monitoring)

**Perfusion and viability:**
- PET scan
- SPECT

**Wall motion abnormalities:**
- Dyssynchrony

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FIGURE 1. Contrast-enhanced, retrospectively ECG-gated first generation DSCT study of a 65-year-old patient with prior history of acute coronary syndrome and myocardial infarct. Figures A and D display myocardium in short axis, and Figures B and E display myocardium in long axis. End-systolic cardiac phase (A, B) and end-diastole (D, E) show myocardial thinning of the inferoposterior wall and decreased contraction along with decreased wall thickening (arrows). Blue and purple colors indicate decreased contractility and wall thickening in peak systole; green color indicates normal contractility; and orange and yellow colors indicate excellent wall contractility and thickening. The polar map in panel C shows decreased thickening of the inferior wall (blue color in center). Green color indicates normal wall thickening; red color indicates excellent wall thickening. Wall thickening values are displayed as a 3-dimensional color-coded image in panel F, showing blue color that indicates reduced wall thickening in the inferoposterior territory (arrows). G, Curved multiplanar reformatted view of the right coronary artery delineates an occluded distal stent and the presence of noncalcified plaque proximal to the stent (arrows).
FIGURE 4. Forty-five-year-old male patient with known CAD. SPECT examination as standard functional imaging modality at stress (A) and rest (B) revealed the presence of stress-induced reversible ischemia in the anterolateral wall. First-pass contrast-enhanced MR perfusion images show at stress (C) and rest (D) the reversible ischemia in the anterolateral territory (black arrows) along with a small mainly subendocardial reversible ischemia of the inferior myocardial region (white arrowhead). Adenosine stress second generation DECT using adenosine stress test (E) also delineates a reversible perfusion defect of the corresponding anterolateral (black arrows) and inferior wall (white arrowhead). DECT shows normal perfusion at rest (D, F).
FIGURE 6. Adenosine stress dynamic multidetector computed tomography (d-MDCT) imaging of the mid left ventricle in a canine model of left-anterior descending artery stenosis. Panels A-D demonstrate d-MDCT at 0, 15, 21, and 70 seconds. Note the area of hypoenhancement (arrows) in the anterior myocardial wall as contrast first arrives in the left ventricle (panel B and Panel C). No visually significant differences are noted at the end of imaging (Panel D).
Fusion Studies


EAT Volume Measurement

- A, B – epicardium identified
- C – only within retained
- D - fat identified automatically
- E,F – all but EAT eliminated, Summed over slices

What is Epicardial Adipose Tissue?

- Visceral fat within the pericardial sack
- Juxtaposed with epicardial coronaries
  - No intervening facial planes
- Most prominent in AV/ IV grooves and RV free wall
- Adipocytes predominate
**EAT Volume & CAD**

**Framingham, MDCT**
- EAT correlates with CAC
- VAT correlates with CRFs more closely (though both moderately correlated)


**EAT volume independent predictor of incident CAD in MESA cohort**


**Associated with CAD severity**
- CT-Angiography
- Invasive angiography
- Autopsy

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**EAT Volume & Ischemia on PET/CT**

- No prior studies looking at EAT volume and ischemia
- PET/CT at EUH to rule out ischemia
- No known CAD or CM
- 45/382 had ischemia
  - Divided “mild-mod” (5-14%) or “severe” (>15%) ischemia
- 52 “no ischemia” matched controls chosen
- All had gated CT for CAC score, used for EAT volume
EAT Volume & Ischemia on PET/CT (2)

* EAT volume predicts ischemia MPI when controlled for covariates (CAC, age, sex, BMI).

Janik M et al, J Nucl Cardiol 2010

Obvious Limitations of all this Testing?

- Radiation Exposure
- Over testing
- Cost