The Rapid Progress of Cardiovascular Imaging
Redefining its Role in Biomedical Research and Clinical Practice

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Disclosures

- None
The increasing power of imaging in diagnosis and management of CV disease

- Non-invasive
- High resolution
- Targeted
- Quantitative

**Pericardial disease**

**HCM**

**Amyloidosis**

**PAH**

**Sarcoidosis**

**Vasculitis**

**CAD**
Translational Research – phenotyping of pulmonary and RV remodeling in pulmonary hypertension

Diagnosis and Risk Assessment: atherosclerosis imaging

Clinical risk spectrum

Very Low  |  No testing needed  |  High

Cardiac CT

Invasive Angiography

Exercise ECG

Echo / Nuclear MPI / CMR
Coronary CTA Phenotypes in CAD

- **No CAD**
- **Minimal (1-24%) Stenosis**
- **Mild (25-49%) Stenosis**
- **Moderate (50-69%) Stenosis**
- **Severe (>70%) Stenosis**

Reassurance ➔ Preventive Therapies ➔ Rx; Consider Further Testing

Courtesy of R. Blankstein
Coronary CTA associated with lower annualized incidence of myocardial infarction in stable CAD

Diagnosis and Risk Assessment: atherosclerosis imaging

**NaF**

**FDG**

**FFR\_CT**

Source: Hulten, Blankstein, Di Carli. Curr Prob Cardiol 2016, in press

The absence of obstructive stenosis fails to explain symptoms or risk in many patients with stable chest pain

11,223 patients referred for coronary angiography between 1998–2009

Sources: Jespersen L et al. EHJ 2012;33:734-44; Maddox TM et al JAMA. 2014;312(17):1754-63
51 yo M with CAD, recent STEMI and DES to pLAD in 2/16, HTN, Type 1 DM, diabetic nephropathy s/p renal transplant in 2008, p/w several hours of chest pain and dyspnea.

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Stress</th>
<th>CFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>0.82</td>
<td>1.23</td>
<td>1.50</td>
</tr>
<tr>
<td>LCX</td>
<td>0.83</td>
<td>1.34</td>
<td>1.62</td>
</tr>
<tr>
<td>RCA</td>
<td>0.81</td>
<td>1.13</td>
<td>1.39</td>
</tr>
<tr>
<td>Global LV</td>
<td>0.82</td>
<td>1.23</td>
<td>1.50</td>
</tr>
</tbody>
</table>

Quantitative myocardial blood flow and CFR

LVEF: 62%
ESV: 45 mL

LVEF: 45%
ESV: 74 mL
We can no longer assume that a normal coronary angiogram implies a normal coronary vasculature.

Coronary Arteriogram

Coronary Vasculature

Courtesy of M. Gibson
Microvascular Structural and Functional Abnormalities in Stable CAD Patients with Comorbidities (HTN, Diabetes, CKD)

- Arteriolar remodeling (thickening and obstruction)
- ↓ capillary diameter and density (rarefaction)
- ↑ endothelial swelling and capillary obstruction
- Endothelial dysfunction \( \rightarrow \) impaired vasomotor function

# Functional Assessment of the Coronary Vasculature

<table>
<thead>
<tr>
<th>Technique</th>
<th>Measure</th>
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</thead>
<tbody>
<tr>
<td><strong>Invasive</strong></td>
<td></td>
</tr>
<tr>
<td>• Thermodilution</td>
<td>• Coronary flow (mL/min)</td>
</tr>
<tr>
<td>• Doppler</td>
<td>• Coronary flow velocity (cm/sec)</td>
</tr>
<tr>
<td>• FFR</td>
<td>• Coronary pressure (unit less ratio)</td>
</tr>
<tr>
<td>• TIMI frame count</td>
<td>• Coronary artery flow (frames)</td>
</tr>
<tr>
<td>• Contrast blush</td>
<td>• Myocardial perfusion (discrete grades)</td>
</tr>
<tr>
<td><strong>Non-invasive</strong></td>
<td></td>
</tr>
<tr>
<td>• PET</td>
<td>• Myocardial blood flow (mL/min/g)</td>
</tr>
<tr>
<td>• MRI</td>
<td>• Myocardial blood flow (mL/min/g)</td>
</tr>
<tr>
<td>• Echo</td>
<td>• Coronary flow velocity (cm/sec)</td>
</tr>
<tr>
<td>• CT FFR</td>
<td>• Coronary pressure (unit less ratio)</td>
</tr>
</tbody>
</table>
Coronary Flow Reserve

- Measures *integrated* hemodynamic effects of epicardial CAD, diffuse atherosclerosis and vessel remodeling, and micro-circulatory dysfunction (*endothelial dysfunction, obstruction, and rarefaction*) on myocardial tissue perfusion.

**Coronary blood flow**

\[
\text{CFR} = \frac{\text{MBF}_{\text{peak hyperemia}}}{\text{MBF}_{\text{rest}}} 
\]

**Pressure difference**

**FFR**

\[< 400 \mu m\]

**EPICARDIAL ARTERIES**

\[> 400 \mu m\]

**SMALL ARTERIES**

**Micro-circulatory dysfunction**
High Prevalence of MCD in Males and Females Without Obstructive CAD

N=1,218

Female
n=813

- CFR > 2.0: 54%
- CFR < 2.0: 46%

Male
n=405

- CFR > 2.0: 51%
- CFR < 2.0: 49%

Adjusted Cardiac Mortality by Severity of CFR Impairment

![Graph showing adjusted cardiac mortality by severity of CFR impairment.](image)

- **N= 2,783**
- **CD= 137**

**Lower vs. Upper**
HR 5.6 [2.5-12.4] p<0.0001

**Middle vs. Upper**
HR 3.4 [1.5-7.7] p=0.003

Excess CV Risk in Women Relative to Men is Associated with Severely Impaired CFR, not Obstructive Disease

58 yo male with HTN and diabetes evaluated for atypical chest pain

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<th>Stress</th>
<th>CFR</th>
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<tbody>
<tr>
<td>LAD</td>
<td>0.91</td>
<td>2.1</td>
<td>2.3</td>
</tr>
<tr>
<td>LCX</td>
<td>0.87</td>
<td>1.98</td>
<td>2.2</td>
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<tr>
<td>RCA</td>
<td>0.92</td>
<td>1.87</td>
<td>2.0</td>
</tr>
<tr>
<td>Global LV</td>
<td>0.89</td>
<td>1.98</td>
<td>2.1</td>
</tr>
</tbody>
</table>

Quantitative myocardial blood flow and CFR

63 yo male with HTN, diabetes and high cholesterol evaluated for dyspnea

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<th>CFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD</td>
<td>1.0</td>
<td>1.48</td>
<td>1.48</td>
</tr>
<tr>
<td>LCX</td>
<td>0.94</td>
<td>1.41</td>
<td>1.50</td>
</tr>
<tr>
<td>RCA</td>
<td>0.97</td>
<td>1.39</td>
<td>1.43</td>
</tr>
<tr>
<td>Global LV</td>
<td>0.97</td>
<td>1.42</td>
<td>1.47</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Annualized Cardiac Mortality</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD+/DM+ (N=606)</td>
<td>2.9%</td>
<td>0.07</td>
</tr>
<tr>
<td>CAD+/DM- (N=569)</td>
<td>2.0%</td>
<td>0.33</td>
</tr>
<tr>
<td>CAD-/DM+ CFR ≤1.6 (N=227)</td>
<td>2.8%</td>
<td>0.005</td>
</tr>
<tr>
<td>CAD-/DM+ CFR &gt;1.6 (N=339)</td>
<td>0.3%</td>
<td>0.65</td>
</tr>
<tr>
<td>CAD-/DM- NI MPI/EF (N=682)</td>
<td>0.5%</td>
<td></td>
</tr>
</tbody>
</table>

*Adjusted for Duke score, ischemia + scar, rest LVEF and early revascularization

Coronary Flow Reserve, Revascularization, and Outcomes

Only patients with angiographic obstruction AND low coronary flow reserve seem to benefit from revascularization, especially CABG.

Diagnosis and Risk Assessment: cardiac amyloidosis

Guide Therapy and Predict Benefit – Aortic Stenosis

Treatment Monitoring – Cardiac and Vascular Inflammation

Imaging Markers as Intermediate Endpoints in Clinical Trials

# Incorporating Microvascular Function in Risk Assessment and Management

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Trial</th>
<th>Therapy/biology</th>
<th>PI</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes and CAD</td>
<td>CIRT-CFR</td>
<td>Methotrexate</td>
<td>Di Carli</td>
<td>enrolling</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>LiiRA</td>
<td>TNF inhibitors</td>
<td>Liao</td>
<td>enrolling</td>
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<tr>
<td>ESRD on HD</td>
<td>SpinD</td>
<td>Spironolactone/L-Arginine</td>
<td>Charytan</td>
<td>enrolling</td>
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<tr>
<td>Hyperuricemia</td>
<td>HUMETS</td>
<td>None</td>
<td>Kim/Solomon</td>
<td>enrolling</td>
</tr>
<tr>
<td>HIV</td>
<td>MIRACLE</td>
<td>Eplerenone</td>
<td>Grinspoon/Adler</td>
<td>enrolling</td>
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<tr>
<td>Non-obstructive atherosclerosis</td>
<td>NOCAD-CFR</td>
<td>PCSK9/SGLT 2 inhibitors</td>
<td>Di Carli</td>
<td>pending funding</td>
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<tr>
<td>Obstructive CAD</td>
<td>TRIANGLE</td>
<td>PCI</td>
<td>van de Hoef</td>
<td>pending funding</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>- Piek: EU coordinator</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Di Carli: US coordinator</td>
<td></td>
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<tr>
<td>Women with ANOCA</td>
<td>None</td>
<td>None</td>
<td>Shaw</td>
<td>pending funding</td>
</tr>
</tbody>
</table>
Summary

• We have seen fantastic progress
• But, many challenges and opportunities remain:
  – Enhance focus on last mile of ‘translation highway’ → clinical application
  – Improve access
  – Define effectiveness and value
    • Outcomes research
    • Cost and comparative effectiveness
  – Redefine training in CV imaging
    • Patient-centered, multimodality imaging skills
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