Does Coronary CTA Fail to Live Up to Its PROMISE in Suspected CAD?

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- Consultant – GE Healthcare and Novartis

PRECISION MEDICINE

- PRECISION IN DIAGNOSIS
- PRECISION IN TREATMENT
- SUPERIOR PATIENT OUTCOMES
Background

- Cardiovascular disease is still the number one killer worldwide
- 4 million stress tests performed annually in the United States
- Little consensus about which diagnostic strategy is preferable and the impact on outcome
- Current testing practices raise concerns regarding frequent testing of very low risk populations and high rates of finding no obstructive coronary artery disease in patients undergoing elective catheterization

Promise of CCTA

- Coronary CT angiography (CTA) could reduce unneeded invasive testing and improve outcomes
  - Higher positive and negative predictive accuracy for CAD
  - Ability to detect a broader spectrum of CAD, including prognostically important non-obstructive disease
  - CTA is superior to usual care in 4 RCTs of acute CP patients
- The impact of the information derived from an initial strategy of noninvasive anatomic versus functional test data on subsequent management and clinical outcomes in stable chest pain patients is unknown

CASE 1

- 51 y/o Female / History of Chest pain and syncope 2 months ago / Work up was negative in outside hospital
- Presenting again to the hospital with recurrent CP
- Cardiac Enzymes = normal
- Echocardiogram = EF 70%, Preserved global and regional LV Function
- MIBI scan = EF 65%, No evidence of myocardial ischemia or infarct
- Questionable attenuation to the inferior wall, which normalizes upon repeat imaging in the prone position
CASE 1 – NUCLEAR MPI

CASE 1 – CORONARY CTA

Focal high grade stenosis in the mid RCA = 90%

CASE 1 – CARDIAC CATH

RCA = 95% stenosis  Post-Stent
EVINCI STUDY


ACCURACY

91%  85%  70%  77%  68%

CTA as the Gatekeeper to the Cath Lab

- NCDR data – 661,063 patients (2009 – 2011)
- Rate of obstructive CAD by Cardiac cath – 42%
- Preprocedure noninvasive test – 64% of patients (n=387,633)
- 78% had SPECT/ Only 2% had CTA

<table>
<thead>
<tr>
<th>Table 1 – Findings among patients without history of CAD who had a noninvasive stress test before elective coronary angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-invasive test</td>
</tr>
<tr>
<td>-------------------</td>
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<tr>
<td>Standard exercise test</td>
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<tr>
<td>Stress echocardiogram</td>
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<tr>
<td>Stress testing with BEI-CT</td>
</tr>
<tr>
<td>Stress testing with CMRI</td>
</tr>
</tbody>
</table>

Patel MR et al. AHJ. 2014;167(6):846-852
Cury RC et al. JCCT. 2014 Nov/Dec 2014 President’s Page

ORiGINAL RESEARCH

The Optimal Imaging Strategy for Patients With Stable Chest Pain
A Cost-Effectiveness Analysis


- The strategy that maximized QALYs and was cost-effective, began with CTA, followed by cardiac stress imaging if at least a 50% stenosis was found and ended with ICA if ischemia was demonstrated

- Coronary CTA is a cost-effective triage test for 60-year-old patients who have non-acute chest pain and a low to intermediate probability of CAD

PROMISE Study Hypothesis and Design
PROspective Multicenter Imaging Study for Evaluation of chest pain

- **Hypothesis:** As compared to functional testing, an initial strategy of anatomic testing with CTA would improve the health outcomes of patients with symptoms suspicious for CAD who require further testing

- **Design:** Multicenter, randomized, pragmatic comparative effectiveness trial comparing these two contemporary diagnostic strategies
Randomization and Follow-up
(n=10,003; 193 NA sites; July 2010 – Sept 2013)

Allocation
- Anatomic testing strategy (CTA) (n=4986)
- Functional testing strategy (n=5007)

Follow-up
- Received CTA/CAC as 1st test (n=4885, 94%)
  - Received other test as 1st test (n=154, 3%)
  - No test (n=248, 5%)
- Received functional test as 1st test (n=4692, 94%)
  - Received other test as 1st test (n=154, 3%)
  - No test (n=248, 5%)

12-month follow-up
- Completed 4750 (95%)
- Completed 4600 (92%)
- Received CTA/CAC as 1st test (n=4686, 94%)
- Received other test as 1st test (n=154, 3%)
- No test (n=156, 3%)

Median follow-up: 25 months (IQR 16, 34)
Maximum follow-up: 50 months

Primary Endpoint:
Death, MI, Unstable Angina, Major Complications

CTA: Functional
Hazard Ratio: 1.04
(95% CI: 0.83, 1.29)
P = 0.750

Secondary Endpoint:
Death or Non-fatal MI

CTA: Functional
Hazard Ratio: 0.88
(95% CI: 0.67, 1.15)
P-value: 0.348
PROMISE TRIAL - Secondary Endpoint:
Catheterization Without Obstructive CAD ≤ 90 days

<table>
<thead>
<tr>
<th></th>
<th>CTA (n=4996)</th>
<th>Functional (n=5007)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive catheterization without obstructive CAD — N (%)</td>
<td>170 (3.4)</td>
<td>213 (4.3)</td>
<td>0.022</td>
</tr>
<tr>
<td>Obstructive CAD by cardiac cath</td>
<td>439 (72%)</td>
<td>193 (47.5%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Invasive catheterization</td>
<td>609 (12.2%)</td>
<td>406 (8.1%)</td>
<td></td>
</tr>
<tr>
<td>Revascularization</td>
<td>311 (6.2%)</td>
<td>158 (3.2%)</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>72</td>
<td>38</td>
<td></td>
</tr>
</tbody>
</table>

Secondary Endpoint:
Cumulative Radiation Exposure ≤90 days

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</thead>
<tbody>
<tr>
<td>All patients</td>
<td>12.0 ± 8.5</td>
<td>10.1 ± 9.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No radiation exposure</td>
<td>4%</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>Intended nuclear stress test randomization stratum</td>
<td>12.0 ± 8.4</td>
<td>14.1 ± 7.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intended stress echo randomization stratum</td>
<td>12.6 ± 9.0</td>
<td>1.3 ± 4.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intended exercise ECG randomization stratum</td>
<td>10.4 ± 7.8</td>
<td>2.3 ± 5.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
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Selected Medication and Lifestyle Relative Changes
Baseline vs. Day 60 Visit: CTA vs Functional
Conclusions

- Compared to usual care using a functional testing strategy, use of an initial anatomic testing strategy employing CTA did not improve clinical outcomes in patients with suspected CAD.
- Our results suggest that CTA is a viable alternative to functional testing.
- These real-world results should inform noninvasive testing choices in clinical care as well as provide guidance to future studies of diagnostic strategies in suspected heart disease.

Results from the PROspective Multicenter Imaging Study for Evaluation of chest pain (PROMISE) Trial

Purpose: To compare the medical costs of initial anatomic imaging with coronary CT angiography (CTA) to usual care with functional stress testing in subjects with chest pain.

Trial Design: Prospective, multicenter, open-label, randomized with parallel assignment. Patients presenting with new chest pain randomized to coronary CTA or functional stress testing. N= 10,003. Primary Endpoint: time to first event – composite of major cardiovascular (CV) events Secondary Endpoint: medical costs, resource use, and increase in cost effectiveness.

<table>
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<tr>
<th>Trial Results</th>
<th>Cost at 90 days</th>
<th>Cost at 2 years</th>
<th>Cost Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>$2,034</td>
<td>$2,255</td>
<td>Cost Difference = $279.</td>
</tr>
<tr>
<td>Functional stress testing</td>
<td>$2,255</td>
<td>$2,255</td>
<td>Cost Difference = $0.</td>
</tr>
</tbody>
</table>

Conclusions: the difference in costs for the use of these tests was small and not significant. The use of either approach produced clinical and economic results that were very similar.

SCOT HEART STUDY

Scottish Computed Tomography of the HEART (SCOT-HEART) Trial

Trial Population

Randomization 1:1

- Standard of Care
  - n=2,073
- Standard of Care + CT Coronary Angiogram
  - n=2,073
- Computed Tomography Coronary Angiogram n=3
  - 100% Data for the Primary Endpoint
  - Intention-to-Treat Analysis
- CT Coronary Angiogram n=1,728
  - 3% Completion
  - 97% Target coverage
  - Hospital readmission
- Data for Primary Endpoint n=2,073
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Trial Population.

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SCOT HEART STUDY

Conclusions
In patients presenting with suspected angina due to coronary heart disease, the addition of computed tomography coronary angiography

- Clarifies the diagnosis: 1 in 4
- Increases the diagnosis of CHD but appears to reduce the diagnosis of angina due to CHD
- Alters subsequent investigations: 1 in 6
- Changes treatments: 1 in 4
- Does not affect short-term anginal symptoms
- May increase coronary revascularisation and reduce fatal and non-fatal myocardial infarction

Lubbers M. et al. Eur Heart J. 2016; Jan 7 Epub ahead of print
THE GOAL: IMAGE QUALITY
One Beat/ 16cm/ 280ms/ High-definition/ motion free

80 kV | 500 mA | 61 BPM | 23 BMI | 0.9 mSv
CAD rule out

Revolution CT @ Miami Baptist

THE GOAL: IMAGE QUALITY
One Beat/ 16cm/ 280ms/ High-definition/ motion free

80 kV | 500 mA | 61 BPM | 23 BMI | 0.9 mSv
CAD rule out

Revolution CT @ Miami Baptist

100 kV | 325 mA | 52-90 BPM | 29 BMI | 1.2 mSv
Patient with irregular heart rate

Revolution CT @ Miami Baptist

PRECISION MEDICINE

- PRECISION IN DIAGNOSIS
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Conclusions

1. Large body of evidence supporting CCTA as an effective gatekeeper to the cath lab
2. Three large Randomized Trials (PROMISE, SCOT-HEART and CRESCENT) demonstrating that CCTA is not only a viable alternative to functional imaging, but has the potential to change patient management resulting in reduction in CV death and MI
3. PRECISION MEDICINE starts with PRECISION IN DIAGNOSIS
4. Promising applications of 3D Printing

3D PRINTING

PRECISION IN DIAGNOSIS LEADING TO PRECISION IN TREATMENT AND BETTER PATIENT OUTCOMES
Why 3D models?

- Planning: surgeon does not get complete picture with 2D data
- Informing: patient does not understand condition or surgery without model
- Educating: models for teaching/illustration and procedure simulation
- Sizing/templating: planning the “fit” of prostheses/implants
- Mirroring: giving model of the “good side” for procedure planning
- Dosing: patient-specific dose planning or delivery (rad onc)
- Treating: 3D piece or organ itself may be implanted (the future!)