Chest Pain Evaluation: No Test, Stress Test or CT Angio?

Pamela S Douglas, MD, MACC, FASE, FAHA
Ursula Geller Professor of Research in Cardiovascular Diseases
Duke University
Past President, American College of Cardiology
Past President, American Society of Echocardiography
Chest Pain Evaluation: No Test, Stress Test or CT Angio?

- Many diagnostic choices with no clear ‘best’ strategy
  - Functional testing vs anatomic testing? (SCOT HEART, PROMISE)
  - New technology (FFR_{CT} PLATFORM)
  - Immediate vs deferred testing (no testing)?

- **Evaluation goals:** The optimal strategy will
  - Clarify the diagnosis
  - Provide risk stratification (prognosis)
  - Direct subsequent care
  - Maximize efficiency
  - Optimize clinical outcomes
  - Minimize cost
A Randomized Comparison of Anatomic versus Functional Diagnostic Testing Strategies in Symptomatic Patients with Suspected Coronary Artery Disease

Pamela S. Douglas, Udo Hoffmann, Manesh R. Patel, Daniel Mark, Lawton Cooper, and Kerry Lee

*On behalf of the PROMISE Investigators*

*Duke Clinical Research Institute, Massachusetts General Hospital, and the National Heart, Lung, and Blood Institute*

Supported by R01HL098237, R01HL098236, R01HL98305 and R01HL098235 from the National Heart, Lung, and Blood Institute
Case Presentation

- 61 yo woman with new onset chest pain
- Risk factors: obesity, hypertension, hyperlipidemia, past smoker, sedentary life style
- Symptoms are atypical, occur at rest and with exertion
- 53% likelihood of significant CAD (Diamond-Forrester)
- 17% risk of a cardiac event in next 10 years (Framingham Risk Score)

What more do you need to know about this patient? What would you do next?
1:1 Randomization — 10,000 patients
Stratified by site and intended functional test

**Anatomic strategy**
- 64+ slice CTA

**Functional strategy**
- Exercise ECG or exercise imaging
- Pharmacologic stress imaging

Tests site read; Results immediately available; Subsequent testing/management by site care team, per guidelines

Minimum follow-up 12 months; Mean 25.2 months

1º = Death, MI, complications, UA hospitalization
2º = MACE components, cath w/o CAD; Costs; QOL

Symptoms suspicious for significant CAD
Requiring non-emergent noninvasive testing

PROMISE Trial Design – 10,003 Subjects

NEJM 2015; 372:1291
Primary Endpoint: Death, MI, Unstable Angina, Major Complications

*CTA*: Functional
Hazard Ratio: 1.04
(95% CI: 0.83, 1.29)
P = 0.75

12 Months
HR 0.94; p=0.68

<table>
<thead>
<tr>
<th>Months since randomization</th>
<th>CTA</th>
<th>Functional</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4996</td>
<td>5007</td>
</tr>
<tr>
<td>6 Mo.</td>
<td>4703</td>
<td>4536</td>
</tr>
<tr>
<td>12 Mo.</td>
<td>4362</td>
<td>4115</td>
</tr>
<tr>
<td>18 Mo.</td>
<td>3551</td>
<td>3331</td>
</tr>
<tr>
<td>24 Mo.</td>
<td>2652</td>
<td>2388</td>
</tr>
<tr>
<td>30 Mo.</td>
<td>1705</td>
<td>1518</td>
</tr>
<tr>
<td>36 Mo.</td>
<td>902</td>
<td>832</td>
</tr>
<tr>
<td>42 Mo.</td>
<td>269</td>
<td>258</td>
</tr>
</tbody>
</table>
**Secondary Endpoint:**  
Catheterization Without Obstructive CAD ≤90 days

<table>
<thead>
<tr>
<th>Invasive testing</th>
<th>CTA (n=4996)</th>
<th>Functional (n=5007)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive catheterization</td>
<td>609 (12.2%)</td>
<td>406 (8.1%)</td>
<td></td>
</tr>
<tr>
<td>With obstructive CAD (% of caths)</td>
<td>439 (72.1%)</td>
<td>193 (47.5%)</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>
<tr>
<td>Invasive catheterization without obstructive CAD — N (%)</td>
<td>170 (3.4%)</td>
<td>213 (4.3%)</td>
<td>0.022</td>
</tr>
</tbody>
</table>

NEJM 2015 372:1291
Test Results, Events and Prognostic Value

CTA Test Positivity Rate: 11.9%
Stress Test Positivity Rate: 12.7%

CTA Event Rate by Test Result:
- Test +: HR 3.74
- Test -: HR 3.47

Stress Event Rate by Test Result:
- Test +: HR 3.74
- Test -: HR 3.47

% Events in Test Category:
- CTA: 64%
- Stress: 64%

CTA Stenosis

Event rate:
- ≥ 50%: 9.2%
- 1-49%: 3.0%
- 0%: 0.9%
Summary

- PROMISE enrolled a symptomatic, intermediate likelihood population for whom noninvasive testing is currently recommended.
- There were no significant differences in outcomes between an initial anatomic (CTA) or functional testing strategy with respect to the primary endpoint overall or in any subgroup.
- However, an initial CTA strategy was associated with:
  - Lower rate of ICA without obstructive CAD
  - Lower radiation exposure than in nuclear testing
  - More favorable changes in preventive medications
  - Better risk reclassification and higher prognostic value
  - No difference in costs or QOL
SCOT-HEART Trial: Major Results

- 4146 pts with stable CP; Randomized after initial evaluation (including Ex ECG) to usual care or added CTA
- 42% had obstructive CAD by CTA (vs 12% in PROMISE)
- Endpoints: MD assessments for angina and CAD
  - Certainty: Yes/No versus Probable/Unlikely
  - Frequency: Yes/Probable versus Unlikely/No

### Primary: Diagnosis of angina due to CHD?

<table>
<thead>
<tr>
<th>Certainty</th>
<th>Frequency</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes/No</td>
<td></td>
<td>1.79 [1.62-1.96]</td>
</tr>
<tr>
<td>Probable/Unlikely</td>
<td></td>
<td>0.93 [0.85-1.02]</td>
</tr>
</tbody>
</table>

### Secondary: Diagnosis of coronary heart?

<table>
<thead>
<tr>
<th>Certainty</th>
<th>Frequency</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes/No</td>
<td></td>
<td>2.56 [2.33-2.79]</td>
</tr>
<tr>
<td>Probable/Unlikely</td>
<td></td>
<td>1.09 [1.02-1.17]</td>
</tr>
</tbody>
</table>

Lancet 2015; 385:2383
Secondary Endpoints: Clinical Outcome

**CHD Death/Non-Fatal MI**

- **Event rate (%)**
  - CTCA: Event rates are lower compared to Standard Care over the follow-up periods.
  - **HR 0.62 [0.38-1.01] P=0.053**

- **Secondary Endpoints: Clinical Outcome**
  - CHD Death/Non-Fatal MI

- **Follow Up (years)**
  - CTCA: Improved outcomes with lower event rates.

- **50% reduction in events after delay**
- **CTA costs $1900 vs 1438 (Δ 462); p< 0.001**

**References**

Lancet 2015; 385:2383

JACC 2016; 67:1759
**PLATFORM Primary Endpoint**

**Invasive Catheterization w/o Obstructive CAD**

- **Design:** Stable pts with planned ICA; Usual care vs CTA/FFR<sub>CT</sub> guided care
- **Study Flow:** CTA/FFR<sub>CT</sub> →60% of ICAs cancelled; 2x ↑ availability of functional data at PCI/CABG
- **Results:** Rate of finding no obstructive CAD at ICA was lower with FFR<sub>CT</sub> at 12% vs. 73% w usual care
  - Similar results in all subgroups
  - No differences in MACE, radiation or revasc
  - Costs > 30% lower with CTA/FFR<sub>CT</sub>
  - Similar pt reported outcomes

**Graph:**

- Planned ICA
- Usual Care: N (%): 137 (73.3) vs. FFRCT 24 (12.4)
- P < 0.0001

*JACC 2016;68:435*
Patients with suspected CAD

Usual Care Cohort

Invasive coronary angiography (ICA)

No need for ICA

CTA/FFR<sub>CT</sub>-Guided Cohort

Invasive coronary angiography (ICA)

No need for ICA

Douglas et al, EHJ 2015; doi:10.1093/eurheartj/ehv444
1.3.4 Diagnostic testing for people in whom stable angina cannot be excluded by clinical assessment alone

1.3.4.3 Offer 64-slice (or above) CT coronary angiography if:

- clinical assessment indicates typical or atypical angina or
- clinical assessment indicates non-anginal chest pain but 12-lead resting ECG has been done and indicates ST-T changes or Q waves. [new 2016]

1.3.4.4 For people with confirmed CAD (for example, previous MI, revascularisation, previous angiography), offer non-invasive functional testing when there is uncertainty about whether chest pain is caused by myocardial ischaemia. An exercise ECG may be used instead of functional imaging. [2010]

https://www.nice.org.uk/guidance/CG95/
Immediate vs Delayed Testing (No Test)?

- **In favor** of a ‘watchful waiting’ strategy
  - Very low annual event rates in recent trials (1-2%/yr)
  - Excellent preventive and anti-anginal therapeutics
  - Similar outcomes with revascularization vs med Rx (eg COURAGE)

- **Against** a ‘watchful waiting’ strategy
  - ACC/AHA GL recommend testing for non-acute chest pain (Class I A)
  - Risk assessment tools are outdated
  - Not testing may miss LM/3VD for whom revascularization is lifesaving
  - Not testing may require multiple visits/medication changes
  - Patient/Provider preferences for action/answers; Physician liability
  - No supporting prospective data: A ‘deferred testing’ strategy has not been evaluated even in an observational setting for outcomes or costs
Temporal Use of Stress Testing Post PCI by Quartile of Overall Use Intensity

- NCDR Cath-PCI + Medicare; 656 sites
- 15 mo post PCI test performed in 32%
- Hospital use ranged 9-66% of patients
- Surveillance vs symptom driven testing
Chest Pain Evaluation: No Test, Stress Test or CT Angio?

- In current US care, stable chest pain patients evaluated for suspected CAD using noninvasive testing, rarely has obstructive CAD, and has a very low event rate.
- Impact of test choice on outcomes varies by CAD prevalence.
- Deferred testing is an appealing but untested strategy.
- CTA has several advantages over stress testing making it a viable alternative to functional testing, and, given these new trial data, is a reasonable strategy to consider alongside functional testing as a first line choice.