ORBITA trial
“Objective Randomised Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina”

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• This trial suggests that in patients with stable angina and significant single vessel disease (PCI) may not increase exercise time, compared to placebo.
• However, PCI significantly reduced ischemia as assessed by FFR, iFR and stress echo.
• This is the first placebo-controlled randomized trial of PCI in this patient population.
Introduction

• Percutaneous coronary intervention (PCI) is commonly utilized for stable angina, with the aim of reducing events (such as myocardial infarction and death) and reducing symptoms.

• The previous COURAGE trial (2007) randomized patients with stable angina to either PCI or medical therapy and found no difference with regard to myocardial infarction and death.

• There was a suggestion that patients who received (unblinded) PCI were more likely to be free of angina with a higher quality of life at 6 months, although this benefit was no longer statistically significant 36 months.

• Meta-analyses including COURAGE and other similar trials have also failed to demonstrate a clear benefit to PCI in patients with stable angina.
As a result of these findings, current consensus guidelines recommend medical therapy as first-line for treatment of stable angina, but continue to support the use of PCI in patients with obstructive coronary disease who remain symptomatic despite medical therapy.
**ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 Appropriate Use Criteria for Coronary Revascularization in Patients With Stable Ischemic Heart Disease**

### Table 1: Revascularization to Improve Survival Compared With Medical Therapy

<table>
<thead>
<tr>
<th>3-vessel disease with or without proximal LAD artery disease*</th>
<th>CABG</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PCI</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>With complex 3-vessel LAD (eg., SYNTAX score ≥22) who are good candidates for CABG</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2-vessel disease with proximal LAD artery disease*</th>
<th>CABG</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PCI</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>With extensive ischemia</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PCI</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>With extensive ischemia without extensive ischemic</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1-vessel proximal LAD artery disease</th>
<th>CABG</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PCI</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>With LAD for long-term benefit</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PCI</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

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### Table 1.1: One-Vessel Disease

<table>
<thead>
<tr>
<th>One-Vessel Disease</th>
<th>Asymptomatic</th>
<th>Ischemic Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Proximal LAD or Proximal Left Dominant LAD Involvement</td>
<td>CABG</td>
<td>PCI</td>
</tr>
<tr>
<td>1. Low-risk findings on noninvasive testing</td>
<td>M (0)</td>
<td>M (0)</td>
</tr>
<tr>
<td>2. Intermediate- or high-risk findings on noninvasive testing</td>
<td>M (1)</td>
<td>M (0)</td>
</tr>
<tr>
<td>3. No stress test performed or, if performed, results are indeterminate</td>
<td>M (2)</td>
<td>M (0)</td>
</tr>
<tr>
<td>4. With LAD for long-term benefit</td>
<td>M (3)</td>
<td>M (0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Proximal LAD Proximal Left Dominant LAD Involvement Present</th>
<th>CABG</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Low-risk findings on noninvasive testing</td>
<td>M (4)</td>
<td>M (0)</td>
</tr>
<tr>
<td>5. Intermediate- or high-risk findings on noninvasive testing</td>
<td>M (5)</td>
<td>M (0)</td>
</tr>
<tr>
<td>6. No stress test performed or, if performed, results are indeterminate</td>
<td>M (6)</td>
<td>M (0)</td>
</tr>
</tbody>
</table>

*On 1 AA Drug (BB Preferred) vs. On 2 AA Drugs
• The previous trials have not blinded patients to treatment allocation, raising the question of whether symptomatic improvement is mediated by the placebo effect.

• A placebo-controlled randomized trial of PCI in stable angina was needed to test for an effect beyond any placebo element.

**Clinical Question**

• In patients with stable angina despite medical therapy and single-vessel disease, does PCI improve angina as measured by treadmill exercise time compared to placebo procedure?
**Design**

- Multicenter
- Double-blinded (neither patients nor their physicians knew which group they were assigned)
- Randomized trial
- N = 200
  - Angiography-guided PCI (n=105)
  - Sham PCI (n=95)
  (coronary angiography and iFR/FFR measurement but no stent placement)
- Enrollment: 2013-2017
- Duration of follow-up: 6 weeks
- Primary Outcome: Difference in treadmill exercise time increment (s)

**Population**

**Inclusion Criteria**

- Aged 18-85
- Both of:
  - Angina or equivalent symptoms
  - At least one angiographically significant (≥70%) lesion in a single vessel that is appropriate for PCI
Exclusion Criteria

- Angiographic stenosis ≥50% in a non-target vessel
- Acute coronary syndrome
- Previous CABG
- Left main disease
- Contraindication to drug eluting stent
- Chronic total occlusion
- Severe valvular disease
- Severe left ventricular systolic dysfunction
- Moderate or greater pulmonary hypertension
- Life expectancy <2 years
- Inability to provide informed consent

Baseline Characteristics

*From all groups.*

- Demographics: Age 66 years, male 73%
- Comorbidities: BMI 28.7, smoker 13%, HTN 69%, Dyslipidemia 72%, DM 18%, previous MI 6%, previous PCI 13%
- Cardiac: Normal LV function 92%
- Angina: CCS I 3%, CCS II 59%, CCS III 39%
- Angina duration: 12.5 months
- Angiographic: LAD culprit 69%, RCA culprit 16%, LCx culprit 10%, QCA area stenosis 84.4%, FFR 0.69, iFR 0.76
Interventions

• Patients randomized 1:1 to PCI or sham PCI
• Patients were approached after diagnostic angiography and enrolled after giving informed consent
• Patients allocated to PCI underwent stenting of all lesions deemed angiographically significant

• In the placebo group, patients were kept sedated for at least 15 minutes on the table and the coronary catheters were withdrawn with no intervention performed

• After enrollment, the study consisted of two consecutive phases
  – Phase 1: 6-week medical optimization phase focused on initiation and uptitration of guideline-directed medical therapy
  – Baseline prerandomization assessment
  – Phase 2: 6-week post-randomization blinded period
• Medical optimization was focused on antianginal therapy, with goal of at least two antianginal medications per patient

• All patients underwent cardiopulmonary exercise testing, symptom questionnaires, and dobutamine stress echocardiography before and six weeks after the procedure.

• All patients were pretreated with dual antiplatelet therapy and were continued until the last assessment visit

• Coronary angiography was performed via a radial or femoral arterial approach with auditory isolation achieved using headphones

• After follow-up assessment, patients were unblinded and given the opportunity to undergo PCI after consultation with their physician
**Primary Outcome**

*Comparisons are PCI vs. sham PCI*

- Change in treadmill exercise time (s):
  
  28.4 (95% CI 11.6 to 45.1) vs. 11.8 (95% CI -7.8 to 31.3), difference 16.6 (95% CI -8.9 to 42.0), $p=0.20$
Secondary Outcomes

• **Peak stress wall motion index score (DSE):**
  Patients randomized to PCI showed significant improvement in peak stress wall motion score versus placebo (difference of differences 0.09, P value 0.001) which indicates that the PCI was technically successful in reducing the ischemic burden.

• **Change in peak oxygen uptake (mL/min):**
  2.0 (95% CI -54.1 to 50.1) vs. 10.9
  (95% CI -47.2 to 69.0), difference -12.9 (95%
  CI -90.2 to 64.3), p=0.74

• **Time to 1mm ST depression (s):**
  472.7 vs. 470.1, p=0.16

• **Change in SAQ - Angina frequency:**
  14.0 (95% CI 9.0 to 18.9) vs. 9.6 (95% CI 3.6 to 15.5), difference 4.4 (95% CI -3.3 to 12.0),
  p=0.26
• Change in Duke treadmill score:
  1.22 (95% CI 0.37 to 2.07) vs. 0.10 (95% CI – 0.99 to 1.19), difference 1.12 (95% CI -0.23 to 2.47), p=0.10

• ≥ 1 CCS angina class improvement:
  27 (26%) vs. 22 (24%), p=NS

Adverse Events

• No deaths
• Four wire complications in the placebo group requiring PCI
• Five major bleeding events;
  - Two in the PCI group and
  - Three in the placebo group.
Criticisms

1- It was a very small study, the results can not be generalized

2- Patients in the study has single vessel, normal LV function, no LMT

3- FFR or iFR was not used to select patients for participation:

~30% of patients had FFR values in excess of 0.80. ORBITA is therefore likely to have underestimated the benefit of PCI in low-FFR patients.

4- The pre-randomization medical optimization phase was very intensive, involving 1-3 telephone consultations per week and regular monitoring of home BP and HR measurements.

In a real-world setting, such speed of uptitration would not be necessary or possible.

5- The 6-week follow up period cannot rule out development of angina relief after 6 weeks.
6-Medical therapy included ranolazine which is often expensive and it is not always covered by insurance companies

Conclusions

• ORBITA is the first placebo controlled randomized trial of PCI in stable angina

• Angiography guided PCI for single vessel disease did not increase exercise time, however decreased ischemic burden compared to placebo procedure

• Health-care providers should focus their attention on treating patients with stable coronary artery disease with optimal medical therapy, and improving the lifestyle choices (heart-healthy diets, regular physical activity)
• These findings need to be validated in a larger randomized controlled trial

• ORBITA highlights the importance of including sham controls and double blinding in order to avoid the powerful placebo effect of procedures such as PCI

Thank You