A 21st Century Approach to Stable Ischemic Heart Disease

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Disclosure

No conflicts
21st Century Guidelines for SIHD

2014 ACC/AHA/AATS/PCNA/SCAI/STS Focused Update of the Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease


European Heart Journal (2013) 34, 2949–3003
doi:10.1093/eurheartj/eht296

2013 ESC guidelines on the management of stable coronary artery disease
The Vexing Problem of Guidelines and Conflict of Interest: A Potential Solution

Gordon Guyatt, MD, MSc; Elie A. Akl, MD, PhD; Jack Hirsh, MD; Clive Kearon, MD, PhD; Mark Crowther, MD; David Gutterman, MD; Sandra Zelman Lewis, PhD; Ian Nathanson, MD; Roman Jaeschke, MD, MSc; and Holger Schünemann, MD, PhD
Background
Taxonomy of Ischemic Coronary Syndromes: (What’s in a Name?)

- Acute Coronary Syndromes
  - Sudden cardiac death
  - ST-elevation myocardial infarction
  - Non-ST-elevation myocardial infarction
  - Unstable angina

- Stable Ischemic Heart Disease
  - Implies a single entity with a single cause and a single treatment
Prevalence of Stable Angina

~8.7 million Americans (M=F) have stable angina
565,000 new cases per year
Goals of Treatment

• Improve Quantity of Life
  • Prevent death and MI
• Improve Quality of Life
  • Relieve angina
• Spend as little of society’s money as possible
Facts
Fact #1: PCI Does Not Reduce Mortality in SIHD

12 RCT’s; N=6589.

Fact #2: PCI Does Not Prevent MI in SIHD

12 RCT's; N=7665.

OMT in 2018

- Aspirin or clopidogrel
- Disease-modifying therapy
  - ACE/ARB
  - High potency statin
- Anti-ischemic therapy
  - Beta blockers
  - Calcium channel blockers
  - Nitrates
- Mediterranean diet
- Regular Exercise/Cardiac Rehab
- Smoking Cessation
- BP and glycemic control
- Weight loss
Fact #3: No High-Risk SIHD Subgroups Benefit from PCI

<table>
<thead>
<tr>
<th>High-Risk Subsets</th>
<th>Worse Outcomes (Death, MI)</th>
<th>Outcomes Improved by PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetics</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Diabetics with high-risk anatomy</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Older patients</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Low LVEF</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>More extensive CAD</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>3V CAD + low LVEF</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Proximal LAD</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Fact #4: PCI Does Not Improve Death, MI in Patients with Ischemia

Fact #5:
PCI Is Not Effective Therapy for Angina

N=1784 patients with angina at the time of randomization

Incremental Benefit of PCI in Relief of Angina

- PCI + OMT
- OMT

0 months: 100%
1 month: 90% (11% increment)
3 months: 81% (13% increment)
6 months: 76% (11% increment)
12 months: 73% (9% increment)
24 months: 70% (8% increment)
36 months: 67% (5% increment)
**Principle Hypothesis:** PCI increases **exercise time** more than a sham procedure

**Sample size calculation:** To detect an increase in exercise time of 30 seconds with 80% power and a SD of 75 seconds requires 200 randomized patients
ORBITA Results Summarized

• Stent compared to sham
  • **No significant improvement in:**
    • Exercise time (with 2 different statistical methods)
    • Time to 1 mm ST depression
    • Peak oxygen uptake
    • SAQ physical limitation (with 2 different statistical methods)
    • SAQ angina frequency (with 2 different statistical methods)
    • SAQ angina stability
    • SAQ quality of life (with 2 different statistical methods)
    • EQ-5D-5L QoL (with 2 different statistical methods)
    • Duke treadmill score
    • CCS angina grade (with 2 different statistical methods)
  • **Significant improvement in:**
    • Peak stress wall motion index score (with 2 different statistical methods)
    • Freedom from angina at 4 weeks (49.5 vs. 31.5%)
Fact #6: Half of Patients with Angina and an Abnormal Stress Test Have Do Not Obstructive CAD


N=398,978
Fact #7: Coronary Spasm is Found in 58% of Patients with Angina and Non-obstructive CAD

Coronary Heart Disease

Clinical Usefulness, Angiographic Characteristics, and Safety Evaluation of Intracoronary Acetylcholine Provocation Testing Among 921 Consecutive White Patients With Unobstructed Coronary Arteries

Peter Ong, MD; Anastasios Athanasiadis, MD; Gabor Borgulya, MD, MSc; Ismail Vokshi, MBBS; Rachel Bastiaenen, MBBS; Sebastian Kubik; Stephan Hill, MD; Tim Schäufele, MD; Heiko Mahrholdt, MD; Juan Carlos Kaski MD, DSc®; Udo Sechtem, MD®

Patients without obstructive coronaries: n=921

Intracoronary acetylcholine testing performed: n=847

ACH-test with pathologic response: n=488 (58%)

Epicardial spasm n = 283 (33.4%)
Microvascular spasm n = 205 (24.2%)
ACH-test inconclusive n = 242 (28.6%)
ACH-test uneventful n = 317 (37.6%)

Circulation. 2014;129:1723-1730
Therapy of Coronary Artery Spasm

- Smoking Cessation*
- Calcium Antagonists*
- Long-acting Nitrates*
- Statin therapy*

* Included in OMT
Fact #8: 90% of Resistance to Coronary Blood Flow Occurs in the Arteries Not Visible by Angiography
Fact #9: Microvascular Dysfunction is Found in 64% of Patients With Angina But Without Obstructive CAD

Prevalence of Coronary Microvascular Dysfunction Among Patients With Chest Pain and Nonobstructive Coronary Artery Disease

Jaskanwal D. Sara, MBChB,* R. Jay Widmer, MD, PhD,* Yasushi Matsuzawa, MD, PhD,* Ryan J. Lennon, MS,j Lilach O. Lerman, MD, PhD,† Amir Lerman, MD*
PET perfusion imaging has become the gold standard of evaluation due to the linear relationship between myocardial blood flow (MBF) and radioisotope signal intensity, allowing highly accurate MBF quantification.

Outcomes of Patients with Microvascular Dysfunction

MACE = death, MI, revascularization, CHF admission

*Circulation.* 2014;129:2518-2527
Mortality in Patients with Abnormal CFR

<table>
<thead>
<tr>
<th>Study name</th>
<th>Odds ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marks 2004</td>
<td>3.125</td>
<td>1.198</td>
<td>8.149</td>
<td>2.330</td>
<td>0.020</td>
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<tr>
<td>Herzog 2009</td>
<td>4.331</td>
<td>1.845</td>
<td>10.166</td>
<td>3.367</td>
<td>0.001</td>
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<tr>
<td>Cortigiani 2012</td>
<td>4.413</td>
<td>3.266</td>
<td>5.961</td>
<td>9.670</td>
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<tr>
<td>Lowenstein 2014</td>
<td>6.517</td>
<td>2.276</td>
<td>18.661</td>
<td>3.492</td>
<td>0.000</td>
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<tr>
<td>Murthy 2014</td>
<td>2.474</td>
<td>1.262</td>
<td>4.851</td>
<td>2.637</td>
<td>0.008</td>
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<tr>
<td>Gan 2017</td>
<td>8.750</td>
<td>2.217</td>
<td>34.542</td>
<td>3.096</td>
<td>0.002</td>
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<tr>
<td></td>
<td>4.172</td>
<td>3.277</td>
<td>5.311</td>
<td>11.593</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Odds ratio and 95% CI

- Normal CFR
- Abnormal CFR
There is No Proven Treatment of Coronary Microvascular Dysfunction

*Included in OMT

European Heart Journal May 2014, 35 (17) 1101-1111
There are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns - the ones we don't know we don't know.

— Donald Rumsfeld —
Left Main CAD

2.1% of 13,000 coronary angiograms at University of Virginia

Survival in Subgroups of Patients with Left Main Coronary Artery Disease
Veterans Administration Cooperative Study of Surgery for Coronary Arterial Occlusive Disease

Prepared by Timothy Takaro, M.D., Peter Peduzzi, Ph.D., Katherine M. Detre, M.D., Dr. P.H., Herbert N. Hultgren, M.D., Marvin L. Murphy, M.D., Johanna van der Bel-Kahn, M.D., James Thomsen, M.D., and William R. Meadows, M.D.

Methods
The screening and selection of patients have been described. In brief, during 1972–1974, 686 adult male patients with angina pectoris entered the randomized controlled trial of the effect of the saphenous vein bypass graft operation on long-term survival. Review of all baseline coronary arteriograms revealed 91 pa-
Diagnostic Modalities for Left Main CAD

- Treadmill Stress Test
  - No radiation, low cost, high NPV (94%), low PPV (26%)
- Nuclear Stress Test
  - Radiation, low sensitivity (64%), high specificity (94%)
- Stress Echo
  - No radiation, high NPV (100%), high PPV (100%)
- Coronary CTA
  - Radiation, anatomical detail, high NPV (100%), high PPV (100%)
Multivessel CAD with Depressed LVEF- 
STICH Trial


N=1212, CAD suitable for CABG, EF <35%
Let’s Talk About Some Real Patients

National Library of Medicine
A doctor, a patient and hospital staff in grand rounds in the 1920s.
Case #1

• 61-year old executive with hypertension who developed chest pain while walking briskly outside on a cold day
• LDL 120 mg/dl
• The pain resolved spontaneously with rest
• He had one additional similar episode and presented to his PCP
What Next?

A. Exercise Stress Test
B. Nuclear Stress Test
C. Stress Echo
D. Coronary CT Angiogram
E. Cardiac Cath/PCI/CABG
F. Begin Medical Therapy and Reassess
G. Other
CCTA
Stress Echo

POST EXERCISE STUDY:

- PEAK BP: 166/70 mm Hg
- PEAK HR: 154

Parasternal Long Axis
- MAS 1
- BAS 1

Parasternal Short Axis
- MAS 1
- LCX 1

Apical Four Chamber
- LAD 1
- RCA 1

Apical Two Chamber
- LAD 1
- RCA 1

POST-EXERCISE COMMENTS:

The patient exercised for 9 min. 45 sec. on Bruce Protocol. Test Terminated.

Echocardiographic images obtained immediately after exercise showed:
- Development of apical and septal apical akinesia/dyskinesia; these changes persisted up to 20 minutes post-exercise (myocardial stunning); eventually normalized after one NTG 0.4 mg and 30 min post-cessation of exercise.

STRESS ECG COMMENTS:

- 1 mm ST elevation in AVR, VPC, sps
- IMPRESSION: Contrast enhancement was employed after initial imaging due to sub-optimal quality related to co-morbidity defined by patient’s body habitus. Maximal Exercise Stress Echocardiogram, POSITIVE for myocardial ischemia in the LAD/diagonal coronary artery distribution. Duke treadmill score of 8/5.
OMT is Medication and Lifestyle Modification
Case #2

- 41-year old man with elevated triglycerides but no history of hypertension, diabetes or smoking develops exertional chest pain at work as a construction supervisor
- His pain was relieved by sublingual nitroglycerin
- He had undergone 2 coronary angiograms previously that were normal
- He had his gall bladder removed which did not improve his symptoms
What Next?

A. Exercise Stress Test
B. Nuclear Stress Test
C. Stress Echo
D. Coronary CT Angiogram
E. Cardiac Cath/PCI/CABG
F. Begin Medical Therapy and Reassess
G. Other
Repeat Coronary Angiography with Acetylcholine Injection

DX: Diffuse coronary spasm
RX: High dose diltiazem and atorvastatin
Case #3

• 73-year old woman with type 2 diabetes, obesity and exertional angina for 2 years.

• Recent normal coronary angiogram
What Next?

A. Exercise Stress Test  
B. Nuclear Stress Test  
C. Stress Echo  
D. Coronary CT Angiogram  
E. Cardiac Cath/PCI/CABG  
F. Begin Medical Therapy and Reassess  
G. Other
Repeat Coronary Angiography with Physiologic Assessment

- Normal FFR
- Reduced CFR 1.3
- No spasm induced with acetylcholine

DX: Microvascular Dysfunction
RX: Atorvastatin, lisinopril, carvedilol
A Broader View of Myocardial Ischemia

ISCHEMIC HEART DISEASE

- Structural CAD
  - Atherosclerotic CAD
  - Non-atherosclerotic CAD

- Functional CAD
  - Variant Angina
  - Vasospastic Angina

- Coronary Microvascular Disorders
  - Primary Microvascular Disorders
  - Secondary Microvascular Disorders

Coronary Vasomotor Disorders
2018 Missouri ACP
Stable Ischemic Heart Disease Guideline

• For patients with appropriate risk factors and stable angina
  • Initiate OMT
  • CCTA, nuclear stress or stress echo to rule out left main disease/severe LV dysfunction—not to treat ischemia
  • Consider cath for persistent angina on maximally tolerated medical therapy with acetylcholine testing to rule out spasm and measurement of coronary flow reserve OR
  • Vasodilator PET scan to assess CFR
    • Enroll in clinical trial if microvascular dysfunction
Thank You!