The Future of Interventional Cardiology: Will Prevention Replace Intervention?

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Speaker's honoraria (moderate, Novartis, Genzyme, Bayer HealthCare, AstraZeneca), no relation to the topic of the lecture.
The Future of Interventional Cardiology: Will Prevention Replace Intervention?

1. AVOIDING THE PITFALLS OF THE TITLE...
Will prevention replace intervention?

Some questions need to be answered before I can give an adequate answer:

• **Which patient populations do you mean?**
  - Acute coronary syndromes
  - Stable CAD
  - Asymptomatic patients with a high risk
  - The general population?

• **What do you mean by „prevention“?**
  - Optimal medical therapy
  - OMT + exercise
  - aggressive lipid lowering with LDL-C <70 mg/dL
The Pyramid of Cardiovascular Prevention

Clinical disease
- Angina, MI, CHF, PAD, stroke, sudden death

Subclinical disease
- Left ventricular dysfunction, carotid stenosis, coronary calcification, endothelial dysfunction, autonomic dysfunction, myocardial ischemia, arrhythmias, more vulnerable plaque, potential for thrombosis

Risk factors
- Traditional
  - Age, family history, smoking, hypertension, dyslipidemia, diabetes, sedentary lifestyle, obesity
- Nontraditional
  - Psychosocial stressors, air pollution, inflammation, other (?)
Prevention and intervention do not exclude one another, but they are obligatory components of an outcome-oriented approach in treating cardiovascular patients.
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2. THE EASY ANSWER: ACUTE CORONARY SYNDROMES
## The Acute Care of STEMI Patients

### Recommendations for PCI in acute STEMI patients

<table>
<thead>
<tr>
<th>Indication</th>
<th>Time from FMC</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary PCI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is recommended in patients with chest pain/discomfort &lt;12 h + persistent ST-segment elevation or previously undocumented left bundle branch block.</td>
<td>As soon as possible and at any rate &lt; 2 h from FMC&lt;sup&gt;d&lt;/sup&gt;</td>
<td>I</td>
<td>A</td>
<td>83, 84, 94</td>
</tr>
<tr>
<td>Should be considered in patients with ongoing chest pain/discomfort &gt;12 h + persistent ST-segment elevation or previously undocumented left bundle branch block.</td>
<td>As soon as possible</td>
<td>IIa</td>
<td>C</td>
<td>—</td>
</tr>
<tr>
<td>May be considered in patients with history of chest pain/discomfort &gt;12 h and &lt;24 h + persistent ST-segment elevation or previously undocumented left bundle branch block.</td>
<td>As soon as possible</td>
<td>IIb</td>
<td>B</td>
<td>88, 89</td>
</tr>
<tr>
<td><strong>PCI after fibrinolysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Routine urgent PCI is indicated after successful fibrinolysis (resolved chest pain/discomfort and ST-segment elevation).</td>
<td>Within 24 h&lt;sup&gt;0&lt;/sup&gt;</td>
<td>I</td>
<td>A</td>
<td>77–79</td>
</tr>
<tr>
<td>Rescue PCI should be considered in patients with failed fibrinolysis.</td>
<td>As soon as possible</td>
<td>IIa</td>
<td>A</td>
<td>80, 87</td>
</tr>
<tr>
<td><strong>Elective PCI/CABG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is indicated after documentation of angina/positive provocative tests.</td>
<td>Evaluation prior to hospital discharge</td>
<td>I</td>
<td>B</td>
<td>36, 41–43</td>
</tr>
<tr>
<td>Not recommended in patients with fully developed Q wave MI and no further symptoms/signs of ischaemia or evidence of viability in the infarct related territory.</td>
<td>Patient referred &gt;24 h</td>
<td>III</td>
<td>B</td>
<td>90, 91</td>
</tr>
</tbody>
</table>

*FMC*: First medical contact, *PCI*: percutaneous coronary intervention.
The Benefit of a Routine Invasive Strategy Depends on the Risk Profile

Fox KAA, J Am Coll Cardiol, 2010;55;2435-2445
Intervention versus Prevention in NSTEMI-ACS

1. Clinical Evaluation
2. Diagnosis/Risk Assessment
3. Coronary angiography

**Evaluation**
- STEMI
- reperfusion

**Validation**
- urgent <120 min
- early <24 h
- <72 h
- no/elective

**Primary**
- Relevant rise or fall in troponin
- Dynamic ST- or T-wave changes (symptomatic or silent)

**Secondary**
- Diabetes mellitus
- Renal insufficiency (eGFR <60 mL/min/1.73 m²)
- Reduced LV function (ejection fraction <40%)
- Early post infarction angina
- Recent PCI
- Prior CABG
- Intermediate to high GRACE risk score *(Table 5)*
-19% relative risk reduction with routine invasive approach

Fox KAA, J Am Coll Cardiol, 2010;55;2435-2445
The Underestimated Importance of Diet and Exercise After an Acute Coronary Syndrome

Chow CK, Circulation 2010(121):750-58
The Future of Interventional Cardiology: Will Prevention Replace Intervention?

3. THE COMPLEX ANSWER: STABLE CORONARY ARTERY DISEASE
What is the Target Lesion in Stable Angina?

Patient, 65 years old
- Exercise-induced angina pectoris
- No symptoms at rest
- Normal left ventricular function
- Clinically stable situation for 6 months

The "oculostenotic reflex"
What is the Target Lesion in Stable Angina?

Criteria for a Target Lesion:

• The stenosis is responsible for the patient’s symptoms.
  • Yes, if there is objective evidence of exercise-induced myocardial ischemia

• Interventional treatment of the stenosis confers a symptomatic benefit.
  • Yes, most likely.

• Interventional treatment of the stenosis prevents an imminent future myocardial infarction.
  • ?

• The interventional treatment of the stenosis improves patient survival.
  • Yes, if the location of the stenosis is one of the following: Left main, proximal LAD, three-vessel-disease
  • Else: ?
Fact #1:
It is not the degree of stenosis that determines if the target lesion will become the culprit lesion for a future myocardial infarction, but the composition of the plaque.

Thick Fibrous Cap

Thin Fibrous Cap
Acute vs. Chronic Coronary Syndromes: Plaque Composition

Lipid Content >40%

Macrophages (%)

Smooth Muscle (%)

*Stable plaque = smooth surface
†Unstable plaque = fissured

Fact #2:
Most myocardial infarctions are caused by moderate degree coronary stenoses.

Falk E, Circulation 1995(92):657-71
Does PCI in Stable Angina Prevent a Future Myocardial Infarction?

Summary from Imaging Studies:

• The worst looking (i.e. highest degree of relative stenosis lesions are the least likely to rupture.

• Less severely obstructive plaques are more numerous.

• Less severely obstructive plaques are responsible for most coronary events.

Conclusion:

PCI of a high degree stenosis is unlikely to prevent future myocardial infarction.

Does PCI in Stable Angina Improve Survival?

Effects on Cardiac Mortality

Risk Ratio (95% CI) | Weight, %
--- | ---
Sievers et al., 1993 | 0.33 (0.01-7.97) | 0.6
ACME 1, 1997 | 1.10 (0.57-2.11) | 6.7
ACME 2, 1997 | 0.88 (0.39-1.99) | 3.9
Dakik et al., 1998 | 1.11 (0.07-16.47) | 0.4
AVERT, 1999 | 0.93 (0.06-14.69) | 0.4
MASS, 1999 | 1.00 (0.34-2.95) | 2.3
Bech et al., 2001 | 0.51 (0.09-2.59) | 1.5
ALKK, 2003 | 0.36 (0.15-0.88) | 6.5
RITA-2, 2003 | 1.02 (0.68-1.53) | 16.4
MASS-II, 2004 | 3.63 (1.03-12.82) | 1.2
OAT, 2006 | 1.04 (0.78-1.38) | 32.4
COURAGE, 2007 | 0.91 (0.66-1.25) | 28.7
Hambrecht et al., 2004 | (Excluded) | 0.0
Overall (95% CI) | 0.97 (0.82-1.14) | ---

Risk Ratio

Favors PTCA | Favors MT

Conservative versus Invasive Treatment Strategies in Stable CAD - Novel Meta-Analyses -

**Effects on Cardiac Mortality**

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk Ratio (95% CI)</th>
<th>Weight, %</th>
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<td>0.33 (0.01-7.97)</td>
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<td>0.97 (0.82-1.14)</td>
<td></td>
</tr>
</tbody>
</table>

*Cecil WT, Am J Manag Care. 2008;14(8):521-528*
**COURAGE: Prospective Comparison of Optimal Medical Therapy versus PCI**

Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE)

- 35,539 Patients underwent assessment
  - 32,468 Were excluded
    - 867 Did not meet inclusion criteria
    - 5155 Had undocumented ischemia
    - 3961 Did not meet protocol for vessels
    - 6534 Were excluded for logistic reasons
    - 18,360 Had one or more exclusions
      - 4513 Had undergone recent (<6 mo) revascularization
      - 4939 Had an inadequate ejection fraction
      - 2987 Had a contraindication to PCI
      - 2542 Had a serious coexisting illness
      - 1285 Had concomitant valvular disease
      - 1203 Had class IV angina
      - 1071 Had a failure of medical therapy
      - 947 Had left main coronary artery stenosis ≥50%
      - 722 Had only PCI restenosis (no new lesions)
      - 528 Had complications after myocardial infarction
  - 3071 Met eligibility criteria
  - 784 Did not provide consent
    - 450 Did not receive physician’s approval
    - 237 Declined to give permission
    - 97 Had an unknown reason

- 2287 Consented to participate (74% of patients with protocol eligibility)
  - 1149 Were assigned to PCI group
    - 46 Did not undergo PCI
      - 27 Had a lesion that could not be dilated
      - 1006 Received at least one stent
  - 107 Were lost to follow-up
  - 1149 Were included in the primary analysis

- 1138 Were assigned to medical-therapy group
  - 97 Were lost to follow-up
  - 1138 Were included in the primary analysis

Kein Vorteil der PTCA gegenüber der medikamentösen Therapie bei stabiler KHK


A) Survival Free of Death from Any Cause and Myocardial Infarction

- Hazard ratio, 1.05; 95% CI (0.87–1.27); P=0.62

B) Overall Survival

- Hazard ratio, 0.87; 95% CI (0.65–1.16); P=0.38

C) Survival Free of ACS

- Hazard ratio, 1.07; 95% CI (0.84–1.37); P=0.56

D) Survival Free of Myocardial Infarction

- Hazard ratio, 1.13; 95% CI (0.89–1.43); P=0.33

No. at Risk

Medical therapy

PCI

A) 1138 1025 956 833 662 418 236 127

1149 1027 957 835 667 431 246 134

B) 1138 1073 1029 917 717 468 302 38

1149 1094 1051 929 733 488 312 44

C) 1138 1025 956 833 662 418 236 127

1149 1027 957 835 667 431 246 134

D) 1138 1019 962 834 638 409 192 120

1149 1015 954 833 637 418 200 134
Prognostic Relevance of the „Area at Risk“

Shaw JL, Circulation 2008(117):1283-91

% Ischaemic Myocardium
## ESC Guidelines on Revascularisation in Stable CAD

<table>
<thead>
<tr>
<th>Subset of CAD by anatomy</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For prognosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main &gt;50%</td>
<td>I</td>
<td>A</td>
<td>30, 31, 54</td>
</tr>
<tr>
<td>Any proximal LAD &gt;50%</td>
<td>I</td>
<td>A</td>
<td>30–37</td>
</tr>
<tr>
<td>2VD or 3VD with impaired LV function</td>
<td>I</td>
<td>B</td>
<td>30–37</td>
</tr>
<tr>
<td>Proven large area of ischaemia (&gt;10% LV)</td>
<td>I</td>
<td>B</td>
<td>13, 14, 38</td>
</tr>
<tr>
<td>Single remaining patent vessel &gt;50% stenosis</td>
<td>I</td>
<td>C</td>
<td>—</td>
</tr>
<tr>
<td>IVD without proximal LAD and without &gt;10% ischaemia</td>
<td>III</td>
<td>A</td>
<td>39, 40, 53</td>
</tr>
<tr>
<td><strong>For symptoms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any stenosis &gt;50% with limiting angina or angina equivalent, unresponsive to OMT</td>
<td>I</td>
<td>A</td>
<td>30, 31, 39–43</td>
</tr>
<tr>
<td>Dyspnoea/CHF and &gt;10% LV ischaemia/viability supplied by &gt;50% stenotic artery</td>
<td>IIa</td>
<td>B</td>
<td>14, 38</td>
</tr>
<tr>
<td>No limiting symptoms with OMT</td>
<td>III</td>
<td>C</td>
<td>—</td>
</tr>
</tbody>
</table>
To assess whether aggressive lipid-lowering therapy is a useful alternative to angioplasty or other catheter-based revascularization procedures in patients with significant CAD.

Randomised to Atorvastatin 80 mg vs. PCI + Usual Care

Cumulative Incidence of a First Ischemic Event (Myocardial Infarction of Unstable Angina)

The Future of Prevention: Regression is possible!
Correlation Between LDL-Lowering and Reduction in Cardiovascular Event Rate

Each 1 mg/dL LDL-Reduction leads to a 1% RR reduction for CV events.

O'Keefe Jr. et al., JACC 43, 2004
Correlation Between LDL-C and Change in Atheroma Volume in IVUS-Studies

The primary endpoint of percent change in atheroma volume from baseline to 6 weeks did not differ between treatment groups (−3.4% in the CSL group vs. −1.6% in the placebo group, p=0.48).

Figure 2  Structure of a synthetic HDL, as compared to a spherical plasma α-HDL.

Tardif JC, JAMA 2007(297):1675-82
Use of Cardiovascular Protective Drug Therapies in Europe

<table>
<thead>
<tr>
<th>Drug</th>
<th>Survey 1</th>
<th>Survey 2</th>
<th>Survey 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelets</td>
<td>80,8%</td>
<td>83,6%</td>
<td>93,2%</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>56,0%</td>
<td>69,0%</td>
<td>85,5%</td>
</tr>
<tr>
<td>ACE/ARB’s</td>
<td>31,0%</td>
<td>49,2%</td>
<td>74,5%</td>
</tr>
<tr>
<td>Statins</td>
<td>18,1%</td>
<td>57,3%</td>
<td>87,0%</td>
</tr>
</tbody>
</table>
“To salvage the acutely ischaemic myocardium without addressing the underlying causes of the disease is futile; we need to invest in prevention.”
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3. THE CLEAR ANSWER: PREVENTION AT POPULATION LEVEL
The Obesity Epidemic—Prevalence of a BMI $>30$ kg/m$^2$

What can be achieved by CV prevention?

Remaining lifetime risks for atherosclerotic CVD in men and women at 50 years of age. Optimal risk factors (RFs) are defined as:

- untreated total cholesterol <4.65 mmol/L (<180 mg/dL),
- untreated blood pressure <120/<80 mm Hg,
- nonsmoker, and
- nondiabetic.

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4. SUMMARY
Why is treating the target lesion not enough?

Stents treat lesions that are selected on luminal stenosis.

_Plaque events are determined more by plaque biology, rather than stenosis._

Coronary disease is diffuse and progressive.

_PCI at discrete sites does not alter disease burden or progression._

Channon K, Radcliffe Hospital, Oxford, UK
„In fact, use of PTCA in patients with stable CAD without first attempting to modify risk factors is currently considered by some experts to be suboptimal therapy.“

Nash DT, Am J Cardiol 2002(89):567-570
Blumenthal RS, J Am Coll Cardiol 2000 (36):668-673
Thank you for your kind attention!
# Definition of Ideal Cardiovascular Health


<table>
<thead>
<tr>
<th>Goal/Metric</th>
<th>Ideal Cardiovascular Health Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current smoking</strong></td>
<td></td>
</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>Never or quit &gt;12 mo ago</td>
</tr>
<tr>
<td>Children 12–19 y of age</td>
<td>Never tried; never smoked whole cigarette</td>
</tr>
<tr>
<td><strong>Body mass index</strong></td>
<td></td>
</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>&lt;25 kg/m²</td>
</tr>
<tr>
<td>Children 2–19 y of age</td>
<td>&lt;85th Percentile</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>≥150 min/wk moderate intensity or ≥75 min/wk vigorous intensity or combination</td>
</tr>
<tr>
<td>Children 12–19 y of age</td>
<td>≥60 min of moderate- or vigorous-intensity activity every day</td>
</tr>
<tr>
<td><strong>Healthy diet score</strong>*</td>
<td></td>
</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>4–5 Components*</td>
</tr>
<tr>
<td>Children 5–19 y of age</td>
<td>4–5 Components*</td>
</tr>
<tr>
<td><strong>Total cholesterol</strong></td>
<td></td>
</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>&lt;200 mg/dL†</td>
</tr>
<tr>
<td>Children 6–19 y of age</td>
<td>&lt;170 mg/dL†</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td></td>
</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>&lt;120/&lt;80 mm Hg†</td>
</tr>
<tr>
<td>Children 8–19 y of age</td>
<td>&lt;90th Percentile†</td>
</tr>
<tr>
<td><strong>Fasting plasma glucose</strong></td>
<td></td>
</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>&lt;100 mg/dL†</td>
</tr>
<tr>
<td>Children 12–19 y of age</td>
<td>&lt;100 mg/dL†</td>
</tr>
</tbody>
</table>

*The committee selected 5 aspects of diet to define a healthy dietary score. The score is not intended to be comprehensive. Rather, it is a practical approach that provides individuals with a set of potential concrete actions. A comprehensive rationale is set forth in the text of this document, and a comprehensive set of nutrition recommendations is provided in the 2006 Nutrition Guidelines.12,54,55
†Untreated values.