ESC Andreas Grüntzig Lecture on Interventional Cardiology

From coronary angioplasty to Percutaneous Interventional Cardiovascular Medicine

W. Wijns (Aalst, BE)
Disclosures

- Consulting Fees: on my behalf go to the Cardiovascular Research Center Aalst
- Contracted Research between the Cardiovascular Research Center Aalst and several pharmaceutical and device companies
- Ownership Interest: Cardiovascular Research Center Aalst is co-founder of Cardio³BioSciences (cell-based regeneration cardiovascular therapies)
- Chairman of PCR /EuroPCR, the annual Course of EAPCI
FIM Percutaneous Coronary Angioplasty
1978

Perfect surgical candidate with a simple to deal with lesion (focal, large vessel, easily accessible, straight proximal segment)

From symptomatic to prognostic indications
2010

Acute Presentations of CAD
• Primary PCI for STEMI
• High-risk unstable angina

Elective / stable patients
• Equipoise with CABG for subsets of patients with left main stenosis (± multivessel disease)
PCI or CABG for Left Main Disease

Unprotected LM Revascularization Trials

- PRECOMBAT (completed)  clintrials.gov NCT 00422968
- Leipzig (recruiting)  clintrials.gov NCT 00176397
- EXCEL (recruiting)  clintrials.gov NCT 01205776
- NOBLE (recruiting)  BCIS + Western Denmark
Percutaneous Interventional Cardiovascular Medicine

Changing the Focus from ...

How?

To ...

Who? and When?
Percutaneous Interventional Cardiovascular Medicine

- Current paradigm denies prognostic value to revascularisation of stable / elective cases
- What if the benefit of revascularisation was confounded by ...
  - less than perfect PCI results
  - failure to restrict PCI to ischemic stenoses
Measurement of FFR in the LAD
Pressure wire pullback under iv adenosine

Courtesy B. De Bruyne
Understanding the importance of combining anatomic and functional evaluation of CAD

I=PCI inappropriate
II=PCI questionable
III=PCI appropriate
IV=PCI deferral is inappropriate

Angiographic Diameter Stenosis (%)

Pressure-derived FFR

N = 2334

Wijns, de Bruyne, Vanhoenacker, JNC 2007;93:856-61
Prognostic Value of Stress 99mTc-sestamibi Perfusion Imaging

Average Annual Hard Events (Death or MI) in > 12000 Patients

- Normal: 0.6%
- Abnormal: 7.4%

Iskander S, Iskandrian A E  JACC 1998
Patient with stenoses ≥ 50% in at least 2 of the 3 major epicardial vessels

Indicate all stenoses ≥ 50% amenable for stenting

Randomization

Angiography-guided PCI

Stent all indicated stenoses

1-year follow-up

FFR-guided PCI

Measure FFR in all indicated stenoses

Stent only those stenoses with FFR ≤ 0.80
FAME trial: Event-free Survival

Absolute difference in MACE-free survival

- **30 days**: 2.9%
- **90 days**: 3.8%
- **180 days**: 4.9%
- **360 days**: 5.3%

Days since Randomization
# ANGIO-group

<table>
<thead>
<tr>
<th>Indicated lesions per patient</th>
<th>ANGIO-group</th>
<th>FFR-group</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=496</td>
<td>2.7 ± 0.9</td>
<td>2.8 ± 1.0</td>
</tr>
</tbody>
</table>

**FFR results**

- Lesions successfully measured, No (%)
  - ANGIO-group: -
  - FFR-group: 1329 (98%)

- FFR in ischemic lesions
  - ANGIO-group: -
  - FFR-group: 0.60 ± 0.14

- FFR in non-ischemic lesions
  - ANGIO-group: -
  - FFR-group: 0.88 ± 0.05

- Lesions with FFR ≤ 0.80, No (%)
  - ANGIO-group: -
  - FFR-group: 874 (63%)

- Lesions with FFR > 0.80, No (%)
  - ANGIO-group: -
  - FFR-group: 513 (37%)

**Stents**

- DES per patient
  - ANGIO-group: 2.7 ± 1.2
  - FFR-group: 1.9 ± 1.3

- Lesions successfully stented, No (%)
  - ANGIO-group: 1237 (92%)
  - FFR-group: 819 (94%)

- DES, total, No
  - ANGIO-group: 1359
  - FFR-group: 980
FFR cheaper
Angio cheaper
USD
Fearon WJ et al Circulation 2010

FAME Trial: Economic Evaluation

ICER of 50,000 $ / QALY

FFR Guidance
Improve Outcomes

FFR Guidance
Saves Resources
Evidence for Optimal Medical Therapy (OMT) vs OMT + Revascularisation by PCI

**Evidence for benefit**
- If moderate / large ischemia
  - 1997: ACIP trial
  - 2003: Nuclear imaging studies
  - 2008: Nuclear substudy COURAGE
  - 2009: Substudy of BARI 2 D
  - 2012: FAME 2 randomised trial

**Evidence for lack of benefit**
- In the absence of ischemia
  - 1998: Nuclear imaging studies
  - 2005: Besançon randomised trial*
  - 2007: Defer randomised trial
  - 2010: FAME 1 randomised trial
  - 2012: FAME 2 randomised trial

*Legalery, Eur Heart J 26:2623
Flow Chart

Stable patients scheduled for 1, 2 or 3 vessel DES stenting

FFR in all target lesions

Randomised Trial

At least 1 stenosis with FFR ≤ 0.80

Randomisation 1:1

PCI + OMT

OMT

Registry

When all FFR >0.80

OMT

50% randomly assigned to FU

Follow-up after 1, 6 months, 1, 2, 3, 4, and 5 years
Primary End-Points

The primary end-point defined as a composite of

• all cause death
• myocardial infarction
• unplanned hospitalisation with urgent revascularisation

as adjudicated by an independent Clinical Event Committee (CEC)
Stable patients scheduled for 1, 2 or 3 vessel DES stenting

FFR in all target lesions

- When all FFR > 0.80
- At least 1 stenosis with FFR ≤ 0.80

Randomised Trial
- At least 1 stenosis with FFR ≤ 0.80
- 691 (72%)

Registry
- When all FFR > 0.80
- 264 (28%)

FAME II
50% randomly assigned to FU

B de Bruyne et al.
Rate of Urgent Revascularisation

RCT:OMT vs. RCT:PCI+OMT = 6.0% vs. 0.6%
HR (95% CI): 11.2 (2.62-47.9); logrank p<.0001

RCT:PCI+OMT vs. REGISTRY:OMT, p=0.71

Cumulative incidence (%)
Months after randomisation

No. at risk
RCT:OMT only
339 235 127 125 121 119 85 19 10 10 10 8
RCT:PCI+OMT
352 257 146 144 144 143 116 25 18 18 18 18
REGISTRY:OMT only
131 88 41 40 40 35 4 1 1 1 1 1
Rate of Any Revascularisation

RCT: OMT vs. RCT: PCI+OMT = 12.1% vs. 1.7%
HR (95% CI): 7.63 (3.24-18.0); logrank p<.0001

No. at risk
RCT: OMT only 339 238 123 119 115 112 83 20 10 10 10 8
RCT: PCI+OMT 352 256 144 141 140 139 114 25 18 18 18 18
REGISTRY: OMT only 131 88 41 40 40 40 35 4 1 1 1 1
Coronary angiography works well in many cases
- when abnormalities are severe
- in the context of acute CAD

Coronary angiography does not work well in equally many cases
- for elective procedures in stable CAD
- in the presence of either moderate stenosis or multivesSEL disease

Combined anatomic-functional assessment integrated with global clinical appraisal has become “The” decision-maker granting both appropriateness of PCI and good outcomes
Percutaneous Interventional Cardiovascular Medicine

From Symptoms to Prognosis
• Coronary Intervention
• Structural Heart Disease
• Resistant Hypertension & Heart Failure
• . . . / . . .
Perfect surgical candidate with a simple to deal with lesion (focal, large vessel, easily accessible, straight proximal segment)

Compassionate use
End stage disease, no option for surgery, moribund patient
Partner US randomised trial

**Cohort B**: non-surgical candidates

### All Cause Mortality (ITT)

**Crossover Patients Followed**

- **Standard Rx**
- **TAVR**

<table>
<thead>
<tr>
<th>Months</th>
<th>0%</th>
<th>20%</th>
<th>40%</th>
<th>60%</th>
<th>80%</th>
<th>100%</th>
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<tr>
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<td>100%</td>
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<td>24</td>
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<td>67.6%</td>
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**HR [95% CI]** = 0.57 [0.44, 0.75]  
**p (log rank)** < 0.0001

**Δ at 1 yr = 20.0%**  
**NNT = 5.0 pts**

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**Δ at 2 yr = 24.3%**  
**NNT = 4.1 pts**

### Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>Standard Rx</th>
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<tr>
<td>24</td>
<td>179</td>
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<td>18</td>
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<td>110</td>
<td>67</td>
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<tr>
<td>0</td>
<td>83</td>
<td>51</td>
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Partner US randomised trial

**Cohort A**: high risk surgical patients

**All-Cause Mortality (ITT)**

- **TAVR**
- **AVR**

**HR [95% CI]** = 0.88 [0.70, 1.12]

**p (log rank)** = 0.310

Numbers at Risk:

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>AVR</th>
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<tbody>
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- 24.3% at 12 months
- 26.8% at 18 months
- 33.9% at 36 months
- 35.0% at 36 months
Percutaneous Interventional Cardiovascular Medicine

From Symptoms to Prognosis
• Coronary Intervention
• Structural Heart Disease
• Resistant Hypertension & Heart Failure
• . . . / . . .
Prevalence of resistant hypertension in US

245 million adults

51 million treated hypertension

\( \approx 6.5 \text{ million resistant hypertension} \)
Primary Endpoint (at 6 months post randomisation)

-3 2
-1 2
0

RDN (n = 49) Control (n = 51)

∆ from Baseline to 6 Months (mmHg)

Systolic
-32
-12

Diastolic

p <0.01 for difference between RDN and Control

Blood pressure reduction in Symplicity

Expanded results presented at the American College of Cardiology Annual Meeting 2012 (Esler, M.)
Systolic Blood Pressure and CV Mortality

**Stroke**

- Age at risk:
  - 80-89 years
  - 70-79 years
  - 60-69 years
  - 50-59 years

**Ischemic Heart Disease**

- Age at risk:
  - 80-89 years
  - 70-79 years
  - 60-69 years
  - 50-59 years
  - 40-49 years
Afferent:
- Renal ischemia
- Adenosine ↑

Efferent:
- Gluconeogenesis ↑
- Insulin resistance
- LVH
- Ischemia Heart Failure
- Vasoconstriction
- Atherosclerosis
- Renin secretion
- Sodium retention
- Proteinuria
Step 4 medication
Renal denervation

Pay attention, inform, adapt drug regimen, use loop diuretics, refer to nephrologist
Consider etiologic treatment

Step 4 medication
Renal denervation

Pay attention, inform, adapt drug regimen, use loop diuretics, refer to nephrologist

Perform ABPM

BP at goal

Aldo/renin ratio metanephrines CT- or MR-angio

Curable HTN?

Consider etiologic treatment

Side effects
Non-compliance
Sub-optimal Rx
Pressor agents
Low GFR

Resistance to triple Rx

Pay attention, inform, adapt drug regimen, use loop diuretics, refer to nephrologist

no

no

yes

yes

no
Consider etiologic treatment

Step 4 medication
Renal denervation

Do not miss the 2012 Great Debate at ESC
Current role of interventional renal denervation in the treatment of severe hypertension
FOCUS session on August 28, 11:00

Pay attention, inform, adapt drug regimen, use loop diuretics, refer to nephrologist

Resistance to triple Rx
Side effects
Non-compliance
Sub-optimal Rx
Pressor agents
Low GFR

BP at goal
no
yes

Aldo/renin ratio metanephrines
CT- or MR-angio

Curable HTN?
no
yes

Consider etiologic treatment

Perform ABPM
BP at goal
no
yes
Percutaneous Interventional Cardiovascular Medicine

- After 3 decades of technical (r)evolutions, a new and mature discipline has emerged
- By focusing on “who” and “when” (once the “how” has been solved), interventional therapies can contribute to multidisciplinary patient care, in synergy with available medical and surgical options
- The less invasive endovascular approach does offer patient comfort, quality of life and improved outcomes, a route now adopted by many other medical and surgical disciplines
THE PCR-EAPCI TEXTBOOK

Take ownership of the Textbook!
With your contributions it will become a participative encyclopaedia
ESC Andreas Grüntzig Lecture on Interventional Cardiology

Special Thanks to ...

The ESC and EAPCI leadership
Our industry partners
My mentors
The PCR family
My colleagues, fellows and team in Aalst