Has the Approach to Coronary Revascularization Changed after Recent Clinical Trials?

1. What Coronary Revascularization?
2. Which Trials?
Approaches to Coronary Revascularization

Conservative

PCI

Bypass Surgery
Has the Approach to Coronary Revascularization Changed after Recent Clinical Trials?

1. What is Coronary Revascularization?
2. Which Trials?
Guidelines are based on Evidence:
What is Evidence?
Demand Bayer Aspirin

SAY "BAYER ASPIRIN"—Genuine

Unless you see the "Bayer Cross" on tablets, you are not getting the genuine Bayer Aspirin prescribed by physicians and proved safe by millions over 25 years for:

Colds  Headache  Neuritis  Lumbago
Pain  Neuralgia  Toothache  Rheumatism

DOES NOT AFFECT THE HEART

Safe
Accept only "Bayer" package which contains proven directions. Handy "Bayer" boxes of 12 tablets. Also bottles of 24 and 100—Druggists.

Aspirin is the trade mark of Bayer Manufacture of Monomethylsalicylate of Salicylic acid.
Only Randomized Trials
(no „adjustments“ necessary)
The Power for the Clinical Outcome must also be considered!
Guidelines for Percutaneous Coronary Interventions

The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology

Authors/Task Force Members: Sigmund Silber, Chairperson* (Germany), Per Albertsson (Sweden), Francisco F. Avilés (Spain), Paolo G. Camici (UK), Antonio Colombo (Italy), Christian Hamm (Germany), Erik Jørgensen (Denmark), Jean Marco (France), Jan-Erik Nordrehaug (Norway), Witold Ruzyillo (Poland), Philip Urban (Switzerland), Gregg W. Stone (USA), William Wijns (Belgium)

the basis of evidence (Table on Levels of evidence). To verify the applicability of the recommendations to a specific area, the expert panel emphasized the importance of the primary endpoint for the randomized trials, giving high priority to the importance of significantly improving patients’ outcome as the primary endpoint investigated in an adequately powered sample size.

European Heart Journal (2005) 26, 804–847
How did major randomized trials presented after March 2005 affect the ESC guidelines?
Has the Approach to Coronary Revascularization Changed after Recent Clinical Trials?
Has the Approach to Coronary Revascularization Changed after Recent Clinical Trials?
ASSENT-4 PCI:
The ASsessment of the Safety and Efficacy of a New Treatment Strategy for Acute Myocardial Infarction

Frans Van de Werf, MD, PhD, FESC
University of Leuven
Leuven, Belgium

on behalf of the ASSENT-4 PCI investigators
ASSENT IV Study Design

ASSENT IV - Trial Design

STEMI patients < 6 hrs, PCI within 1-3 hrs
N=4000

Randomization 1:1, Open Label

UFH and Aspirin

Clopidogrel only after angiogram when decision for stent implantation is made

Pre-treatment with TNK followed by PCI
Ilb/Ilia not allowed

Primary Endpoint: Composite of Death or Cardiogenic Shock or Congestive Heart Failure within 90 Days

UFH and Aspirin

Primary PCI
Ilb/Ilia if needed
Kaplan-Meier Curves for 30 DAY MORTALITY

TNK + PCI
N = 829

PCI alone
N = 838

Log rank test
p<0.05
Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial

Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) investigators*

Interpretation A strategy of full-dose tenecteplase with antithrombotic co-therapy, as used in this study and preceding PCI by 1–3 h, was associated with more major adverse events than PCI alone in STEMI and cannot be recommended.
term ‘facilitated PCI’ is not uniformly used for identical settings: it should be used as initially planned PCI, following shortly after initiating thrombolysis and/or GP IIb/IIIa inhibitors. Therefore, in randomized studies testing the concept of facilitated PCI, all patients (with or without pre-treatment) should undergo planned primary PCI.

we prefer primary PCI over thrombolysis in the first 3 h of chest pain to prevent stroke and, in patients presenting 3–12 h after the onset of chest pain, to salvage myocardium and also prevent stroke. At the moment, there is no evidence to recommend facilitated PCI.
Take Home Messages from ASSENT-4:

- If thrombolysis is performed, do not start PCI within 3 hours.
- This is a prothrombotic period, potentially dangerous for stenting.
- ASSENT-4 did not change the ESC PCI guidelines (no recommendation of facilitated PCI) and was implemented in the recent ESC STEMI guidelines.
Has the Approach to Coronary Revascularization Changed after Recent Clinical Trials?
Do drug-eluting stents increase deaths?

TWO SEPARATE, independent meta-analyses, presented in Hot Line session I, suggest drug-eluting stents (DES) may increase death, Q-wave myocardial infarction (clinical surrogates of in-stent thrombosis) and cancer deaths, bringing the long-term safety of DES firmly into the spotlight. Discussant Salim Yusuf (McMaster University, Canada) hailed the data as one of the most important presentations to come out of this year’s meeting.

“Six million people in the world have been implanted with DES, yet their long-term safety and efficacy is unknown,” said Yusuf. “I’ve a feeling the data we’re seeing today is only the tip of the iceberg. We need to encourage more

obtain this data from the manufacturer,” said Nordmann. He speculated that the increase in cancer might be due to a rapid impairment of the immune system.

Yusuf widened the debate to include percutaneous coronary intervention (PCI). “The overuse of PCI is an insidious change in the culture of cardiology that needs to be reversed,” he said. The use of PCI was established in MI, high-risk unstable angina and cardiogenic shock. However, its use in stable disease was a totally different question.

“There’s no beneficial influence on mortality – PCI does nothing to prevent heart attack. All we are doing is providing short-term relief of chest pain. It’s not re-stenosis that kills, but the
ANGIOGRAPHIC FOLLOW-UP AFTER PLACEMENT OF A SELF-EXPANDING CORONARY-ARTERY STENT

Patrick W. Serruys, M.D., Bradley H. Strauss, M.D., Kevin J. Beatt, M.B., B.S.,
Michel E. Bertrand, M.D., Jacques Puel, M.D., Anthony F. Rickards, M.B., B.S.,
Bernhard Meier, M.D., Jean-Jacques Goy, M.D., Pierre Vogt, M.D., Lukas Kappenberger, M.D.,
and Ulrich Sigwart, M.D.

Table 2. Deaths after Stent Implantation.

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Time after Implantation</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;24 hr</td>
<td>Stent occlusion after vessel closure during PTCA</td>
</tr>
<tr>
<td>2</td>
<td>48 hr</td>
<td>Sudden death</td>
</tr>
<tr>
<td>3</td>
<td>2 days</td>
<td>Stent occlusion after 11 days, followed by emergency bypass procedure</td>
</tr>
<tr>
<td>4</td>
<td>8 days</td>
<td>Stent occlusion during implantation, myocardial infarction, shock</td>
</tr>
<tr>
<td>5</td>
<td>11 days</td>
<td>Sudden death</td>
</tr>
<tr>
<td>6</td>
<td>1 1/2 mo</td>
<td>Sudden death</td>
</tr>
<tr>
<td>7</td>
<td>2 1/2 mo</td>
<td>Surgery for new lesion of left main artery, after bypass procedure</td>
</tr>
<tr>
<td>8</td>
<td>6 mo</td>
<td>Chronic congestive heart failure</td>
</tr>
</tbody>
</table>


25% Stent Thrombosis!
Stent Thrombosis presents usually as an Acute Myocardial Infarction
Incidence, Predictors, and Outcome of Thrombosis After Successful Implantation of Drug-Eluting Stents

The clinical consequences were death in 45% of patients and nonfatal MI in the majority of the others.

Mortality of Stent thrombosis: 30% - 45%
Do Drug-eluting Stents Decrease Mortality?

Registry data from real-world practice with DES are showing consistently positive safety, efficacy data.

According to reports presented at TCT 2007, DES have improved outcomes and done so safely, in some cases reducing mortality.

“It is encouraging that these data so consistently show safety and efficacy. The challenge will be synthesizing the data from so many different areas into information for clinical practice,” Gregg Stone, MD, dine treatment beyond one year in patients who were event-free after either treatment with DES or bare-metal stents in single, de novo lesions in native

Vagaonescu concluded that the use of a single DES in the setting of AMI was associated with a significant reduction of two-year all-cause mortality and cardiovascular mortality when compared with the use of a single bare-metal stent.

For complete coverage see Emerging DES Data articles inside.
Safety and Efficacy of Drug-Eluting and Bare Metal Stents

Comprehensive Meta-Analysis of Randomized Trials and Observational Studies

Ajay J. Kirtane, MD, SM; Anuj Gupta, MD; Srinivas Iyengar, MD; Jeffrey W. Moses, MD; Martin B. Leon, MD; Robert Applegate, MD; Bruce Brodie, MD; Edward Hannan, PhD; Kishore Harjai, MD; Lisette Okkels Jensen, MD; Seung-Jung Park, MD, PhD; Raphael Perry, MD; Michael Racz, PhD; Francesco Saia, MD, PhD; Jack V. Tu, MD, PhD; Ron Waksman, MD; Alexandra J. Lansky, MD; Roxana Mehran, MD; Gregg W. Stone, MD

(Circulation. 2009;119:3198-3206.)
In-Stent Restenosis is NOT a benign Disease!

~36% Present as ACS
9.5% as AMI


10% of BMS In-Stent Restenosis Cases Presented as an MI

Conclusions—ST, although infrequent, results in a high incident rate of death and MI, whereas the more frequent occurrence of target lesion revascularization is associated with a finite but lower rate of death and MI. The marked reduction in restenosis with drug-eluting stents compared with BMS may counterbalance the potential excess risk from late ST with drug-eluting stents. *(Circulation. 2007;115;&NA;--)*
Barcelona 2009 looks back to Barcelona 2006 for its update on drug-eluting stent safety

By Janet Fricker
ESC Congress News

THE ESC’S LAST CONGRESS in Barcelona in 2006 will largely be remembered for what’s gone down in cardiology folklore as the “ESC firestorm” or “Barcelona brawl”. It was all about the safety of drug-eluting stents (DES). Returning to Barcelona for ESC Congress 2009, the programme committee has taken the brave decision to revisit the controversy, with a main session titled “Is it time to turn the page on Barcelona 2006?”

At ESC Congress 2006 two independent meta-analyses, presented during a Hot Line session, raised the possibility that first generation DES might increase the risk of death. In one presentation Alain Nordmann from Basel, Switzerland, suggested the sirolimus (but not the paclitaxel) eluting stent was associated with small but significant increases in non-cardiac mortality; while in a second presentation Edoardo Camezind from Geneva, Switzerland, pooled published data from four randomised trials to show rates of overall death and Q wave MI to be higher (6.3%) for the Cypher stent than the BMS stent (3.9%, p=0.03).

The fall-out was immediate. According to data from Morgan Stanley, DES stent penetration in Europe fell from 56.2% in the third quarter of 2006 to 49.4% in the fourth quarter of that year, and to a low of 45.7% in the third quarter of 2007. The decline in DES use was even more dramatic in the USA.

In tomorrow’s session Stefan James from Uppsala Clinical Research Centre, Sweden, will review data from registries, focussing on the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) which analysed outcomes of all the 47,967 patients receiving stents in Sweden between 2003 and 2006.

The latest SCAAR data “add to a growing number of randomised trials, registry studies and updated analyses demonstrating no higher mortality associated with DES than with BMS”.

Kastrati from the German Heart Centre in Munich, Germany, adds to a growing number of randomised trials, registry studies and updated analyses demonstrating no higher mortality associated with DES than with BMS. “Now, three years after Barcelona 2006, there’s abundant evidence to show that the benefit of DES in terms of restenosis is not achieved at the expense of compromised safety,” says Kastrati.

Trials are now under way in more complex cases, such as acute MI, in-stent restenosis, complex and long lesions. Recent changes in design, says Kastrati, include those enrolling “comers” to better reflect real life situations, follow-up lasting at least two years. Moreover, technology continues to evolve with less biodegradable polymers for drug release, poly-free release of drugs, drug-eluting balloon technology and completely biodegradable stents.

Most opinion leaders are agreed that scientific debate sparked by ESC Congress 2006 at least prompted research into stent safety. Then, an unprecedented wave of published safety data in more than 200,000 patients reassured both physicians and patients that proven efficacy of first generation DES was not the cost of safety. Moreover, trial design changed, placing greater emphasis on aspects in the evaluation and approval of second generation DES. And at tomorrow’s session, participants at ESC Congress 2009 undoubtedly listen with particular attention to Camezind’s own presentation simply titled “Yay or Nay?”
Stent Thrombosis solved?

no!
Endothelialization after Stent Implantation:

- immediately after stent implantation
- bare metal stents: 4 weeks
- DES: at least 6-12 months
Angiographically confirmed Bare Metal Stent Thrombosis
(1.56%, 95/6058)

Acute/subacute: 1.16%
Late thrombosis: 0.4%
Very Late thrombosis

Bare Metal Stents

P. Wenaweser, European Heart J, 2005, 26, 1180-87
Sirolimus-Eluting Stent Implanted in Human Coronary Artery for 16 Months
Pathological Findings

Giulio Guagliumi, MD; Andrew Farb, MD; Giuseppe Musumeci, MD; Orazio Valsecchi, MD; Maurizio Tespili, MD; Teresio Motta, MD; Renu Virmani, MD

- small thrombi
- thin Neointima
- Foci without endothelialization

(Circulation. 2003;107:1340-1341.)
Angiographic DES Stent Thrombosis Bern - Rotterdam Cohort Study

Cumulative probability of stent thrombosis (%)

Days after stent implantation

Median 9 Days

Between 30 days to 3 years:
Slope = 0.6% / year

N=8,146 Patients

Courtesy of S. Windecker
Angiographic DES Stent Thrombosis Bern - Rotterdam Cohort Study

- Median 9 Days
- Between 30 days to 3 years: Slope = 0.6% / year
- N=8,146 Patients

very late
Symptomatic Graft Occlusion & Stent Thrombosis to 12 Months

**CABG (N=897)**

- 3.4
- n=27

**TAXUS (N=?)**

- 3.3
- n=28

Reduction of Stent Thrombosis by DES of next generation?
Take Home Messages from DES FIRESTORM:

- The wild beast „increased mortality after DES“ was born in Barcelona at the ESC 2006.
The wild beast „increased mortality after DES“ was born in Barcelona at the ESC 2006.
It was finally buried in Barcelona at the ESC 2009.
The „Barcelona Firestorm“ did not change the ESC guidelines.
Late and very late stent thrombosis occurs also with bare metal stents - but more often with DES, so - although rare - this concern still remains.
The highly effective reduction of restenosis after DES also reduces ACS with subsequent reduction of mortality.
For optimal treatment, new DES must be developed for faster healing to enable shorter need of dual antiplatelet medication, thus hopefully decreasing mortality following DES implantation.
Occluded Artery Trial (OAT)

Presented at
The American Heart Association
Scientific Session 2006

Presented by Dr. Judith S. Hochman
Objective:
To evaluate outcomes of percutaneous coronary intervention (PCI) versus medical therapy among high-risk but stable patients with persistent total occlusion of the infarct-related artery post-myocardial infarction (MI).

Hypothesis:
Routine PCI for total occlusion of the infarct-related artery 3-28 days after acute MI would reduce the composite end point of death, reinfarction, or New York Heart Association (NYHA) class IV heart failure.
The primary endpoint: death, reinfarction, or NYHA class IV heart failure occurred in 17.2% of the PCI group and 15.6% of the medical therapy group ([HR] 1.16, p=0.20).

Presented at AHA 2006
Coronary Intervention for Persistent Occlusion after Myocardial Infarction

Judith S. Hochman, M.D., Gervasio A. Lamas, M.D., Christopher E. Buller, M.D., Vladimir Dzavik, M.D., Harmony R. Reynolds, M.D., Staci J. Abramsky, M.P.H., Sandra Forman, M.A., Witold Ruzylo, M.D., Aldo P. Maggioni, M.D., Harvey White, M.D., Zygmunt Sadowski, M.D., Antonio C. Carvalho, M.D., Jamie M. Rankin, M.D., Jean P. Renkin, M.D., P. Gabriel Steg, M.D., Alice M. Mascette, M.D., George Sopko, M.D., Matthias E. Pfisterer, M.D., Jonathan Leor, M.D., Viliam Fridrich, M.D., Daniel B. Mark, M.D., M.P.H., and Genell L. Knatterud, Ph.D., for the Occluded Artery Trial Investigators*

Hazard ratio, 1.16; 95% CI (0.92–1.45); P=0.20

Hazard ratio, 1.16; 95% CI (0.92–1.45); P=0.20

<table>
<thead>
<tr>
<th>Year after Enrollment</th>
<th>PCI group</th>
<th>Medical therapy group</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No. at Risk
PCI group   1082  895  719  482  265  85
Medical therapy group 1084  909  714  474  268  78
Coronary Intervention for Persistent Occlusion after Myocardial Infarction

Judith S. Hochman, M.D., Gervasio A. Lamas, M.D., Christopher E. Buller, M.D., Vladimir Dzavik, M.D., Harmony R. Reynolds, M.D., Staci J. Abramsky, M.P.H., Sandra Forman, M.A., Witold Ruzyllo, M.D., Aldo P. Maggioni, M.D., Harvey White, M.D., Zygmunt Sadowski, M.D., Antonio C. Carvalho, M.D., Jamie M. Rankin, M.D., Jean P. Renkin, M.D., P. Gabriel Steg, M.D., Alice M. Mascette, M.D., George Sopko, M.D., Matthias E. Pfisterer, M.D., Jonathan Leor, M.D., Viliam Fridrich, M.D., Daniel B. Mark, M.D., M.P.H., and Genell L. Knatterud, Ph.D., for the Occluded Artery Trial Investigators*

---

### Table 1. Baseline Clinical and Angiographic Core Laboratory Characteristics.*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PCI Group (N = 1082)</th>
<th>Medical Therapy Group (N = 1084)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemia in infarct-related artery territory — no./total no. (%)</td>
<td></td>
<td></td>
<td>0.22</td>
</tr>
<tr>
<td>Severe (ineligible)</td>
<td>0/290 (0)</td>
<td>1/299 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>27/290 (9)</td>
<td>32/299 (11)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>98/290 (34)</td>
<td>80/299 (27)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>165/290 (57)</td>
<td>186/299 (62)</td>
<td></td>
</tr>
</tbody>
</table>
### Guidelines for Percutaneous Coronary Interventions

The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology

---

#### Table 1  Recommendations of PCI indications in stable CAD

<table>
<thead>
<tr>
<th>Indication</th>
<th>Classes of recommendations and levels of evidence</th>
<th>Randomized studies for levels A or B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective large ischaemia</td>
<td>I A</td>
<td>ACME&lt;sup&gt;a&lt;/sup&gt; ACIP&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

---

*European Heart Journal (2005) 26, 804–847*
Randomized Trial of Percutaneous Coronary Intervention for Subacute Infarct-Related Coronary Artery Occlusion to Achieve Long-Term Patency and Improve Ventricular Function

The Total Occlusion Study of Canada (TOSCA)-2 Trial

Vladimír Džavík, MD; Christopher E. Buller, MD; Gervasio A. Lamas, MD; James M. Rankin, MD; G.B. John Mancini, MD; Warren J. Cantor, MD; Ronald J. Carere, MD; John R. Ross, MD; Deborah Atchison, PhD; Sandra Forman, MA; Boban Thomas, MD; Pawel Buszman, MD; Carlos Vozzi, MD; Anthony Glanz, MD; Eric A. Cohen, MD; Peter Mečiar, MD; Gerald Devlin, MD; Alice Mascette, MD; George Sopko, MD; Genell L. Knatterud, PhD; Judith S. Hochman, MD; for the TOSCA-2 Investigators

(Circulation. 2006;114:2449-2457.)
Take Home Messages from OAT (TOSCA-2):

- No reperfusion is the worst „treatment“ of myocardial infarction.
- Reopening an occluded infarct artery one week later is not helpful, especially if there is no proof of residual ischemia.
- OAT (and TOSCA-2) were no CTO studies (no chronic occlusion).
- OAT (and TOSCA-2) did not change the ESC guidelines.
Has the Approach to Coronary Revascularization Changed after Recent Clinical Trials?
Medicine enough for pain in chest?

Study sees way to avoid angioplasty

By Steve Sternberg
USA TODAY
Hypothesis

PCI + Optimal Medical Therapy will be Superior to Optimal Medical Therapy Alone
Survival Free of Death from Any Cause and Myocardial Infarction

Number at Risk

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Therapy</td>
<td>1138</td>
<td>1017</td>
<td>959</td>
<td>834</td>
<td>638</td>
<td>408</td>
<td>192</td>
<td>3</td>
</tr>
<tr>
<td>PCI</td>
<td>1149</td>
<td>1013</td>
<td>952</td>
<td>833</td>
<td>637</td>
<td>417</td>
<td>200</td>
<td>3</td>
</tr>
</tbody>
</table>
# Overall Survival

<table>
<thead>
<tr>
<th>Number at Risk</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Medical Therapy</td>
<td>1138</td>
</tr>
<tr>
<td>PCI</td>
<td>1149</td>
</tr>
</tbody>
</table>

---

**PCI + OMT**

**OMT**

---

![COURAGE Heart Logo](image)
Survival Free of Hospitalization for ACS

Number at Risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Therapy</td>
<td>1138</td>
<td>1025</td>
<td>956</td>
<td>833</td>
<td>662</td>
<td>418</td>
<td>236</td>
<td>127</td>
</tr>
<tr>
<td>PCI</td>
<td>1149</td>
<td>1027</td>
<td>957</td>
<td>835</td>
<td>667</td>
<td>431</td>
<td>246</td>
<td>13</td>
</tr>
</tbody>
</table>
Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O’Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merril Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group*

CONCLUSIONS

As an initial management strategy in patients with stable coronary artery disease, PCI did not reduce the risk of death, myocardial infarction, or other major cardiovascular events when added to optimal medical therapy.
2. Indications for PCI

2.1. Indications for PCI in stable coronary artery disease

In patients with no or mild symptoms, however, the scenario is different and unlikely to be improved by PCI.
2. Indications for PCI

2.1. Indications for PCI in stable coronary artery disease

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Recommendations of PCI indications in stable CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication</td>
<td>Classes of recommendations and levels of evidence</td>
</tr>
<tr>
<td>Objective large ischaemia</td>
<td>I A</td>
</tr>
</tbody>
</table>
Improvement of Prognosis depends on the Extent of Myocardial Ischemia

Cardiac Death after 2 years (%)

% Myocardial Ischemia

0% 1-5% 5-10% 11-20% >20%

Medical Rx Revasc

P > .0001

Guidelines on the management of stable angina pectoris: full text†

The Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology

Authors/Task Force Members, Kim Fox, Chairperson, London (UK)*, Maria Angeles Alonso Garcia, Madrid (Spain), Diego Ardissino, Parma (Italy), Pawel Buszman, Katowice (Poland), Paolo G. Camici, London (UK), Filippo Crea, Roma (Italy), Caroline Daly, London (UK), Guy De Backer, Ghent (Belgium), Paul Hjemdahl, Stockholm (Sweden), José Lopez-Sendon, Madrid (Spain), Jean Marco, Toulouse (France), João Morais, Leiria (Portugal), John Pepper, London (UK), Udo Sechtem, Stuttgart (Germany), Maarten Simoons, Rotterdam (The Netherlands), Kristian Thygesen, Aarhus (Denmark)
### Table 6  Summary of recommendations for revascularization in stable angina

<table>
<thead>
<tr>
<th>Indication</th>
<th>For prognosis&lt;sup&gt;a&lt;/sup&gt;</th>
<th>For symptoms&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Class of recommendation</td>
<td>Level of evidence</td>
</tr>
<tr>
<td>PCI (assuming suitable anatomy for PCI, appropriate risk stratification, and discussion with the patient)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina CCS Classes I to IV despite medical therapy with single vessel disease</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Angina CCS Classes I to IV despite medical therapy with multi-vessel disease (non-diabetic)</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Stable angina with minimal (CCS Class I) symptoms on medication and one-, two-, or three-vessel disease but objective evidence of large ischaemia</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>
### Table 6  Summary of recommendations for revascularization in stable angina

| Indication                                                                 | For prognosis<sup>a</sup> | | | For symptoms<sup>b</sup> |
|---------------------------------------------------------------------------|----------------------------|----------------------------|----------------------------|
|                                                                           | Class of                    | Level of                    | Class of                    | Level of                    |
|                                                                           | recommendation              | evidence                    | recommendation              | evidence                    |
|PCI (assuming suitable anatomy for PCI, appropriate risk stratification, and discussion with the patient) | I                           | A                           | I                           | A                           |
| Angina CCS Classes I to IV despite medical therapy with single vessel disease | I                           | A                           | I                           | A                           |
| Angina CCS Classes I to IV despite medical therapy with multi-vessel disease (non-diabetic) | I                           | A                           | I                           | A                           |
| Stable angina with minimal (CCS Class I) symptoms on medication and one-, two-, or three-vessel disease but objective evidence of large ischaemia | IIb                          | C                           |                             |                             |

<sup>a</sup> For prognosis: I = strong recommendation, IIa = moderate recommendation, IIb = weak recommendation, III = recommendation against

<sup>b</sup> For symptoms: A = high level of evidence, B = moderate level of evidence, C = low level of evidence.
35,539 Patients underwent assessment

32,468 Were excluded
   8677 Did not meet inclusion criteria
   5155 Had undocumented
   3961 Did not meet
   6554 Were excluded
   18,360 Had
   4580 (serious coexistence of disease) revascu-
   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
Take Home Messages from COURAGE:

- Conservative treatment in patients with stable CAD is an option, if
  - Coronary anatomy is known
  - Patients with left main stenosis, depressed LV-EF etc. are excluded
  - No major signs of myocardial ischemia
- COURAGE did not change the ESC guidelines.
FINESSE: Study Design

Acute ST Elevation MI (or New LBBB) within 6h pain onset
Presenting at Hub or Spoke with estimated time to Cath between 1 and 4 hours

Randomize 1:1:1
N=3000

- Double Blind
- Double Dummy

Placebo

Placebo

Placebo

Placebo Abciximab

Reteplase (5U+5U)* Abciximab

Transfer To Cath Lab
ASA, unfractionated heparin 40U/kg (max 3000U)
or enoxaparin (0.5 mg/kg IV + 0.3 mg/kg SC) – substudy only

Abciximab

Placebo

Placebo

Primary PCI with Abciximab Infusion (12 h)

Follow up through 90 days and 1 year
Primary Endpoint

Primary Composite Endpoint at Day 90

- Primary PCI with in lab Abciximab (n=806) - 10.7%
- Abciximab Facilitated PCI (n=818) - 10.5%
- Reteplase/Abciximab Facilitated PCI (n=828) - 9.8%

p=0.55
TIMI Major or Minor Bleeding (nonintracranial) through Discharge/Day 7

**TIMI Bleeding through Discharge/Day 7**

- **TIMI Major**
  - Primary PCI with In Lab Abciximab (n=795)
  - Abciximab Facilitated PCI (n=805)
  - Abciximab/Reteplase Facilitated PCI (n=814)

- **TIMI Minor**
  - p=0.025
  - p=0.547
  - p=0.127

- **TIMI Major or Minor**
  - p<0.001
  - p=0.006
  - p=0.008

- **Percentage**
  - 0%
  - 5%
  - 10%
  - 15%
  - 20%
  - 25%
  - 30%
Facilitation may be finished by FINESSÉ

FINESSÉ and CARESS studies report results
term ‘facilitated PCI’ is not uniformly used for identical settings: it should be used as initially planned PCI, following shortly after initiating thrombolysis and/or GP IIb/IIIa inhibitors. Therefore, in randomized studies testing the concept of facilitated PCI, all patients (with or without pre-treatment) should undergo planned primary PCI.

we prefer primary PCI over thrombolysis in the first 3 h of chest pain to prevent stroke and, in patients presenting 3–12 h after the onset of chest pain, to salvage myocardium and also prevent stroke. At the moment, there is no evidence to recommend facilitated PCI.
FINESSE corroborated the concept of avoiding routine upstream administration of abciximab before primary PCI in STEMI.

FINESSE further confirmed previous ESC guidelines.
TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel

TRITON-TIMI 38
AHA 2007
Orlando, Florida

Disclosure Statement:
The TRITON-TIMI 38 trial was supported by a research grant to the Brigham and Women’s Hospital from Daiichi Sankyo Co. Ltd and Eli Lilly & Co.
Study Design

ACS (STEMI or UA/NSTEMI) & Planned PCI
ASA \[\downarrow\] N = 13,600
Double-blind

- CLOPIDOGREL
  300 mg LD/ 75 mg MD
- PRASUGREL
  60 mg LD/ 10 mg MD

Median duration of therapy - 12 months

1° endpoint: CV death, MI, Stroke
2° endpoints:
  CV death, MI, Stroke, Rehosp-Rec Isch
  CV death, MI, UTVR
  Stent Thrombosis (ARC definite/prob.)
Safety endpoints: TIMI major bleeds, Life-threatening bleeds
Key Substudies: Pharmacokinetic, Genomic
Stent Thrombosis (ARC Definite + Probable)

Any Stent at Index PCI
N= 12,844

 Endpoint (%)

Clopidogrel

 Prasugrel

HR 0.48
P <0.0001
NNT= 77

Days

0 30 60 90 180 270 360 450
Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

Stephen D. Wiviott, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Gilles Montalescot, M.D., Ph.D., Witold Ruzyllo, M.D., Shmuel Gottlieb, M.D., Franz-Joseph Neumann, M.D., Diego Ardissino, M.D., Stefano De Servi, M.D., Sabina A. Murphy, M.P.H., Jeffrey Riesmeyer, M.D., Govinda Weerakkody, Ph.D., C. Michael Gibson, M.D., and Elliott M. Antman, M.D., for the TRITON–TIMI 38 Investigators*

---

**Primary Efficacy End Point**

- Clopidogrel: 12.1
- Prasugrel: 9.9

Hazard ratio: 0.81; 95% CI: 0.73–0.90; P<0.001

**Key Safety End Point**

- Clopidogrel: 1.8
- Prasugrel: 2.4

Hazard ratio: 1.32; 95% CI: 1.03–1.68; P=0.03

---

NOVEMBER 15, 2007

STEMI Subgroup (n = 3534)

CV death / MI / stroke

Clopidogrel: 12.4%
Prasugrel: 10.0%

HR 0.79 (0.65 - 0.97)
P = 0.02
NNT = 42

TIMI major non-CABG bleeds

Clopidogrel: 2.4%
Prasugrel: 2.1%

HR 0.68 (0.54 - 0.87)
P = 0.002

Montalescot G et al Lancet 2009
Diabetic Subgroup (n = 3146)

CV death / MI / stroke

TIMI major non-CABG bleeds

Prasugrel

Clopidogrel

Wiviott SD et al. *Circulation* 2008; 118: 1626-1636
Prasugrel is a serious alternative to Clopidogrel in PCI for ACS. The most benefit is achieved in patients with STEMI and/or Diabetes with a reduction of ischemic events without increased bleeding complications. In patients with stent thrombosis during Clopidogrel, a switch to Prasugrel may be strongly considered. Prasugrel will change future guidelines.
Has the Approach to Coronary Revascularization Changed after Recent Clinical Trials?
Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS)

Mortality and reinfarction at 1 year

F. Zijlstra, MD PhD
Thoraxcenter
University Medical Center Groningen,
The Netherlands
Thrombus Aspiration during Primary Percutaneous Coronary Intervention

Tone Svilaas, M.D., Pieter J. Vlaar, M.Sc., Iwan C. van der Horst, M.D., Ph.D., Gilles F.H. Diercks, M.D., Ph.D., Bart J.G.L. de Smet, M.D., Ph.D., Ad F.M. van den Heuvel, M.D., Ph.D., Rutger L. Anthonio, M.D., Ph.D., Gillian A. Jessurun, M.D., Ph.D., Eng-Shiong Tan, M.D., Albert J.H. Suurmeijer, M.D., Ph.D., and Felix Zijlstra, M.D., Ph.D.

CONCLUSIONS

Thrombus aspiration is applicable in a large majority of patients with myocardial infarction with ST-segment elevation, and it results in better reperfusion and clinical outcomes than conventional PCI, irrespective of clinical and angiographic characteristics at baseline.
<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>Thrombus Aspiration no./total no.</th>
<th>Conventional PCI  no./total no.</th>
<th>Risk Ratio for Aspiration (95% Confidence Interval)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>84/490</td>
<td>129/490</td>
<td>0.65 (0.51–0.83)</td>
<td>0.43</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>52/337</td>
<td>91/356</td>
<td>0.60 (0.44–0.82)</td>
<td>0.34</td>
</tr>
<tr>
<td>Female</td>
<td>32/153</td>
<td>38/134</td>
<td>0.74 (0.49–1.11)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;65 yr</td>
<td>52/202</td>
<td>78/223</td>
<td>0.74 (0.55–0.99)</td>
<td></td>
</tr>
<tr>
<td>≤65 yr</td>
<td>32/288</td>
<td>51/267</td>
<td>0.58 (0.39–0.88)</td>
<td></td>
</tr>
<tr>
<td>Total ischemic time</td>
<td></td>
<td></td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td>≥180 min</td>
<td>58/256</td>
<td>75/243</td>
<td>0.73 (0.55–0.99)</td>
<td></td>
</tr>
<tr>
<td>&lt;180 min</td>
<td>20/222</td>
<td>46/231</td>
<td>0.45 (0.28–0.74)</td>
<td></td>
</tr>
<tr>
<td>Infarct-related vessel</td>
<td></td>
<td></td>
<td></td>
<td>0.19</td>
</tr>
<tr>
<td>RCA</td>
<td>18/177</td>
<td>42/199</td>
<td>0.48 (0.29–0.81)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>66/313</td>
<td>87/291</td>
<td>0.71 (0.53–0.93)</td>
<td></td>
</tr>
<tr>
<td>Infarct-related segment</td>
<td></td>
<td></td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>Proximal lesion</td>
<td>41/290</td>
<td>72/307</td>
<td>0.60 (0.43–0.85)</td>
<td></td>
</tr>
<tr>
<td>No proximal lesion</td>
<td>43/200</td>
<td>57/183</td>
<td>0.69 (0.49–0.97)</td>
<td></td>
</tr>
<tr>
<td>TIMI flow grade before PCI</td>
<td></td>
<td></td>
<td></td>
<td>0.54</td>
</tr>
<tr>
<td>0 or 1</td>
<td>62/275</td>
<td>96/306</td>
<td>0.72 (0.55–0.95)</td>
<td></td>
</tr>
<tr>
<td>2 or 3</td>
<td>22/210</td>
<td>31/179</td>
<td>0.60 (0.36–1.01)</td>
<td></td>
</tr>
<tr>
<td>Thrombus seen on angiography</td>
<td></td>
<td></td>
<td></td>
<td>0.58</td>
</tr>
<tr>
<td>Yes</td>
<td>39/236</td>
<td>60/221</td>
<td>0.61 (0.43–0.87)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>44/241</td>
<td>68/262</td>
<td>0.70 (0.50–0.98)</td>
<td></td>
</tr>
</tbody>
</table>

Cardiac death and reinfarction after 1 year in the Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS): a 1-year follow-up study

Pieter J Vlaar*, Tone Svilaas*, Iwan C van der Horst, Gilles F H Diercks, Marieke L Fokkema, Bart J G L de Smet, Ad F M van den Heuvel, Rutger L Anthonio, Gillian A Jessurun, Eng-Shiong Tan, Albert J H Suarezijer, Felix Zijlstra

![Graph showing the comparison of all-cause mortality between Conventional PCI and Thrombus aspiration.](image)

1. Primary endpoint was a surrogate (myocardial blush), therefore not powered to show a mortality reduction.
2. Aspiration was performed only in 84% of the patients.
3. PCI was performed only in 94%.

The huge and statistically significant reduction in mortality after 1y from 7.6% to 4.0% (almost 50%) is surprising in the light of:

- Only a modest benefit in improvement of the surrogate parameters, like myocardial blush and ST-segment resolution.
- No improvement of peak CK and peak CK-MB.
Cardiac death and reinfarction after 1 year in the Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study (TAPAS): a 1-year follow-up study

Pieter J Vlaar*, Tone Svilaas*, Iwan C van der Horst, Gilles F H Diercks, Marieke L Fokkema, Bart J G L de Smet, Ad F M van den Heuvel, Rutger L Anthonio, Gillian A Jessurun, Eng-Shiong Tan, Albert J H Suurmeijer, Felix Zijlstra

<table>
<thead>
<tr>
<th></th>
<th>Thrombus aspiration (N=535)</th>
<th>Conventional PCI (N=536)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final TIMI flow 3</td>
<td>431/501 (86.0%)</td>
<td>409/496 (82.5%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Distal epicardial vessel</td>
<td>25/446 (5.6%)</td>
<td>25/434 (5.8%)</td>
<td>0.92</td>
</tr>
<tr>
<td>obstruction after PCI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak creatine kinase (total)</td>
<td>N=421</td>
<td>N=418</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>565 (247–1506)</td>
<td>637 (291–1420)</td>
<td>0.24</td>
</tr>
<tr>
<td>Time to peak creatine kinase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(total), h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>8 (5–12)</td>
<td>7 (5–12)</td>
<td>0.84</td>
</tr>
<tr>
<td>Peak creatine kinase-MB</td>
<td>N=406</td>
<td>N=405</td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>58 (24–118)</td>
<td>63 (30–114)</td>
<td>0.46</td>
</tr>
<tr>
<td>Time to peak creatine kinase-MB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>7 (5–10)</td>
<td>7 (5–10)</td>
<td>0.80</td>
</tr>
</tbody>
</table>
Role of adjunctive thrombectomy and embolic protection devices in acute myocardial infarction: a comprehensive meta-analysis of randomized trials

Anthony A. Bavry¹, Dharam I. Kumbhani², and Deepak L. Bhatt³*

Figure 3 Incidence of mortality with similar type adjunctive thrombectomy devices grouped together.
Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation

Table 5  Reperfusion therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reperfusion therapy is indicated in all patients with history of chest pain/discomfort of &lt; 12 h and with persistent ST-segment elevation or (presumed) new left bundle-branch block</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>GPIIb/IIa antagonist</td>
<td>ll&lt;sup&gt;a&lt;/sup&gt;</td>
<td>A</td>
</tr>
<tr>
<td>Abciximab</td>
<td>I&lt;sup&gt;a&lt;/sup&gt;</td>
<td>A</td>
</tr>
<tr>
<td>Tirofibran</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Eptifibatide</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Antithrombin therapy&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>ll&lt;sup&gt;a&lt;/sup&gt;</td>
<td>B</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Adjunctive devices</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombus aspiration</td>
<td>ll&lt;sup&gt;b&lt;/sup&gt;</td>
<td>B</td>
</tr>
</tbody>
</table>
Take Home Messages from TAPAS:

- Before stenting patients with STEMI, manual thrombus extraction should be strongly considered.
- TAPAS was a single center study and should be confirmed by a large multicenter trial.
- TAPAS has already changed the ESC guidelines.
SYNTAX Randomized Trial

De novo disease acceptable for revascularization

N=3300

- Left main disease and/or
- 3-vessel disease

Randomize 1500

CABG registry N=2750

PCI registry N=50

Primary NI endpoint – 1 year MACCE
All cause death, MI, cerebrovascular events, repeat revascularization

Led by Patrick Serruys and Frederick Mohr
The Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery: The SYNTAX Study

Primary Endpoint Results at One Year in the Randomized Cohort

Patrick W. Serruys MD PhD
Friedrich W. Mohr MD PhD
On behalf of the SYNTAX investigators

Conflicts of Interest: None
SYNTAX Eligible Patients

De novo disease

Limited Exclusion Criteria
- Previous interventions
- Acute MI with CPK > 2x
- Concomitant cardiac surgery

Left Main Disease
(isolated, +1, +2 or +3 vessels)

3 Vessel Disease
(revasc all 3 vascular territories)
The primary clinical endpoint is the 12 Month major Cardiovascular or Cerebrovascular event rate *(MACCE)*

- MACCE is defined as:
  - All cause Death
  - Cerebrovascular Accident (CVA/Stroke)
  - Documented Myocardial Infarction (ARC definition)
  - Any Repeat Revascularization (PCI and/or CABG)
- All events CEC Adjudicated

*ARC MACCE definition Circ 2007; 115:2344–2351*
All-Cause Death/CVA/MI to 12 Months

CABG (N=897)  TAXUS (N=903)

$P=0.98^*$

Event Rate ± 1.5 SE. *Fisher's Exact Test
PCI is "not non-inferior" to Bypass Surgery
Repeat Revascularization to 12 Months

CABG (N=897)  TAXUS (N=903)

<table>
<thead>
<tr>
<th>Event Type</th>
<th>CABG Group (%)</th>
<th>PCI Group (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI</td>
<td>4.7</td>
<td>11.4</td>
</tr>
<tr>
<td>CABG</td>
<td>1.3</td>
<td>2.8</td>
</tr>
</tbody>
</table>

P < 0.0001*

Event Rate ± 1.5 SE. *Fisher’s Exact Test

ITT population
CVA to 12 Months

- CABG (N=897)
- TAXUS (N=903)

$p=0.003^*$

Cumulative Event Rate (%)

Months Since Allocation

Event Rate ± 1.5 SE. *Fisher’s Exact Test

ITT population
All-Cause Death to 2 Years

ITT population

P = 0.24

Cumulative Event Rate (%)

Before 1 year*
3.5% vs 4.4%
P = 0.37

After 1 year*
1.5% vs 1.9%
P = 0.53

CABG (N=897)  TAXUS (N=903)

Months Since Allocation

Cumulative KM Event Rate ± 1.5 SE; log-rank P value; *Binary rates

ITT population
Repeat Revascularization to 2 Years

ITT population

CABG (N=897)  TAXUS (N=903)

$P<0.001$

Before 1 year*
5.9% vs 13.5%
$P<0.001$

After 1 year*
3.7% vs 5.6%
$P=0.06$

Cumulative KM Event Rate ± 1.5 SE; log-rank $P$ value; *Binary rates

Cumulative Event Rate (%)

Months Since Allocation

ITT population
2 Year Outcomes in 3VD and LM Subgroups

3 Vessel Disease
- n=1095
- Death/CVA/MI: 8.2%
- Revasc: 7.5%
- MACCE: 14.4%
- P=0.11

Left Main Disease
- n=705
- Death/CVA/MI: 11.8%
- Revasc: 10.2%
- MACCE: 19.3%
- P=0.48

Time-to Event; Log-rank P value

ITT population
There is ‘3-vessel disease’ and ‘3-vessel disease’

SYNTAX-Score > 33:
Consider to prefer Bypass Surgery!
Welcome to the SYNTAX Score website. The SYNTAX Score is a unique tool to score complexity of coronary artery disease. However, it is very important to use this new scoring tool correctly, hence, it is strongly recommended to complete the tutorial first.

Introducing the SYNTAX Score at EuroPCR 2009
SYNTAX score, an excellent by-product

One interesting product of the study is the SYNTAX score. The more complex the coronary anatomy - ie, the higher the SYNTAX score - the better the outcomes of CABG as opposed to PCI. If the SYNTAX score is low, the two therapies seemed comparable in terms of outcomes. This Score taken together with the clinical profile will help in patient selection for the most appropriate technique.

Why does SYNTAX not represent the best surgical management of CABG? “The internal thoracic artery: The drug eluting graft!”

Only 18.9% of patients in the SYNTAX trial had pure
SYNTAX: Diabetic Patients

- Bypass Surgery (n=204)
- TAXUS Stent (n=227)

**Event Rates in Diabetic Patients (%)**

- MI: 4.4% (P=0.83)
- Stroke: 2.5% (P=0.26)
- Repeat Revascularisation: 6.4% (P<0.001)
- Total Event Rate: 20.3%
SYNTAX did not reach its primary endpoint, because repeat revascularization was a part of it.

After 2 years, repeat revascularization was 17.4% in the TAXUS-DES group and still significantly higher than the 8.6% in the CABG group.

The advantage of bypass surgery over PCI was especially prominent in patients with diabetes.

However, stroke was significantly higher after bypass surgery.

With the data from SYNTAX, PCI of unprotected left main stenosis is a true option for some patients with stable CAD.

The SYNTAX-Score is purely anatomic and is helpful for decision making of DES vs. surgery, esp. after correction for functional parameters.

SYNTAX will change future ESC guidelines.
CARDia Trial Design

Diabetic patients with multivessel disease or complex single vessel disease

Suitable for PCI or CABG

Inclusion and exclusion criteria met

CONSENT

Randomisation

Conventional CABG N=254

Optimal PCI stent + abciximab N=256

DES 71%
BMS 29%
CARDIA
(Coronary Artery Revascularization Diabetes Trial)

- 510 diabetic pts randomized to CABG vs PCI (71% DES)

![Graph showing outcomes of CABG vs PCI for various cardiac events]

- Death: 3.3% CABG, 3.9% Stent, p=0.02
- Non-fatal MI: 5.7% CABG, 6.2% Stent
- Non-fatal stroke: 0.0% CABG, 2.5% Stent
- Death, MI, stroke: 10.2% CABG, 10.1% Stent
- Revascularization: 7.3% CABG, 11.0% Stent, p=0.65

ESC, 2008
FRACTIONAL FLOW RESERVE versus ANGIOGRAPHY FOR GUIDING PCI IN PATIENTS WITH MULTIVESSEL CORONARY ARTERY DISEASE

Late Breaking Trial at
TCT, October 14 th , 2008

Nico H.J.Pijls, MD, PhD
Catharina Hospital, Eindhoven
The Netherlands,
on behalf of the FAME investigators
Patient with stenoses ≥ 50% in at least 2 of the 3 major epicardial vessels

Indicate all stenoses ≥ 50% considered 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 study: Event-free Survival

absolute difference in MACE-free survival

Days since Randomization

Survival Free of MACE

30 days 2.9%

90 days 3.8%

180 days 4.9%

360 days 5.3%
Routine measurement of FFR during PCI with DES in patients with multivessel disease, when compared to current angiography guided strategy, furthermore:

- is cost-saving and does not prolong the procedure

- reduces the number of stents used

- decreases the amount of contrast agent used

- results in a similar, if not better, functional status
Guidelines for Percutaneous Coronary Interventions
The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology

50% - 70% Diameter stenosis
ischaemia not documented/
or no prior stress imaging

> 0.80  FFR  < 0.75

Defer PCI  Perform PCI
FFR vs. Angiography for Multivessel Evaluation

FAME
2 Year Follow-Up

William F. Fearon, Pim A.L. Tonino, Bernard De Bruyne, Uwe Siebert and Nico H.J. Pijls, on behalf of the FAME Study Investigators
2 Year Survival Free of MACE

- **FFR-Guided**
- **Angio-Guided**

730 days, 4.5%
FAME corroborated the findings of DEFER for multivessel disease suggesting to obtain from stenting, if FFR is > 0.8.

Thus, FFR may be cost saving, avoiding unnecessary stenting.

FAME further confirmed previous ESC guidelines.
TRANSFER-AMI: Should urgent transfer after fibrinolysis now be standard of care?

Warren J. Cantor, MD

Medical Director, Interventional / Invasive Program,
Southlake Regional Health Centre
Newmarket, Ontario, Canada

Assistant Professor, University of Toronto
High Risk ST Elevation MI within 12 hours of symptom onset

TNK + ASA + Heparin or Enoxaparin + Clopidogrel

Randomization

Pharmacoinvasive Strategy
Urgent Transfer to PCI Centre

Standard Treatment

Assess chest pain, ST\uparrow resolution at 60-90 minutes after randomization

Failed Reperfusion**

Cath / PCI within 6 hrs regardless of reperfusion status

Cath and Rescue PCI ± GP IIb/IIIa Inhibitor

Successful Reperfusion

Elective Cath ± PCI > 24 hrs later

Repatriation of stable patients within 24 hrs of PCI

** ST segment resolution < 50% & persistent chest pain, or hemodynamic instability
TRANSFER-AMI Sites

- Manitoba: 2 PCI Centres, 5 Sites
- Ontario: 8 PCI Centres, 30 Sites
- Montreal: 1 PCI Centre, 1 Site
Primary Endpoint:
30-Day Death, re-MI, Heart Failure, Severe Recurrent Ischemia, Cardiogenic Shock

% of Patients

<table>
<thead>
<tr>
<th>Standard (n=496)</th>
<th>Pharmacoinvasive (n=508)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.6</td>
<td>10.6</td>
</tr>
</tbody>
</table>

OR = 0.537
(0.368, 0.783)
p = 0.0013
Routine Early Angioplasty after Fibrinolysis for Acute Myocardial Infarction

Warren J. Cantor, M.D., David Fitchett, M.D., Thomas G. Lessing, M.D., John Ducas, M.D., Michael Heffernan, M.D., Eric A. Colby, M.D., Jon J. T. Stone, M.D., Anatoly Langer, M.D., Vladimir Dzavik, M.D., Shant H. Manoharan, M.D., James Lazzam, M.D., Brian Schwartz, M.D., Amparo Casanova, M.D., Ph.D., and Daniel Eisenberg, M.D., for the TRANSFER-AMI Trial Investigators

CONCLUSIONS

Among high-risk patients who had a myocardial infarction with ST-segment elevation and who were treated with fibrinolysis, transfer for PCI within 6 hours after fibrinolysis was associated with significantly fewer ischemic complications than was standard treatment.
Guidelines for Percutaneous Coronary Interventions
The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology

<table>
<thead>
<tr>
<th>Routine post-thrombolysis coronary angiography and PCI, if applicable</th>
<th>Up to 24 h after thrombolysis, independent of angina and/or ischaemia</th>
<th>I A</th>
</tr>
</thead>
</table>

SIAM III
GRACIA-1
CAPITAL-AMI
The GRACIA – 1 trial

(Gruppo de Análisis de la Cardiopatía Isquémica Aguda)

ESC 2003

Randomised trial comparing stenting within 24 hours of thrombolysis versus conservative ischaemia-guided approach to STEMI

One-year Results

Francisco F. Avilés
(on behalf of the GRACIA group)
GRACIA – 1

One – year outcome

REVASCULARIZATION

CONSERVATIVE: 14%

INTERVENTIONAL: 4%

Log-rank test: p=0.0005
TRANSFER-AMI corroborated the concept of routine coronary angiography with PCI, if applicable, after thrombolysis.

TRANSFER-AMI further confirmed previous ESC guidelines.
Has the Approach to Coronary Revascularization Changed after Recent Clinical Trials?
Of the four studies comparing Cypher stents to Taxus stents, one did not define the primary endpoint (TAXi\textsuperscript{19}), two assumed superiority of the Cypher stent (REALITY\textsuperscript{20} and SIRTAX\textsuperscript{21}), and one was designed as a non-inferiority trial (ISAR-Diabetes\textsuperscript{22}) (Table 5). The multicenter REALITY trial did not reach the primary endpoint, whereas the single-center SIRTAX trial did (Table 5). No randomized, controlled multicenter trial with a primary clinical endpoint and adequate power calculation exists, showing that one DES is superior to another.
CONCLUSIONS
As compared with paclitaxel-eluting stents, the use of sirolimus-eluting stents results in fewer major adverse cardiac events, primarily by decreasing the rates of clinical and angiographic restenosis.
SIRTAX-LATE

5-Year Clinical and Angiographic Follow-up From a Prospective, Randomized Trial Comparing Sirolimus-Eluting With Paclitaxel-Eluting Stents

Lorenz Räber, Mario Togni, Simon Wandel
Mathias Wigger, Lea Wohlwend, Stéphane Cook,
Peter Wenaweser, Christian Seiler, Franz Eberli,
Thomas Lüscher, Bernhard Meier, Peter Jüni
and Stephan Windecker

Funded by Bern University Hospital, Switzerland
Flow of Patients – Clinical F/U Through 5 Years

Randomized (N=1,012)

SES (N=503)  PES (N=509)

Lost to f/u = 3  3 = Lost to f/u
Patient withdrawal = 0  0 = Patient withdrawal

1-year follow-up (N=1,006; 99.4%)

SES (N=500)  PES (N=506)

Lost to f/u = 12  20 = Lost to f/u
Patient withdrawal = 0  0 = Patient withdrawal

5-year follow-up (N=974; 96.8%)

SES (N=488)  PES (N=486)
Major Adverse Cardiac Events @ 5 Years

Cumulative Incidence of MACE (%)

1 year HR
0.59 [0.40 – 0.86]  
P<0.01

5 year HR
0.85 [0.65 – 1.10]  
P=0.21

Δ 1 year
5.5%

Δ 5 year
2.9%

SES

PES
Major Adverse Cardiac Events

Landmark-Analysis

1 year HR
0.59 [0.40 – 0.86]
P<0.01

1-5 years HR
1.18 [0.84 – 1.65]
P=0.35
Target lesion Revascularization

Landmark-Analysis

1 year HR
0.54 [0.34 – 0.84]
P < 0.01

1-5 year HR
1.15 [0.77 – 1.73]
P = 0.49

Cumulative Incidence of TLR (%)

Years

SES

PES
There is no clinical difference between Cypher and Taxus.
SIRTAX-LATE further confirmed previous ESC guidelines.
The problem of long-term follow-up with DES:
  when the results are available, the DES will be replaced:
  - Cypher will be replaced by the Nevo Sirolimus-eluting stent
  - Taxus Liberté will be replaced by the Taxus Element Paclitaxel-eluting stent
A Natural History Study of Atherosclerosis Using Multimodality Intracoronary Imaging to Prospectively Identify Vulnerable Plaque

Gregg W. Stone, MD

PROSPECT Investigators

Providing Regional Observations to Study Predictors of Events in the Coronary Tree

The PROSPECT Trial
The PROSPECT Trial

3-vessel imaging post PCI

Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

IVUS

Virtual histology

Palpography (n=\(\sim\)350)

Meds rec
Aspirin
Plavix 1yr
Statin
Repeat biomarkers
@ 30 days, 6 months

F/U: 1 mo, 6 mo, 1 yr, 2 yr, \(\pm\) 3-5 yrs

Repeat imaging in pts with events

MSCT Substudy
N=50-100

Proximal 6-8 cm of each coronary artery
Lesions are classified into 5 main types

1. Fibrotic
2. Fibrocalcific
3. Pathological intimal thickening (PIT)
4. Thick cap fibroatheroma (ThCFA)
5. VH-thin cap fibroatheroma (VH-TCFA) (presumed high risk)
PROSPECT: Correlates of Non Culprit Lesion Related Events

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>HR (95% CI)</th>
<th>P value</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCFA</td>
<td>3.8 (2.2, 6.6)</td>
<td>&lt;0.0001</td>
<td>51.2%</td>
</tr>
<tr>
<td>MLA ≤4.0mm²</td>
<td>5.0 (2.9, 8.7)</td>
<td>&lt;0.0001</td>
<td>49.1%</td>
</tr>
<tr>
<td>PB ≥70%</td>
<td>7.9 (4.6, 13.8)</td>
<td>&lt;0.0001</td>
<td>30.7%</td>
</tr>
<tr>
<td>MLA ≤4mm² + TCFA</td>
<td>6.4 (3.4, 12.2)</td>
<td>&lt;0.0001</td>
<td>17.4%</td>
</tr>
<tr>
<td>PB ≥70% + MLA ≤4mm²</td>
<td>6.7 (3.4, 13.0)</td>
<td>&lt;0.0001</td>
<td>15.4%</td>
</tr>
<tr>
<td>PB ≥70% + TCFA</td>
<td>10.8 (5.5, 21.0)</td>
<td>&lt;0.0001</td>
<td>11.0%</td>
</tr>
<tr>
<td>PB ≥70% + MLA ≤4mm² + TCFA</td>
<td>10.8 (4.3, 27.2)</td>
<td>&lt;0.0001</td>
<td>4.6%</td>
</tr>
</tbody>
</table>

*Likelihood of one or more such lesions being present per patient. PB = plaque burden at the MLA
The combination of IVUS and Virtual Histology is a useful diagnostic tool to assess the non-culprit lesions after having stented the culprit lesion in patients with ACS.

PROSPECT may possibly change future ESC guidelines.
Most of the recent randomized trials have further underlined the existing concepts of coronary revascularization and confirmed the ESC guidelines.

SYNTAX has probably the greatest impact on changing the approaches to coronary revascularization:
- identifying patients predominantly benefiting from bypass surgery
- stenting of unprotected left main as an option

Based on DEFER, FAME and PROSPECT, the combination of FFR (fractional flow reserve), IVUS and VH (virtual histology) may better identify „insignificant“ lesions to be stented or to be treated conservatively in order to improve patients‘ prognosis.
Guidelines for Percutaneous Coronary Interventions

The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology

Authors/Task Force Members: Sigmund Silber, Chairperson* (Germany), Per Albertsson (Sweden), Francisco F. Avilés (Spain), Paolo G. Camici (UK), Antonio Colombo (Italy), Christian Hamm (Germany), Erik Jørgen (Denmark), Jean Marco (France), Jan-Erik Nordlander (Sweden), Witold Ruzyillo (Poland), Philip H. Thompson (UK), William Wijns (Belgium)

European Heart Journal (2005) 26, 804–847