Incorporating randomised trials in guidelines

W. Wijns
Aalst, B

Saturday October 16, 2010
## Evidence basis

<table>
<thead>
<tr>
<th></th>
<th>RCT</th>
<th>Registries (Propensity Matched)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strengths</strong></td>
<td><strong>No Bias</strong></td>
<td>Large Numbers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Represent real clinical practice</td>
</tr>
<tr>
<td><strong>Potential Weaknesses</strong></td>
<td></td>
<td><strong>Confounding/Bias</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Levels of Evidence (LOE)

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Data derived from multiple randomized clinical trials or meta-analyses.</td>
</tr>
<tr>
<td>B</td>
<td>Data derived from a single randomized clinical trial or large non-randomized studies.</td>
</tr>
<tr>
<td>C</td>
<td>Consensus of opinion of the experts and/or small studies, retrospective studies, registries.</td>
</tr>
</tbody>
</table>
## Evidence basis

<table>
<thead>
<tr>
<th></th>
<th>RCT</th>
<th>Registries</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The Gold standard</td>
<td>(Propensity Matched)</td>
</tr>
<tr>
<td><strong>Strengths</strong></td>
<td><strong>No Bias</strong></td>
<td>Large Numbers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Represent real clinical practice</td>
</tr>
<tr>
<td><strong>Potential Weaknesses</strong></td>
<td>Small numbers of patients</td>
<td>Confounding/Bias</td>
</tr>
<tr>
<td></td>
<td>Small % of eligible population</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atypical patient populations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Short duration of follow-up</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Large numbers of cross-overs</td>
<td></td>
</tr>
</tbody>
</table>

[Joint 2010 ESC - EACTS Guidelines on Myocardial Revascularisation](www.escardio.org/guidelines)
Acute Cardiac Care 2010
Stent or Lysis? It’s a matter of time
Incorporating randomised trials (RCT) in guidelines

- Levels of evidence
- Endpoints of RCT
- Weight of RCT
- Meta-analyses
- Integration
- C level

Saturday October 16, 2010
Endpoints for RCT

• Hard event endpoints: (cardiac) death, stroke, MI (wild type)
• Soft(er) endpoints: periprocedural MI, revascularization, ischaemia
Cardiovascular death

18,624 ACS UA/NSTEMI or STEMI (if primary PCI)
All receiving ASA; clopidogrel-treated or -naïve

HR 0.79 (95% CI 0.69–0.91), P=0.001
NNT = 90
Endpoints for RCT

- Hard event endpoints: (cardiac) death, stroke, MI (wild type)
- Soft(er) endpoints: periprocedural MI, revascularization, ischaemia
- Surrogate endpoints, mostly angiographic:
  TIMI flow rate / infarct size / QCA metrics (late loss)
Validated drug-eluting stents (DES) for clinical use

<table>
<thead>
<tr>
<th>DES</th>
<th>Eluted Drug</th>
<th>Trials and references</th>
</tr>
</thead>
<tbody>
<tr>
<td>BioMatrix Flex</td>
<td>Biolimus A9</td>
<td>LEADERS</td>
</tr>
<tr>
<td>Cypher</td>
<td>Sirolimus</td>
<td>SIRIUS</td>
</tr>
<tr>
<td>Endeavor</td>
<td>Zotarolimus</td>
<td>ENDEAVOR-II, -III and -IV</td>
</tr>
<tr>
<td>Resolute</td>
<td>Zotarolimus</td>
<td>RESOLUTE-AC</td>
</tr>
<tr>
<td>Taxus Liberté/Element</td>
<td>Paclitaxel</td>
<td>TAXUS-IV and -V/PERSEUS-WH</td>
</tr>
<tr>
<td>Xience V</td>
<td>Everolimus*</td>
<td>SPIRIT-III and –IV</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical primary endpoint reached</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Angiographic primary endpoint reached</strong></td>
</tr>
</tbody>
</table>

Selection is based on adequately powered RCT with a primary clinical or angiographic endpoint.

With the exception of LEADERS and RESOLUTE (all-comers trials), efficacy was investigated in selected de novo lesions of native coronary arteries.

*Promus Element device elutes everolimus from a different stent platform.
Endpoints for RCT

- Hard event endpoints: (cardiac) death, stroke, MI (wild type)
- Soft(er) endpoints: periprocedural MI, revascularization, ischaemia
- Surrogate endpoints, mostly angiographic:
  - TIMI flow rate / infarct size / QCA metrics
- Intermediate endpoints, mostly mechanistic (imaging based)
- Composite endpoints
  - Triple, quadruple, or multiple mix

Issues are hierarchy, (in)consistency
Optimal timing for invasive treatment

Meta-analysis of 4 major trials (n = 4013)
EARLY (1.2-14 hours) vs DELAYED (20-86 hours)

Katritsis et al. Eur H J;2010, online August 13
Organization of STEMI patient disposal describing pre- and in-hospital management, and reperfusion strategies within 12 h of First Medical Contact (FMC)

Symptoms of STEMI

EMS
- Pre-hospital diagnosis & care
  - Ambulance to Cath
  - Primary PCI capable centre

GP / Cardiologist
- Immediate transfer to Cath Lab
  - Primary PCI

Self referral
- Private transportation
  - Non-primary PCI capable centre
    - PCI possible < 2 h
      - yes
        - Immediate transfer to Cath Lab
      - no
        - Immediate fibrinolysis
  - no

Self referral
- Yes
  - Primary PCI

Self referral
- No
  - Primary PCI
Reperfusion Strategies

‘High Risk’ ST Elevation MI within 12 hours of symptom onset

TNK + ASA + Heparin / Enoxaparin + Clopidogrel

“Pharmacoinvasive Strategy”
Urgent Transfer to PCI Centre (within 6 h)

“Standard Treatment”
Assess chest pain, ST↑ resolution at 60-90 minutes after randomization

Failed Reperfusion*
Successful Reperfusion

PCI Centre
Cath Lab
Cath / PCI within 6 hrs regardless of reperfusion status
Cath and Rescue PCI ± GP IIb/IIIa Inhibitor
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

Randomisation stratified by age (≤75 vs. > 75) and by enrolling site

Reperfusion Strategies

Primary Endpoint: 30-Day Death, re-MI, CHF, Severe Recurrent Ischemia, Shock


OR=0.64 (0.47, 0.87); p=0.004

Standard (n=496)  
Pharmacoinvasive (n=508)

Days from Randomization

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=496</td>
<td>422</td>
<td>415</td>
<td>415</td>
<td>414</td>
<td>414</td>
<td>412</td>
<td></td>
</tr>
<tr>
<td>n=508</td>
<td>468</td>
<td>466</td>
<td>463</td>
<td>461</td>
<td>460</td>
<td>457</td>
<td></td>
</tr>
</tbody>
</table>
## Recommendations for PCI in STEMI

<table>
<thead>
<tr>
<th>Indication</th>
<th>Time from FMC</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PCI after fibrinolysis:</strong></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</td>
<td>I</td>
<td>A</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>
</tr>
</tbody>
</table>

In order to reduce delay for patients with no reperfusion, transfer to PCI center of all post-fibrinolysis patients is recommended.
Organization of STEMI patient disposal describing pre- and in-hospital management, and reperfusion strategies within 12 h of First Medical Contact (FMC)

Symptoms of STEMI

EMS
- Pre-hospital diagnosis & care
- Ambulance to Cath
- Primary PCI capable centre
- Primary PCI
- Rescue PCI

GP / Cardiologist

Self referral
- Private transportation

Non-primary PCI capable centre
- PCI possible < 2 h
- yes
- no

Successful fibrinolysis?
- yes
- Immediate fibrinolysis
- no
- Transfer to ICU of PCI-capable centre
- Immediate transfer to Cath Lab

Coronary Angiography 3 to 24 h after FMC
- Delayed PCI as required
Endpoints for RCT

- Hard event endpoints: (cardiac) death, stroke, MI (wild type)
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- Surrogate endpoints, mostly angiographic:
  - TIMI flow rate / infarct size / QCA metrics
- Intermediate endpoints, mostly mechanistic (imaging based)
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Benefit / Risk ratio
# ACUITY: Primary Endpoint Measures

## UFH/Enoxaparin + GPI vs. Bivalirudin Alone

<table>
<thead>
<tr>
<th>Primary endpoint</th>
<th>Risk ratio ±95% CI</th>
<th>Bival alone</th>
<th>UFH/Enox + IIb/IIIa</th>
<th>RR (95% CI)</th>
<th>p value (non inferior) (superior)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net clinical outcome</td>
<td>10.1% 11.7% 0.86 (0.77-0.97)</td>
<td>10.1%</td>
<td>11.7%</td>
<td>0.86 (0.77-0.97)</td>
<td>&lt;0.001 0.015</td>
</tr>
<tr>
<td>Ischemic composite</td>
<td>7.8% 7.3% 1.08 (0.93-1.24)</td>
<td>7.8%</td>
<td>7.3%</td>
<td>1.08 (0.93-1.24)</td>
<td>0.02 0.32</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>3.0% 5.7% 0.53 (0.43-0.65)</td>
<td>3.0%</td>
<td>5.7%</td>
<td>0.53 (0.43-0.65)</td>
<td>&lt;0.001 &lt;0.001</td>
</tr>
</tbody>
</table>

Bivalirudin alone better | UFH/Enox + IIb/IIIa better

*NEJM 2006;355:2203*
Acute Cardiac Care 2010
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- Meta-analyses
- Integration
- C level

Saturday October 16, 2010
Weight of RCT

- Size: mega vs large vs small
- Relevance
  - Robust finding (p value)
  - Case selection
  - Generalisable
  - Subgroup analysis (absolute vs RRR)
  - Obsolescence
Intended Early Invasive vs. Conservative Strategy

Long term outcome by initial Risk Score

Meta-analysis of 3 major trials

Fox KA et al. JACC 2010;55(22):2435-45
### 15 RCT of PCI vs CABG in ‘Multivessel’ Disease (Pre-SYNTAX)

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>N</th>
<th>Stent</th>
<th>Included /Eligible</th>
<th>1 or 2 VD</th>
<th>EF &gt;50%</th>
<th>Left Main</th>
<th>Proximal LAD</th>
<th>Diabetes</th>
<th>ITA</th>
</tr>
</thead>
<tbody>
<tr>
<td>RITA</td>
<td>1011</td>
<td>-</td>
<td>4%</td>
<td>88</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>6</td>
<td>74</td>
</tr>
<tr>
<td>ERACI</td>
<td>127</td>
<td>-</td>
<td>9%</td>
<td>55</td>
<td>100</td>
<td>0</td>
<td>-</td>
<td>11</td>
<td>75</td>
</tr>
<tr>
<td>LAUSANNE</td>
<td>134</td>
<td>-</td>
<td>3%</td>
<td>100</td>
<td>-</td>
<td>0</td>
<td>100</td>
<td>12</td>
<td>100</td>
</tr>
<tr>
<td>GABI</td>
<td>359</td>
<td>-</td>
<td>4%</td>
<td>82</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>10</td>
<td>37</td>
</tr>
<tr>
<td>EAST</td>
<td>392</td>
<td>-</td>
<td>4%</td>
<td>60</td>
<td>100</td>
<td>0</td>
<td>70</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>CABRI</td>
<td>1054</td>
<td>-</td>
<td>3%</td>
<td>60</td>
<td>100</td>
<td>0</td>
<td>-</td>
<td>12</td>
<td>75</td>
</tr>
<tr>
<td>MASS</td>
<td>142</td>
<td>-</td>
<td>69%</td>
<td>-</td>
<td>100</td>
<td>0</td>
<td>100</td>
<td>21</td>
<td>100</td>
</tr>
<tr>
<td>BARI</td>
<td>1829</td>
<td>-</td>
<td>12%</td>
<td>59</td>
<td>100</td>
<td>0</td>
<td>36</td>
<td>24</td>
<td>80</td>
</tr>
<tr>
<td>TOULOSE</td>
<td>152</td>
<td>-</td>
<td>3%</td>
<td>71</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>14</td>
<td>58</td>
</tr>
<tr>
<td>SIMA</td>
<td>121</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>100</td>
<td>0</td>
<td>100</td>
<td>11</td>
<td>100</td>
</tr>
<tr>
<td>ERACI II</td>
<td>450</td>
<td>+</td>
<td>2%</td>
<td>44</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>17</td>
<td>88</td>
</tr>
<tr>
<td>AWESOME</td>
<td>454</td>
<td>+</td>
<td>-</td>
<td>55</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>70</td>
</tr>
<tr>
<td>MASS II</td>
<td>408</td>
<td>+</td>
<td>2%</td>
<td>59</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ARTS</td>
<td>1205</td>
<td>+</td>
<td>?5%</td>
<td>68</td>
<td>100</td>
<td>0</td>
<td>-</td>
<td>19</td>
<td>93</td>
</tr>
<tr>
<td>SOS</td>
<td>988</td>
<td>+</td>
<td>?5%</td>
<td>62</td>
<td>100</td>
<td>0</td>
<td>45</td>
<td>14</td>
<td>81</td>
</tr>
<tr>
<td>SUMMARY</td>
<td>8826</td>
<td>5/15</td>
<td>5%</td>
<td>65%</td>
<td>100%</td>
<td>0%</td>
<td>41%</td>
<td>16%</td>
<td>79%</td>
</tr>
</tbody>
</table>

**RCT effectively excluded patients who are known to have the greatest benefit from CABG in favour of those who do not.**

Taggart, ATS 2006
Weight of RCT

- Size: mega vs large vs small
- Relevance
  - Robust finding (p value)
  - Case selection
  - Generalisable
  - Subgroup analysis (absolute vs RRR)
  - Obsolescence

New designs  “All-Comer” Trials
Combined RCT & Registry arms
SYNTAX Trial Design

Heart Team (surgeon & interventional cardiologist)

Amenable for both treatment options

Amenable for only one treatment approach

Stratification: LM and Diabetes

Randomized Arms
N=1800

CABG n=897
3VD n=549 (66.3%)
LM n=348 (33.7%)

TAXUS* n=903
3VD n=546 (65.4%)
LM n=357 (34.6%)

Two Registry Arms
N=1275

CABG n=1077

PCI n=198

*TAXUS Express

62 EU Sites + 23 US Sites

23 US Sites
MACCE to 3 Years

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

Before 1 year
12.4% vs 17.8%
P = 0.002

1–2 years
5.7% vs 8.3%
P = 0.03

2–3 years
4.8% vs 6.7%
P = 0.10

P < 0.001

CABG (N=897)  TAXUS (N=903)
MACCE to 3 Years
SYNTAX CABG Registry

CABG Registry (N=644)

Cumulative KM Event Rate ± 1.5 SE; log-rank P value
Calculated by core laboratory; ITT population

Months Since Allocation

Cumulative Event Rate (%)

Before 1 year*
8.8%

1-2 years*
5.0%

2-3 years*
4.0%

16.4%
MACCE to 3 Years
SYNTAX PCI Registry

PCI Registry (N=192)

Cumulative Event Rate (%)

Months Since Allocation

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

Calculated by core laboratory; ITT population
Weight of RCT

- Size: mega vs large vs small
- Relevance
  - Robust finding (p value)
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  - Generalisable
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  - Obsolescence

New Analyses  “Delphi” Method
MACCE to 3 Years by SYNTAX Score Tercile *Low Scores (0–22)*

### CABG (N=118) vs. PCI (N=104)

<table>
<thead>
<tr>
<th>Event</th>
<th>CABG</th>
<th>PCI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>6.0%</td>
<td>&gt; 2.6%</td>
<td>0.21</td>
</tr>
<tr>
<td>CVA</td>
<td>4.1%</td>
<td>&gt; 0.9%</td>
<td>0.12</td>
</tr>
<tr>
<td>MI</td>
<td>2.0%</td>
<td>&lt; 4.3%</td>
<td>0.36</td>
</tr>
<tr>
<td>Death, CVA or MI</td>
<td>11.0%</td>
<td>&gt; 6.9%</td>
<td>0.26</td>
</tr>
<tr>
<td>Revasc.</td>
<td>13.4%</td>
<td>&lt; 15.4%</td>
<td>0.69</td>
</tr>
</tbody>
</table>

*Site-reported Data; ITT population*

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

TCT 2010 • Three-year Outcomes of the SYNTAX Trial: Left Main Subgroup • Serruys • Slide 29
MACCE to 3 Years by SYNTAX Score Tercile  
*Left Main SYNTAX Score ≥33*

### Cumulative Event Rate (%)

<table>
<thead>
<tr>
<th>Months Since Allocation</th>
<th>CABG (N=149)</th>
<th>PCI</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Left Main SYNTAX Score ≥33**

- **Death:** 7.6% vs. 13.4%; $P=0.10$
- **CVA:** 4.9% vs. 1.6%; $P=0.13$
- **MI:** 6.1% vs. 10.9%; $P=0.18$
- **Death, CVA or MI:** 15.7% vs. 20.1%; $P=0.34$
- **Revasc.:** 9.2% vs. 27.7%; $<0.001$

**P value**

- **Death:** 0.10
- **CVA:** 0.13
- **MI:** 0.18
- **Death, CVA or MI:** 0.34
- **Revasc.:** <0.001

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

Site-reported Data; ITT population
Stent or Lysis? It’s a matter of time
Incorporating randomised trials (RCT) in guidelines

- Levels of evidence
- Endpoints of RCT
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- Integration
- C level

Saturday October 16, 2010
On the current epidemic outburst of meta-analytic rage in interventional cardiology.
### Specific PCI devices and pharmacotherapy

<table>
<thead>
<tr>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

| Manual catheter thrombus aspiration should be considered during PCI of the culprit lesion in STEMI. |
| For PCI of unstable lesions, intravenous abciximab should be considered for pharmacological treatment of no-reflow. |
| Drug-eluting balloons* should be considered for the treatment of in-stent restenosis after prior BMS. |

Based on registries, 1 positive RCT and meta-analyses

**BUT**

the TAPAS RCT is single-center, not powered for differences in mortality (n=1.071), there was no reduction in peak CK and aspiration was performed in 84% of cases
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Saturday October 16, 2010
## Antithrombotic treatment options in myocardial revascularisation

### NSTE-ACS

<table>
<thead>
<tr>
<th>Antiplatelet therapy</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Clopidogrel (with 600 mg loading dose as soon as possible)</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Clopidogrel (for 9-12 months after PCI)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>+ GPIIb-IIIa antagonists (in high-risk patients with elevated Troponin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abciximab (with DAPT)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Tirofiban, Eptifibatide</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Upstream GPIIb-IIIa antagonists</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>

Depending on drug approval and availability.
## Antithrombotic treatment options in myocardial revascularisation

<table>
<thead>
<tr>
<th>NSTE-ACS</th>
<th>Anticoagulation</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>very high-risk of ischaemia</td>
<td>UFH (+ GPIIb-IIIa antagonists)</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>medium-to-high-risk of ischaemia</td>
<td>Bivalirudin (monotherapy)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>low-risk of ischaemia</td>
<td>Fondaparinux</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>Enoxaparin</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

Joint 2010 ESC - EACTS Guidelines on Myocardial Revascularisation
## Antithrombotic treatment options in myocardial revascularisation

<table>
<thead>
<tr>
<th>STEMI</th>
<th>Anticoagulation</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bivalirudin (monotherapy)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>UFH</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>Fondaparinux</td>
<td>III</td>
<td>B</td>
</tr>
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</table>
## Antithrombotic treatment options in myocardial revascularisation

<table>
<thead>
<tr>
<th>STEMI</th>
<th>Antiplatelet therapy</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASA</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>Clopidogrel</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>(with 600 mg loading dose as soon as possible)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prasugrel</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>Ticagrelor</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>+ GPIIb-IIIa antagonists</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>(in patients with evidence of high intracoronary thrombus burden)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abciximab</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>Eptifibatide</td>
<td>IIa</td>
<td>B</td>
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<td></td>
<td>Tirofiban</td>
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Depending on drug approval and availability.
Acute Cardiac Care 2010
Stent or Lysis? It’s a matter of time
Incorporating randomised trials (RCT) in guidelines

- Levels of evidence
- Endpoints of RCT
- Weight of RCT
- Meta-analyses
- Integration
- C level

Saturday October 16, 2010
Levels of Evidence (LOE)

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence A</td>
<td>Data derived from multiple randomized clinical trials or meta-analyses.</td>
</tr>
<tr>
<td>Evidence B</td>
<td>Data derived from a single randomized clinical trial or large non-randomized studies.</td>
</tr>
<tr>
<td>Evidence C</td>
<td>Consensus of opinion of the experts and/or small studies, retrospective studies, registries.</td>
</tr>
</tbody>
</table>

Out of 190 recommendations, 85 (44.7%) are LOE « C » and *may* represent gaps in knowledge.
Parachutes appear to reduce the risk of injury but ... their effectiveness has not been proved with randomised controlled trials.

Level of Evidence = C

Evidence of the « C » level is not necessarily weak!
Incorporating randomised trials in guidelines

W. Wijns
Aalst, B

Saturday October 16, 2010