Management of heavy Thrombotic Burden in STEMI Patients

Hany Eteiba
President, Scottish Cardiac Society
Vice President, Royal College of Physicians and Surgeons
Consultant Interventional Cardiologist
Regional and National Medicine Director
West of Scotland Heart and Lung Centre, Golden Jubilee National
University Department of Cardiology, Glasgow Royal Infirmary

NSTEMI vs STEMI
Thrombus Presence in STEMI

High Thrombus Burden in STEMI

Impact of Thrombus Burden

STEMI ≤ 12 h. 812 patients
Definition: Major thrombus burden ≥ 2 vessel diameter

Sianos G., J Am Coll Cardiol 2007
Distal embolization in AMI is a predictor of more extensive myocardial damage and a poor prognosis.

Occurred in 27/178 pts (15%) after primary PCI.

No-reflow (MVO) portends an adverse prognosis after acute MI.

Half of acute MIs are complicated by microvascular obstruction leading to reduced survival.

Impact of antiplatelet therapy

Early stent thrombosis (Day 0–30)

Proportion of patients (%)

<table>
<thead>
<tr>
<th>Days</th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
<th>p-value</th>
<th>RRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>20</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
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<tr>
<td>30</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
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</tbody>
</table>

Late stent thrombosis (Day 30–450)

Proportion of patients (%)

<table>
<thead>
<tr>
<th>Days</th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
<th>p-value</th>
<th>RRR</th>
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<tbody>
<tr>
<td>90</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
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<tr>
<td>150</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
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<tr>
<td>210</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
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<tr>
<td>270</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
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<tr>
<td>330</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
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<tr>
<td>390</td>
<td>0.0</td>
<td>0.0</td>
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</tr>
<tr>
<td>450</td>
<td>0.0</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
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</table>

Clopidogrel vs. Prasugrel:
- p=0.0001
- RRR=71%

ATTEMPT: “individual patients data” metanalysis. Thrombectomy and GP IIb/IIIa in STEMI

n=2686 pts

Mortality

<table>
<thead>
<tr>
<th>Intervention</th>
<th>30d</th>
<th>12 month</th>
<th>15 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombectomy - IIb/IIIa inb -</td>
<td>7.4%</td>
<td>5.0%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Thrombectomy - IIb/IIIa inb +</td>
<td>5.0%</td>
<td>4.8%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Thrombectomy + IIb/IIIa inb -</td>
<td>7.4%</td>
<td>5.0%</td>
<td>3.3%</td>
</tr>
<tr>
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Burzotta et al, 2009

p=0.02
Aspiration Thrombectomy
No current proof in adequately powered RCT that it reduce hard clinical end point

Distal protection devices
Demonstrated benefit in SVG

Mesh Covered stents
Improve ST resolution, but ? Impact on clinical outcome

IIa/IIb antagonist
IC No benefit
Via clear way, reduce infarct size but no clinical benefit
Pathophysiology of MVO

*Fibrin rich microthrombii*

Capillary obstruction with fibrin-microthrombii

→ Capillary damage border zone (viable)

→ Haemorrhagic transformation / clot in core

Prevention of MVO

• Empirical: reduce ischaemic time, anti-thrombotic therapy

Treatment of MVO

• Intra-coronary vasodilators (no evidence for benefit and potential for harm cf REFLOW trial).

• Glycoprotein IIbIIIa – ineffective (INFUSE-AMI trial)

Overall, there are no evidence-based treatments for MVO. Therapy is empirical.
**Rationale**
In selected patients with risk factors for no-reflow, restored flow & anti-thrombotic therapies reduce thrombus burden such that stenting 4 – 16 hrs later is **safe and effective**.

**Results**

**Primary Endpoint**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Immediate Stenting</th>
<th>Deferred Stenting</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>No-reflow (TIMI 0/1)</td>
<td>2</td>
<td>6</td>
<td>0.054</td>
</tr>
<tr>
<td>No/slow-reflow (TIMI&lt;3)</td>
<td>29</td>
<td>33</td>
<td>0.006</td>
</tr>
<tr>
<td>Complications (IPTEs)</td>
<td>33</td>
<td>10</td>
<td>0.008</td>
</tr>
</tbody>
</table>
MRI Results
Secondary Endpoint

Median time to deferred stenting: 9 (6 – 12) hrs

Myocardial salvage index

Fibrinolysis
Back to the future?

Pharmacology

- Man-made, recombinant form of tPA
- Second-generation thrombolytic (T_{1/2} = 5 min)
- Fibrin-specific
- Standard dose = 100 mg for MI, stroke, PTE
- 10 mg dose for venous catheter blockages
- Full dose thrombolysis + primary PCI is harmful
- Optimise pharmaco-invasive strategy?
UK Multicentre Randomised Control Trial
Intra-coronary Fibrinolysis For MV obstruction

Participating sites

Chief Investigator: Prof Colin Berry
Principle Investigator: Dr Hany Eteiba

www.glasgowctu.org/TTIME

Hypothesis for efficacy
Compared with placebo, intra-coronary low dose fibrinolysis will reduce microvascular obstruction which in turn will be associated with improvements in surrogate outcomes.

Hypothesis for safety
Reduced dose intra-coronary alteplase will be safe and will not be associated with an excess of bleeds.
Current Research : T-Time

Intra-Coronary Administration of Study Drug
(10 ml + 10 ml)

Guide catheter

Aorta

+/- Thrombectomy catheter - local infusion

Clot

Placebo 10 ml

Alteplase 10 mgs

Alteplase 20 mgs

Conclusions

Heavy Thrombus burden in STEMI patient carries an increased risk of MVO

Mechanical devices may be helpful at times but no proof of its efficacy on reducing hard clinical end points in adequately powered randomized trials

A period of optimum pharmacotherapy with timely mechanical intervention is a pragmatic approach which could be effective in selected patients with high thrombotic burden

Reduced IC Thrombolytic therapy is an emerging concept currently being explored in T-Time randomised trial.
Case Presentation

- AW 70 year-old retired General Surgeon, ACS with dynamic ST-T changes
- ex-smoker, positive family history of IHD
- Past History: hypertension, dyslipidaemia
- CABG 1993: LIMA to LAD, SVG to D1 and SVG to a large dominant RCA
- PCI to RCA (BMS) 2004

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