Revived indications for thrombus aspiration during primary PCI: Unanswered questions after TAPAS

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Disclosures

• Gregg W. Stone MD
  - Research support from Abbott Vascular, Boston Scientific and Atrium
AMI: Pathophisiology

Ruptured plaque with occlusive thrombus
Impact of Macroscopic Distal Emboli

DE occurred in 27 of 178 (15%) pts after primary PTCA

⇒

↓ ST res

↑ Infarct size

↑ Mortality

Henriques JPS et al. EHJ 2002;23:1112-7
Mechanical Approaches to Thrombus

Thrombus aspiration
(Export, Pronto, Rescue, Diver CE, Rinspirator, etc.)

Thrombectomy
(AngioJet, X-Sizer)

Distal protection
(GuardWire, FilterWire, AngioGuard, etc.)
EMERALD: Primary endpoint
ST-Segment Resolution (n=501)

GuardWire (n=233)  Control (n=216)

Complete STR (%)

P=0.77

P=NS for all

Stone GW et al. JAMA 2005;293:1063-72
Infarct Size: Primary endpoint
by Tc-99m-SPECT (N=437)

% left ventricle

GuardWire (n=229)  Control (N=208)

Means  18.3%  16.2%  12.0%  9.5%

1° endpoint

Medians  ±19.4  ±19.1  [2, 26]  [0, 23.5]

P=0.26  P=0.016

Stone GW et al. JAMA 2005;293:1063-72
6 Month MACE (LV): EfficacyRelated to Myocardial Salvage

Death, new onset severe heart failure, new onset sustained hypotension, or rehospitalization for left ventricular failure

p=0.57

GuardWire 16.1%
Control 14.3%

Stone GW et al. JAMA 2005;293:1063-72
126 consecutive aspirates were collected from 62 pts at different times of the procedure in the roll-in phase and submitted to a core lab (R. Virmani, AFIP)

76% of patients had plaque and/or thrombus

Specimen type in patients with debris

- Clot: 83%
- Plaque: 81%
- Clot only: 19%
- Plaque only: 17%
- Clot and Plaque: 64%
Case 35-605, Pre-dilatation Sample

Major axis 6.28 mm
Area 5.00 mm²
AIMI Randomized Trial
(N=480)

STR >70% @ 90 mins

- AngioJet: 60%
- Control: 68%
P = 0.14

Infarct size (mean)
- AngioJet: 12.5%
- Control: 9.8%
P < 0.02

Ali A et al. JACC 2006;48:244-52
MACE by 30 Days

1 Month Events (%)

- **Death**: 4.6% (P<0.02)
- **Reinfarction (Q-wave)**: 0% (P<0.02) 0%
- **Stroke**: 1.7% (0.8%)
- **SAT/TLR**: 2.1% (0.4%)
- **MACE**: 6.7% (1.7%)

Ali A et al. JACC 2006;48:244-52
Reasons Why Thrombus Retrieval May Not Work

- Reperfusion achieved too late
- Infarct already too large
- Multifactorial causes of impaired myocardial recovery
- Device specific limitations
TAPAS: 1,071 pts with STEMI undergoing primary PCI randomized to aspiration (Export) vs. control

- Consecutive pts with possible STEMI (0.1 mm ST↑)
- Single center: U. Med Cntr Groningen, 1/05 – 12/06
- Anterior (43%) and non anterior MI with symptoms <12°
- Randomization in ER before anatomy known
- 1005/1071 (94%) underwent PCI; analysis by ITT
- Thrombus present in 43%; baseline TIMI-3 flow in 26%
- Aspiration performed in 448/535 (84%) assigned pts; atherothrombotic material retrieved in 73%

Svilaas T et al. NEJM 2008;358;557-67
TAPAS: 1,071 pts with STEMI undergoing PCI randomized in the ER to aspiration (Export) vs. control

Myocardial Blush (1° EP)

- Thrombus aspiration
- Conventional PCI

ST-segment Resolution (~44' post)

- Thrombus aspiration
- Conventional PCI

Svilaas T et al. NEJM 2008;358;557-67
TAPAS: 1,071 pts with STEMI undergoing primary PCI randomized in the ER to manual aspiration (Export) vs. control


30 days
4.0% vs. 2.1% P=0.07

1 year
7.6% vs. 4.0% P=0.04
Why the Results of TAPAS are Surprising

- Patient presentation was relatively late (symptoms <12º)
- Aspiration was not performed in 16% of pts; even PCI wasn’t performed in 6%
- There was no reduction in distal embolization with aspiration (5.6% vs. 5.8%)
- ST resolution was not relatively better in thrombotic Isns and other situations where aspiration should benefit
- The modest benefits in ST resolution and blush which occurred with aspiration wouldn’t be expected to reduce mortality by an absolute 3.6% (~50% relative decrease)!

Svilaas T et al. NEJM 2008;358;557-67
Microcirculatory Protection Devices in STEMI

Meta-analysis of 30 studies, 6415 randomized pts

Bavry AA et al. *Eur Heart J* 2008

Mortality

Mean 5 mo FU (range d/c – 12 mo)

Device: 3.2%
Control: 3.7%

RR [95%CI] = 0.87 [0.67, 1.13]
P=0.29

$I^2 = 0$
P$_{bias} = 0.62$

Favors PCI alone: 0.87 (0.67-1.13)
Microcirculatory protection devices in STEMI
Meta-analysis of 30 studies, 6415 randomized pts

13 aspiration catheter thrombectomy studies (n=3026)
5 active mechanical thrombectomy studies (n=934)
12 distal protection device studies (n=2442)

Bavry AA et al. Eur Heart J 2008
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### Stroke

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<td>3.43 [0.85, 14]</td>
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RR = 3.01
P = 0.02

Bavry AA et al. Eur Heart J 2008

Favors PCI alone
AMI: Attempts to Decrease Infarct Size

Have been mostly met with frustration

The concept of reducing embolic load

- **Emerald (n=501)**
  - Distal protection (GuardWire Plus)
  - Stone GW et al. *JAMA* 2005
  - Infarct size: 16.2%
  - *P*=0.26

- **AIMI (n=480)**
  - Active thrombectomy (AngioJet)
  - Ali A et al. *JACC* 2006
  - Infarct size: 9.8%
  - *P*=0.018

- **Kaltoft et al (n=225)**
  - Simple thrombus aspiration (Rescue)
  - Kaltoft A et al. *JAMA* 2005
  - Infarct size: 7.5%
  - *P*=0.004
TAPAS: Infarct Size Measurement

Peak enzyme

- Peak CPK
  - Control: 637
  - Export aspiration: 565
  - P = 0.24

- Peak CPK-MB
  - Control: 63
  - Export aspiration: 58
  - P = 0.46

EXPIRA: 175 pts with STEMI <9° with TIMI 0-1 flow (44% LAD) undergoing PCI randomized to Export aspiration vs. control; cMRI substudy in 75 pts at 2-5 days and 3 months

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<td>MBG ≥2</td>
<td>59.8%</td>
<td>88.6%</td>
<td>&lt;0.0001</td>
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<tr>
<td>90’ complete STR</td>
<td>39.1%</td>
<td>63.6%</td>
<td>0.001</td>
</tr>
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<td>MVO acute, %</td>
<td>72.9%</td>
<td>31.5%</td>
<td>0.0005</td>
</tr>
<tr>
<td>CPK peak, ng/ml</td>
<td>108 ± 111</td>
<td>109 ± 119</td>
<td>0.6</td>
</tr>
<tr>
<td>Infarct size acute, %LV</td>
<td>13 ± 7</td>
<td>14 ± 12</td>
<td>0.6</td>
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<tr>
<td>Infarct size 3 mos, %LV</td>
<td>11 ± 5</td>
<td>9 ± 2</td>
<td>0.2</td>
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<td>Death, 9 months</td>
<td>4.6%</td>
<td>0%</td>
<td>0.02</td>
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INFUSE-AMI Trial

450 pts with anterior STEMI
Anticipated sx to PCI <5 hrs, TIMI 0/1 flow in prox or mid LAD

PCI with bivalirudin
IC abcx bolus (ClearWay)

PCI with bivalirudin
Standard of care

Primary endpoint: Infarct size at 30 days (MRI)
2º endpoints: TIMI flow, blush, ST-resolution, MACE (30d, 1 yr)

Sponsor and IDE holder: CRF; Funding support: Atrium
PI: Gregg W. Stone; Co-PI: C. Michael Gibson
Conclusions: Microcirculatory protection

• Despite completion of 31 randomized trials, we still don’t know with confidence whether microcirculatory protection during PCI in STEMI reduces (or increases) infarct size or improves clinical outcomes, and whether the results vary significantly with different devices.

• We have been unable to identify patients or lesions specifically likely to benefit (or be harmed).

• The ongoing European Jetstent trial (AngioJet in thrombotic lesions) may be enlightening, and a large, multicenter randomized trial is required to validate the TAPAS results.
Conclusions: Microcirculatory protection

• Pending guidance from future clinical trials, it is presently reasonable to:
  - Use simple catheter-based aspiration for large thrombus burden in proximal coronary vessels - but this is not required for all occluded coronary arteries
  - Use distal protection devices for diseased saphenous vein grafts